Document D3.1
Scientific study protocols for each of the three multicentre studies
Version 1.5

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Approved by: Janne Rasmussen
Filename: D3.1 v1.5 United4Health scientific study protocols

Abstract
This document provides the final study protocols for the three pilots, which have been prepared, discussed and agreed in associated with the three Scientific Committees, one for each of the three diseases of interest, diabetes, COPD and heart failure. The three protocols have been approved during the 3rd PA in Edinburgh, on 30th October 2013.

Key Word List
Telemedicine, telemonitoring, remote monitoring, observational study, diabetes mellitus, chronic obstructive pulmonary disease, cardiovascular disease, congestive heart failure.
Executive Summary

United4Health aims to reach new frontiers in the evaluation and deployment of ICT services for the management of people living with chronic diseases in home settings, on a large scale. This document provides the final study protocols for the three pilots, which have been prepared, discussed and agreed in the associated three Scientific Committees, one for each of the three diseases. The starting point for these protocols was the grant agreement and the experience accumulated during the Renewing Health Pilot A which has similar objectives to United4Health, but a wide range of interventions. In the case of United4Health, three interventions have been selected from the basket of those already validated or under validation in Renewing Health; these interventions will be studied in several regions to guarantee aggregation of data and comparability of results. The interventions selected address the three main chronic diseases found among the EU population, namely diabetes, chronic obstructive pulmonary disease, and heart failure; for each of these pathologies, all the pilot sites will implement the same intervention. The main challenge of this project is to achieve a balance on the one hand of the target of the large scale deployment in real life, most of the partners have decided to offer these services to all of their patients with the specific disease, and on the other hand of the local commitment to the protocols of the selected services given the different clinical routines and settings.

This document provides also an overview of the study design and the evaluation methodology, with special focus on the assessment of the economic and organisational outcomes using all the available data sources, adopting a common approach among all the sites and a valid methodology.
Change History

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1.1 17th November 2013
1.2 22nd November 2013
1.3 3rd December 2013
1.4 2nd March 2014
1.5 31st March 2014

Version Changes
0.1 First draft
1.1 Final draft for review
1.2 Formatting changes, and minor text changes following review
1.3 Further minor changes
1.4 Minor clarifications of protocols
1.5 Minor updates

Outstanding issues
Confirm questionnaire for patient satisfaction in Section 5.3
Will be reissued as public document following approval by Commission
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1. Introduction

1.1 Purpose of this document

This document contains the U4H study protocols and the common evaluation methodology.

1.2 Glossary

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AECOPD</td>
<td>Acute Exacerbations of Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>CAT</td>
<td>COPD Assessment Test</td>
</tr>
<tr>
<td>CEAP</td>
<td>Clinically Employed Allied Professional</td>
</tr>
<tr>
<td>CHD</td>
<td>Coronary Heart Disease</td>
</tr>
<tr>
<td>CHF</td>
<td>Congestive Heart Failure</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CONSORT</td>
<td>Consolidated Standards of Reporting Trials</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular Disease</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>EHR</td>
<td>Electronic Healthcare Record</td>
</tr>
<tr>
<td>EMR</td>
<td>Emergency Medical Room</td>
</tr>
<tr>
<td>ESRD</td>
<td>End-Stage Renal Disease</td>
</tr>
<tr>
<td>FEV1</td>
<td>Forced expiratory volume in one second</td>
</tr>
<tr>
<td>GOLD</td>
<td>Global Initiative for Chronic Obstructive Lung Disease</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Glycated Haemoglobin</td>
</tr>
<tr>
<td>HDL</td>
<td>High Density Lipoprotein</td>
</tr>
<tr>
<td>HF</td>
<td>Heart Failure</td>
</tr>
<tr>
<td>HIS</td>
<td>Hospital Information System or Health Information System</td>
</tr>
<tr>
<td>HTA</td>
<td>Health Technology Assessment</td>
</tr>
<tr>
<td>HTN</td>
<td>Hypertension</td>
</tr>
<tr>
<td>ICD</td>
<td>Implantable Cardioverter-Defibrillator</td>
</tr>
<tr>
<td>ICD-10</td>
<td>International Classification of Diseases and Related Health Problems 10th Revision</td>
</tr>
<tr>
<td>ICS</td>
<td>Inhaled Corticosteroids</td>
</tr>
</tbody>
</table>
### D3.1 Scientific study protocols for each of the three multicentre studies

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDF</td>
<td>International Diabetes Federation</td>
</tr>
<tr>
<td>LABA</td>
<td>Long-Acting Beta2 Agonists</td>
</tr>
<tr>
<td>LAMA</td>
<td>Long-Acting Muscarinic Antagonist</td>
</tr>
<tr>
<td>LDL</td>
<td>Low Density Lipoprotein</td>
</tr>
<tr>
<td>LOS</td>
<td>Length Of Stay</td>
</tr>
<tr>
<td>MAST</td>
<td>Model for the Assessment of Telemedicine</td>
</tr>
<tr>
<td>MDMW</td>
<td>My Diabetes My Way (in Scotland)</td>
</tr>
<tr>
<td>NIV</td>
<td>Non-Invasive Ventilation</td>
</tr>
<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
</tr>
<tr>
<td>PD4</td>
<td>Phosphodiesterase type 4</td>
</tr>
<tr>
<td>PDA</td>
<td>Personal Digital Assistant</td>
</tr>
<tr>
<td>PHR</td>
<td>Personal Health Records</td>
</tr>
<tr>
<td>PHS</td>
<td>Personal Health Systems</td>
</tr>
<tr>
<td>POCT</td>
<td>Point of Care Testing</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
</tr>
<tr>
<td>RH</td>
<td>Renewing Health project</td>
</tr>
<tr>
<td>SABA</td>
<td>Short-Acting Beta-2 Agonists</td>
</tr>
<tr>
<td>SAMA</td>
<td>Short-Acting Muscarinic Antagonist</td>
</tr>
<tr>
<td>SF-36</td>
<td>Short Form (36) Health Survey</td>
</tr>
<tr>
<td>SMBG</td>
<td>Self-Monitoring of Blood Glucose</td>
</tr>
<tr>
<td>TMon</td>
<td>Telemonitoring</td>
</tr>
<tr>
<td>U4H</td>
<td>UNIversal solutions in Telemedicine Deployment for European HEALTH care (United4Health)</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>WSD</td>
<td>Whole System Demonstrator</td>
</tr>
</tbody>
</table>
2. **Background**

2.1 **Project objectives**

The Project aims to demonstrate that the PHS-based solutions for the management of people living with chronic diseases in home settings, already validated or under validation in RENEWING HEALTH[1,2], can be successfully transferred to other regions and deployed at scale. Similarly, by comparing results of RENEWING HEALTH regarding efficacy (under controlled conditions) and the results of United4Health[1] regarding effectiveness in real life, we aim to increase the current evidence base of the benefits that these solutions can provide to people living with chronic diseases, their relatives and other informal carers, and healthcare professionals, and the return on investment that they can provide to health authorities and health insurers.

To further increase the base of evidence, and to extend the scope of the pilots in the regions that were already included in RENEWING HEALTH, a good number of these regions will deploy in their territory new solutions validated by other regions in the RENEWING HEALTH project. Due to the consistent use of the same evaluation methodology[3] across participating regions in both RENEWING HEALTH and United4Health, and the increased geographical scope of the pilots, the case for the deployment of PHS-based solutions will be strengthened considerably.

United4Health is going to achieve what, due to different reasons, neither its predecessor Pilot A, RENEWING HEALTH[4], nor the Whole System Demonstrators[5] in England, could achieve: to have a single integrated disease management programme deployed at scale across pilot sites located in different Member States, based on multicentric design (i.e. homogeneous intervention and a homogeneous methodological approach). This will allow both the aggregation of data across pilots to achieve large samples, and consequently will lead to strong statistical power of the results and the possibility to stratify the results by region to see how the impact of the same intervention varies as a function of the local organisational context.

Aggregation of data and comparability of results among pilot sites will be made possible by the use of the same evaluation methodology, MAST[3], in all the pilot sites. MAST, which was originally designed under contract to the European Commission in the context of the MethoTelemed project, has been extensively validated in RENEWING HEALTH[2], and is increasingly the evaluation methodology of choice for telehealth. Moreover, by retaining of the same indicators, data for the same intervention will be compared across the two projects. This will increase even further the statistical power of the results which will be based on samples of unprecedented size.

2.2 **Description of the services**

The services that are going to be piloted in United4Health have been already validated, or are under validation, in the framework of RENEWING HEALTH, which is due to be completed in December 2013. This means that all the services have been abundantly tested from the point of view of functionality and robustness of the technical solution.
Out of the large basket of services used in RENEWING HEALTH, three have been selected by the United4Health Consortium, and will be evaluated within the framework of multi-centre trials. The services selected are:

- Life-long management of diabetes.
- Short-term follow-up after hospital discharge for COPD patients.
- Remote monitoring of congestive heart failure.

Life-long management of diabetes is currently installed in Berlin, Thessaly and Veneto. For the United4Health studies, it will be enhanced with the functionality of patient education and coaching currently installed in North Norway. Within United4Health, this service will be trialled, for a total of 7,410 patients, in:

- Scotland;
- Wales;
- Northwest Moravia;
- Slovenia;
- Campania;
- Calabria;
- South Karelia;
- Central Greece;
- Berlin.

Short-term follow-up after hospital discharge for COPD patients is currently installed in South Denmark. Within United4Health, this service will be trialled, for a total of 2,038 patients, in:

- Scotland;
- Wales;
- Southern Norway;
- Galicia;
- North Norway;
- Berlin.

Remote monitoring of Congestive Heart Failure is currently installed in Thessaly and Veneto. Within United4Health, this service will be trialled, for a total of 1,830 patients, in:

- Scotland;
- Basque Country;
- Northwest Moravia;
- Slovenia;

In general terms, the services are operational, but in regions different from those which will pilot them in United4Health, and none of them is currently used in a cross-border multi-centre trial.

The table below shows the number of patients who will be included in the pilots by region and by pathology.
D3.1 Scientific study protocols for each of the three multicentre studies

### Table 1: Number of patients in the Intervention Group by region and by pathology

<table>
<thead>
<tr>
<th>Pathology</th>
<th>New pilots funded by ICT PSP</th>
<th>New pilots funded from other sources</th>
<th>Existing RENEWING HEALTH partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>5,600</td>
<td>400</td>
<td>0</td>
</tr>
<tr>
<td>COPD</td>
<td>838</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>CHF</td>
<td>1,250</td>
<td>300</td>
<td>80</td>
</tr>
<tr>
<td>HTN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>7,688</td>
<td>300</td>
<td>600</td>
</tr>
</tbody>
</table>

#### 2.3 Expected measurable final results of the project

Considering that the Whole System Demonstrators, RENEWING HEALTH and approximately 130 other randomised controlled trials (RCTs) of telemedicine interventions that have been carried out throughout the world have already demonstrated all that could be demonstrated on the clinical impact of telemedicine on chronic conditions[6,7,8,9], United4Health is aiming at focusing on the organisational aspects, the efficiency gains, and the economic aspects of the telemedicine interventions.

In other words, the expected measurable results of the project are:

- Streamlined care processes made possible by monitoring people living with chronic diseases at home.
- Actual move people living with chronic diseases towards the bottom of the healthcare pyramid by reducing their reliance on the most expensive healthcare facilities (hospitals and emergency rooms).
- Increased productivity of healthcare professionals by the involvement of patients and their informal caregivers in the chronic condition management (coaching and education among lifestyles better adjusted to the actual conditions).
- Thorough analysis of all cost elements involved in the deployment of the telemedicine services adopted in United4Health, and comparison with savings obtained in other areas.
- Use by healthcare providers of familiar, everyday technologies such as telephone, television and internet to improve access to person-centred care, tailored to individuals’ preferences.
- Where chronic patients are admitted to hospital, healthcare providers have established and sustained telehealth and telecare services to safely support...
individuals in order to discharge them back to their home / community as early as possible.

- Identify potential barriers and facilitators of adoption, which will help to design successful implementation strategies, including reasons for non-participation.
- Patient satisfaction with using integrated telemedicine services and having access to specialists, if needed, from his/her home.

### Table 2: Project success indicators

<table>
<thead>
<tr>
<th>Indicator Nr.</th>
<th>Objective/expected result</th>
<th>Indicator name</th>
<th>Method of measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Difference in number of annual admissions to hospital between the Intervention and the Comparator Group</td>
<td>HOSPITAL ADMISSIONS</td>
<td>Hospital Information Systems. The use of historical data could be equally considered.</td>
</tr>
<tr>
<td>2</td>
<td>Difference in number of annual accesses to the ER between the Intervention and the Comparator Group</td>
<td>EMERGENCY</td>
<td>Hospital Information Systems. The use of historical data could be equally considered.</td>
</tr>
<tr>
<td>3</td>
<td>Difference in number of GP consultations between the Intervention and the Comparator Group</td>
<td>GP CONSULTATIONS</td>
<td>GPs EHRs. The use of historical data could be equally considered.</td>
</tr>
<tr>
<td>4</td>
<td>Difference in the total cost of treatment between the Intervention and the Comparator Group</td>
<td>TOTAL COST</td>
<td>Cost-effectiveness analysis based on Drummond et al methodology as adopted by the MAST and the RH project</td>
</tr>
<tr>
<td>5</td>
<td>Acceptance of the telemedicine service in the Intervention group</td>
<td>PATIENT PERSPECTIVE</td>
<td>WSD questionnaire. It will be assessed at the end of the follow up.</td>
</tr>
<tr>
<td>6</td>
<td>Evaluation of the organisational changes after the deployment of the telemedicine service.</td>
<td>ORGANISATIONAL CHANGES</td>
<td>The same methodology used in the RH project will be used to assure the comparability of the results.</td>
</tr>
<tr>
<td>7</td>
<td>Analysis of the reasons of non-participation among the eligible patients</td>
<td>NON-PARTICIPATION REASONS</td>
<td>A questionnaire about the reasons for non-participation based on the experience acquired by the RH project.</td>
</tr>
<tr>
<td>8</td>
<td>Differences in clinical outcomes specific for each different disease</td>
<td>CLINICAL OUTCOMES</td>
<td>STROBE and MAST methodology to assess disease-specific outcomes.</td>
</tr>
</tbody>
</table>
3. **Scientific background and rationale for the study design and the evaluation methodology**

3.1 **Study design**

Renewing Health has demonstrated the efficacy of the interventions in randomised controlled trials. Thus the clinical impact has been demonstrated in studies with a high degree of internal validity and in experimental conditions.

However, real life effectiveness of these interventions has not been demonstrated yet. As described in Hendy et al. (2012)[10] in a study of the implementation of the WSD, the randomised design may result in a number of practical problems for the organisations who carry out the study and perform the data collection. For example, the knowledge and experiences gained during the trial cannot be used to improve the intervention during the study, because the service must remain constant during the latter. Therefore United4Health will study the effectiveness of the interventions in an observational design by comparing a control group treated before the implementation of the telemedicine interventions with an intervention group treated after the implementation of telemedicine. The strengths of this study design are complementary to the evidence of efficacy demonstrated in several efficacy trials[11], and are based on:

1. Long follow-up period which allows for registering and monitoring long-term clinical effects and safety data[12].
2. Big sample size representative of the general population, which allows for stratification analysis and identification of patient subgroups that benefit the most from the intervention[13].
3. Real-life data about impact on costs and organisation (structure and processes) which allows the identification of barriers and facilitators for a wider service implementation[14].

In addition, from an ethical perspective, the service that is proved to be efficacious should be offered to all potential healthcare users. This type of study design will assess the real-life effectiveness of the tried services with a high degree of external validity and generalisability of the results. Due to inclusion of patients from many European countries, this study will be able to provide to other regions in Europe a very valid estimate of the expected impact of the interventions.

3.2 **Assessment methodology**

The evaluation of the three studies will be conducted using the MAST multidimensional evaluation methodology[3]. MAST is based on HTA (Health Technology Assessment), and has been successfully validated in the ICT PSP Type A project Renewing Health[2,4]. It is encountering an increasing level of success among organisations involved in trials of complex interventions such as those piloted in United4Health, because it fills a gap which has been widely felt in this area. MAST was developed under contract with the European Commission (MethoTelemed project) by a multinational team led by the Odense University Hospital which participates in United4Health as part of the South Denmark Regional Partnership. The same team which developed and validated MAST will be in charge of the evaluation of United4Health. The design of the trials will be elaborated taking...
into consideration the kind of evidence that the various stakeholders need to engage in the roll-out of ICT-supported integrated care services for older people, and the statistical validity of the outcomes measured.

3.3 Safety and clinical outcomes

Safety in accordance with MAST methodology is defined as the identification and assessment of harms, and can be divided into clinical safety (of the patients and staff) and technical safety of the telemedicine equipment (technical reliability). Clinical effectiveness is defined as the effects on patients’ health. Effectiveness refers to the performance of a technology in regular clinical practice.

3.4 Patient perception

Regarding patient perception the project will use the WSD questionnaire on patient acceptability\[15\]. This instrument was also used in the Renewing Health project. These data should be collected for the first 100 patients in each region.

3.5 Economic evaluation

An economic evaluation will be performed. Data on economic outcomes (admissions, etc.) will be collected for each patient in the intervention and the control group according to the common protocol; the same methodology was implemented in the Renewing Health project. In addition, data will be collected on the number of contacts with patients through the use of the telemedicine applications, and the duration of each contact. These data should be collected for the first 100 patients in each region. Similar information on the price of the telemedicine application will be collected.

The aim of the economic evaluation is to estimate the mean costs per patient in the intervention and the control group. These data will be used to carry out a cost-analysis in accordance with Drummond et al. (2005)[16].

3.6 Organisational changes

Evaluation of the organisational changes is performed using the common protocol and the same methodology as in the Renewing Health project[2,4]. The method for data collection will mainly be focus group interviews with members of the clinical staff who know the content and the organisation of the telemedicine intervention[2,10].
4. **Pilot protocols**

4.1 **Pilot 1: Long term monitoring of diabetes**

<table>
<thead>
<tr>
<th>WP6 Leader: Anne Reoch, NHS24/SCTT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Members of the DM Scientific Committee:</strong></td>
</tr>
<tr>
<td>1. Anne Reoch (chair)</td>
</tr>
<tr>
<td>2. Sandeep Thekkapat</td>
</tr>
<tr>
<td>3. Sam Rice</td>
</tr>
<tr>
<td>4. Metka Epsek</td>
</tr>
<tr>
<td>5. Alfonso Longobucco</td>
</tr>
<tr>
<td>6. Francesca Faggiano</td>
</tr>
<tr>
<td>7. Tiziana Spinosa</td>
</tr>
<tr>
<td>8. Sebastian Gotzen</td>
</tr>
<tr>
<td>9. Mira Pakanen</td>
</tr>
<tr>
<td>10. Alexandra Mpargiota</td>
</tr>
<tr>
<td>11. Martin Hutyra</td>
</tr>
<tr>
<td>12. Anna Kotzeva</td>
</tr>
<tr>
<td>13. Kristian Kidholm</td>
</tr>
<tr>
<td>14. Panagiotis Stafylas</td>
</tr>
</tbody>
</table>

**Study sites and local investigators**

Participants will be enrolled and the study will be conducted at the following health facilities or community health partnerships.

**Scotland**

NHS Ayrshire and Arran - East CHP, North CHP, South CHP (Leads: Dr Iqbal Malik).

NHS Lanarkshire - North CHP & South CHP (Leads: Dr Sandeep Thekkepat)

NHS GGC – Renfrew CHP & East Renfrew CHP (Leads: Prof Martin McIntyre, Dr Brian Kennon)

Principle Investigator: Sandeep Thekkepat

**Wales**

Prince Philip Hospital, Llanelli, Carmarthenshire,

Glangwili Hospital, Carmarthen, Carmarthenshire

Withybush Hospital, Haverfordwest, Pembrokeshire

Bronglais Hospital, Aberystwyth, Ceredigion

Principle Investigator: Sam Rice MD PhD
Calabria
Azienda Sanitaria Provinciale di Cosenza
Distretto di Cosenza
Via Milelli 23/A di Cosenza, Italy
Principal investigators: Alfonso Longobucco, MD, and Francesca Faggiano MD

South Karelia
South Karelia Social and Health Care District
Valto Käkelän Katu 3, P.O.Box 24,
53101 Lappeenranta, Finland
Principal Investigator: Mira Pakanen MSc, Nurse

Central Greece
General University Hospital of Larissa,
Department of Endocrinology and Metabolic diseases
Mezourlo area, 41110, Larissa, Greece
Principal investigators: Alexandra Mpargiota, MD, with the collaboration of George Dafoulas, MD

Berlin
Pflegewerk
Principal Investigator: Dr Sebastian Gotzen

Northwest Moravia
University Hospital Olomouc
Principal investigator: Dr Martin Hutyra

Slovenia
Slovenj Gradec General Hospital & Healthcare Centre of Ravne
Principal investigator: Dr Metka Epsek

Campania
Agenzia Regionale Sanitaria Campania
Principal investigator: Dr Tiziana Spinosa

Scientific background and rationale
Diabetes mellitus is a major cause of morbidity and mortality worldwide. In 2013, the International Diabetes Federation (IDF) estimated the worldwide prevalence to be 382 million (8.3% of the global population) and predicted that by 2035 the prevalence will have risen to 592 million[17]. It is predicted to become the seventh leading cause of death in the world by the year 2030. Total deaths from diabetes are projected to rise by more than 50% in the next 10 years. There are three major types of diabetes - Type 1 diabetes, Type 2 diabetes and Gestational diabetes. Type 1 diabetes, a result of autoimmune process, needs insulin therapy to survive. Type 2 diabetes (formerly called non-insulin-dependent or adult-onset diabetes), is a disease caused by the body’s ineffective use of insulin - often resulting from excess body weight and physical inactivity. It is characterised by insulin resistance and relative insulin deficiency; either of these may be present at the time that diabetes is diagnosed. The diagnosis of type 2 diabetes usually occurs after the age of 40 years.
but can occur earlier, especially in populations with high diabetes prevalence. Type 2 diabetes can remain undetected, i.e. asymptomatic, for many years; the diagnosis is often made from associated complications, or incidentally through an abnormal blood or urine glucose test. It can lead to microvascular complications, e.g. retinopathy, renal disease, peripheral neuropathy and macrovascular complications, i.e. arterial disease, leading to heart attack, stroke, dementia or amputation. Type 2 accounts for around 90% of all diabetes worldwide[17]. Diabetes results in high healthcare costs, loss of labour productivity, and decreased rates of economic growth. Globally, healthcare expenditure for diabetes totalled USD 465 billion in 2011, equivalent to 11% of total health spending. Without an investment in making effective treatments for preventing diabetes complications widely available, this is predicted to rise to USD 595 billion by 2030[17].

The multi-vascular risk factors and wide-ranging complications mean that the management of type 2 diabetes requires complex and time-consuming healthcare management[18]. The necessary lifestyle changes, complexities of management, and side effects of therapy, make self-monitoring and education a priority for patients who wish to self-manage. Ideally, patients with type 2 diabetes should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If managed in collaboration with healthcare professionals, the preferences of people with diabetes are more likely to be realised and their personal goals attained. As the ratio between people being diagnosed with diabetes and healthcare professionals available to manage them grows wider on a daily basis, we must look at new ways of working – constantly striving to for patient centred care[6,18].

Telemedicine (or the use of technology in accessing healthcare) allows the opportunity for patients to play a new and more direct role in their treatment and care[2,19,20]. Diabetics have undertaken self-monitoring of blood glucose for many years but it is acknowledged that this is not always reliable[21]. Structured self-monitoring of blood glucose improves glycaemic control, and provides guidance in prescribing diabetes medications in patients with relatively well-controlled non-insulin treated type 2 diabetes[19]. Remote home monitoring of blood glucose via telemedicine, has been found to improve glycaemic control[22], and patients find this acceptable[23], resulting in potential for adjustment in medication and access to relevant clinical advice sooner than may have been available with conventional monitoring. Technology also allows access to varied, structured, self-education programmes, offering access to health coaching programmes at any time of day. The use of self-management health information technology (SMHIT) has been found to significantly improve glycaemic control and improve patient centred care[20].

Telemedicine is not designed to replace conventional models of care, but can provide further options for self-care at home, potentially both reducing the requirement for some face-to-face interactions with healthcare professionals, and reducing HbA1c[6,18,22].

### Study Objectives

The study aims to demonstrate that:

### Clinical

Patients with diabetes mellitus can be effectively monitored by simplified, centralised and large-scale telemotoring of blood glucose levels, improving self-management of their disease.
Reduction in face-to-face contacts with healthcare professionals and reduction in HbA1c.

**Patient perception**

Patients with diabetes mellitus type 2 can be effectively monitored by simplified, centralised and large-scale telemonitoring of blood glucose levels, with a high degree of patient acceptability.

**Economic**

This intervention is cost-effective compared to usual care.

**Organisational**

The required organisational changes result in a work-load for staff that is acceptable. The intervention can be successfully transferred to other regions and deployed at large scale.

Identification of challenges in implementation of large scale telemedicine deployment across more than one country in Europe.

### Study Design

This is an observational study using as a comparator group the total population of the patients fulfilling the eligibility criteria who have been treated and followed for at least one year before the implementation of the telemedicine service, and in the same health units as the intervention group, and whose data are available through EMR or other databases (retrospective collection of data regarding demographics, clinical and economic outcomes for the comparator group). Additional data regarding the costs of the telemedicine service, patient perception and organisational aspects will be collected for the intervention group. This is illustrated in the figure below.

![Diagram of Diabetes study design](image)

**Figure 1: Diabetes study design**

Optionally, to reduce bias the regions could collect data on demographics, clinical and economic outcomes for all patients (with diagnosed type 2 diabetes) treated during the intervention period and not just those who follow the inclusion criteria. Thereby it will be possible to do an analysis of results (A) by inclusion of only...
telemedicine users and (B) by inclusion of all patients that potentially could be users of telemedicine.

<table>
<thead>
<tr>
<th>Sample size of intervention group (Total N=7410 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scotland</strong></td>
</tr>
<tr>
<td><strong>Wales</strong></td>
</tr>
<tr>
<td><strong>Northwest Moravia</strong></td>
</tr>
<tr>
<td><strong>Slovenia</strong></td>
</tr>
<tr>
<td><strong>Campania</strong></td>
</tr>
<tr>
<td><strong>Calabria</strong></td>
</tr>
<tr>
<td><strong>South Karelia</strong></td>
</tr>
<tr>
<td><strong>Central Greece</strong></td>
</tr>
<tr>
<td><strong>Berlin</strong></td>
</tr>
</tbody>
</table>

The comparator group will consist of the total population of patients fulfilling the eligibility criteria who have been treated and followed for at least one year before the implementation of the telemedicine service (or MDMW in Scotland), and in the same health units as the intervention group, and whose data are available through EMR or other databases. The final size of this population will be defined before the implementation of the new service.

<table>
<thead>
<tr>
<th>Study start and end dates, duration of the intervention and follow-up period</th>
</tr>
</thead>
<tbody>
<tr>
<td>The enrolment of patients in the Intervention group will be between 1st January 2014 and 30th September 2014.</td>
</tr>
<tr>
<td>The duration of the intervention and the follow-up period will be 12 months. However, patients recruited in first quarter will be followed up for an 18-month period.</td>
</tr>
<tr>
<td>The comparator group will consist of all the patients treated during 12 months before implementation of the telemedicine service at the same GP / hospital / Health District, and who have the same enrolment characteristics as the ones in the intervention group.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Eligibility criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of type 2 diabetes, and already in home monitoring of blood glucose. Optionally, patients with type 1 diabetes will be eligible to participate in order to ensure the recruitment of the total sample size.</td>
</tr>
</tbody>
</table>
Enrolment

Potential participants are selected by screening electronic healthcare records or/and the hospital / national databases and/or during long term condition annual reviews in the community setting. Candidates in the intervention group are informed about the nature and the objectives of the intervention. Once candidates have signed the informed consent form, they participate in the study, or, in the case of Scotland, if patients are happy to participate (which requires no consent form).

Demographic and clinical baseline characteristics

Demographic and clinical baseline characteristics are collected according to the common protocol.

The following common, mandatory, data are collected for all patients in the intervention and control groups:

- Year of birth.
- Gender.
- Smoking.
- Assessment of comorbidity – ICD-10 (use specific codes and define accordingly, YES/NO format).
- Insulin (yes/no).
- Date of diagnosis with Type 2 DM.
- Self-monitoring blood sugar (times/week).

In addition, partners can collect the following optional data:

- Has the patient a formal or informal care giver?
- PC user.
- Mobile phone user.
- Education: seven levels.

Intervention

The intervention aims to promote self-care and self-management by encouraging use of self-monitoring of glucose and lifestyle risk factors, and by providing ongoing health coaching.

The patient at home uses the provided device for the measurement of blood glucose level. The device, used by the patient, collects the data and sends them to the gateway device automatically.

The gateway device transmits data collected by the patient to the server of a Regional eHealth Centre, managed according to local policy.

The telemonitoring software will allow: healthcare professionals to monitor and manage the data as agreed locally, including provision of a summary and access to the web based portal to monitor the patients’ health conditions at any time required.
In Scotland, the patient at home uses their currently provided home glucose monitoring device and a DiaSend device at home. This device allows the transmission of the measurement to the patient's self management website, MDMW (http://www.mydiabetesmyway.scot.nhs.uk/). This will then populate SCI Diabetes (Diabetes database in Scotland), thus allowing both patients and clinicians a digitally captured, up-to-date picture of the individuals blood glucose measurements and trends, a summary of which can be produced anytime, at either the patient or the clinician's end and managed as locally agreed.

The MDMW website also provides health coaching, the 1,200 patients provided with the DiaSend interface, will be encouraged to use this. 4,400 other patients will be registered onto MDMW and encouraged to take part in the health coaching aspects of the site and continue with SMBG as they have been previously.


It should be acknowledged that regions show variations in monitoring intervals as a consequence of the different local management strategies, and the flexibility given by recent scientific guidelines[18,24]:

**Type 1 diabetes and Type 2 Insulin dependent**: daily or twice daily (if stable may be longer interval)

**Type 2 Non-Insulin dependent**: minimal weekly

![Figure 2: System architecture of the diabetes telemonitoring service](image)

**Interventions in the comparator group**

Participants in the comparator group receive usual care. Usual care consists of regular visits to the specialist or a primary care facility. On the occasion of the visits, glucose or/and HbA1c measurements are performed, and the current oral or insulin
therapy is modified if necessary. Patients also receive basic education in the management of diabetes.

### Primary and secondary outcomes

**Primary outcome:** Reduction of the number of face-to-face contacts with GP or diabetologist, depending on local pathway.

**Secondary outcomes:**

- Reduction in HbA1c.
- Number of primary care professional contacts, including GPs, diabetologists, specialised or not nurses, community nurses etc.
- Number of visits to emergency department.
- Duration of use of the telemedicine device.
- Number of outpatient visits (consultant or specialist nurse).
- Number of outpatients visits to a diabetologist.
- Number of outpatients visits to other specialists in charge of the management of diabetes related complications (optional).
- Number of admissions (any admission during 12 months).
- Number of bed days (days of hospitalisation).

### Evaluation time points

Patients will be evaluated at recruitment and at the end of the study. They will be followed, and the data will be collected for all patients, during a period of 12 months. For the sub-population with extended monitoring, there will be assessment at study start, at 12 months and 18 months.

### Economic evaluation

Economic evaluation will be performed according to the common protocol as described in section 5.1.

### Evaluation of organisational changes

Assessment of the organisational changes will be done in accordance with the common protocol and the Renewing Health project methodology as described in section 5.2.

### Evaluation of patient perception

The evaluation of patient satisfaction will be performed in accordance with the common methodology, using the WSD questionnaire, which was also used in the Renewing Health project (see section 5.3).
4.2 Pilot 2: Short-term follow-up after hospital discharge for COPD patients

**WP7 Leader: Keir Lewis, NHS Wales**

**Members of the COPD Scientific Committee**

1. Keir Lewis (chair)
2. Claire Hurlin
3. Hugh Brown
4. Frode Gallefoss
5. Audhild Hjalmarsen
6. Sebastian Gotzen
7. Carlos Zamarrón Sanz
8. Anna Kotzeva
9. Kristian Kidholm
10. Panagiotis Stafylas

**Study sites and local investigators**

Participants will be enrolled and the study will be conducted at the following health facilities:

**Scotland**

- NHS Ayrshire and Arran - East CHP, North CHP, South CHP
- NHS Lanarkshire - North CHP & South CHP
- NHS GGC – Renfrew CHP & East Renfrew CHP

Principal Investigator: Dr Hugh Brown.

**Wales**

- Hywel Dda Health Board.
  Principal Investigator: Dr Keir Lewis

**Southern Norway**

- Sorlandet Hospital.
  Principal Investigator: Dr Frode Gallefoss

**Northern Norway**

- University Hospital North Norway (UNN)
  Principal Investigator: Dr Audhild Hjalmarsen

**Galicia**

- Galician Health Service – SERGAS
  Principal Investigator: Dr Carlos Zamarrón Sanz
Berlin
Pflegewerk
Principal Investigator: Dr Sebastian Gotzen

Scientific background and rationale

Telemonitoring (TMon) for COPD has been associated with reduced emergency admissions and other healthcare contacts[25,26,27,28]. The largest randomised controlled trial (Whole Systems Demonstrator) of telemonitoring for COPD to date has suggested a reduction in mortality by 7-10%, but another large RCT (TeleScot) has shown no convincing clinical benefits; the same also seems to be true of the first available results from RH[5,29,30].

What is less clear is:
A) Which should be the target patient population?
B) Which measurements are most appropriate and useful, e.g. spirometry, pulse oximetry, temperature, symptom management questions and quality of life questions?
C) The added value of video consultation.
D) The optimal duration for comprehensive telemonitoring on an ongoing basis.
E) How telemonitoring could be better utilised to reflect an individual patient’s health status at any given time?

Study Objectives (hypotheses)

The study aims to demonstrate that:

Clinical outcomes
- The introduction of a short-term intensive telemonitoring programme (TMon) followed by a less intensive ‘step down’ TMon for COPD patients discharged from the hospital after an exacerbation, reduces hospital re-admissions from COPD exacerbations over the following year.

Organisational outcomes
- The required organisational changes can be implemented at scale in a timely way. TMon will result in a workload for the staff that is acceptable.
- The required organisational changes and new ways of working are agreed and approved by the appropriate management structures within the relevant local agencies involved in delivery.
- The intervention models can be successfully transferred to other regions and mainstreamed as part of usual care.

Economic outcomes
- TMon for the COPD care pathway is more cost-effective compared to usual care.
Other outcomes

- The new service is acceptable to all stakeholders including patients and health professionals.

### Study Design

Interventional study of telemonitoring using mainly historical comparators. Primary outcome data on admissions will be collected through Emergency Medical Room (EMR) or other databases. Other data regarding demographics, clinical and economic outcomes for both groups will be collected from case records. Additional data regarding the costs of the telemedicine service, patient perception and organisational aspects will be collected for the intervention group. This is illustrated in the figure below.

**Figure 3: COPD study design**

To look for any possible selection bias for those electing to use TMon, regions will also attempt to collect prospective admission data and baseline demographics for all patients with COPD admitted during the one year intervention period. Reasons for exclusion from the study will be listed, wherever allowed by subjects, to enable a better understanding of the uptake / refusal and failures of TMon in a real-life setting.

**Sample size of intervention group (Total N=2038 patients)**

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scotland</td>
<td>838 patients (670 patients + 168 patients)</td>
</tr>
<tr>
<td>Wales</td>
<td>200 patients</td>
</tr>
<tr>
<td>Southern Norway</td>
<td>200 patients</td>
</tr>
<tr>
<td>Galicia</td>
<td>500 patients</td>
</tr>
<tr>
<td>Northern Norway</td>
<td>200 patients</td>
</tr>
<tr>
<td>Berlin</td>
<td>100 patients</td>
</tr>
</tbody>
</table>

In the case of Scotland, 670 patients will be recruited and followed-up in accordance with the study protocol, and 168 more patients will be recruited as part of the decision on deploying the service to the entire population who qualifies for it in
Scotland till 30th September 2015. Clinical, organisational and economic outcomes will be assessed only for the first 670 patients completing follow-up.

The comparator group will consist of the total population of patients fulfilling the eligibility criteria who have been treated and followed for at least one year before the implementation of the telemedicine service, from the same health units as the intervention group. This population will have similar demographics and clinical features, and its total size will be defined from admissions, the year before the implementation of the new service. In one centre (Wales), it is impossible to implement TMon across four different hospitals simultaneously with current resources. They will implement it in two of four hospitals initially, thus also allowing prospective gathering of a comparator group in the other two hospitals (with identical clinical services and similar patient demographics). This would allow additional analysis to reduce possible bias of disease progression within the same cohort if comparing admissions within them over two years.

**Study start and end dates, duration of the intervention and follow-up period**

Intervention group: Recruitment will start between 1st November 2013 and 31st January 2014 according to site capability, and continue until 1st April 2015 or until the target population is recruited (whichever is sooner).

The intervention and follow-up duration (with the three intensity levels of telemonitoring) for an individual patient will be up to 12 months (and a minimum of three months), based on the treating physician’s prescription (see below for the description and duration for each of the three intensity levels of telemonitoring).

**Eligibility criteria**

**Inclusion criteria:**

Hospitalisation for exacerbation of COPD according to the Global Strategy for Diagnosis (GOLD), Management, and Prevention of COPD[31]. We aim to recruit sequential patients until each site’s target is reached.

**The exclusion criteria will include any reason for non-participation, including:**

- Those unwilling or unable to provide written consent. (The study team will ask for a reason, but will emphasise that the potential subject is under no obligation to provide one.)

- Discharged to a locality not covered by the outreach TMon team / hospital (e.g. different geographical area served by another hospital / health institution, or discharged to a new setting, i.e. from home prior to admission and discharged to a nursing home).

- Discharged to a locality with no mobile phone signal.

- Those unable or unwilling to use TMon after teaching, but prior to installation.

- Clinician’s discretion: free text stating the clinical reason will be allowed here (prompts to guide the text include: unreliable behaviour, chaotic social circumstances, including drug or alcohol abuse etc.).

The number of patients who were screened but not included in the study, and the underlying reasons, will be registered and analysed with a common questionnaire
among the three pilots, with a view to identifying patient subgroup populations who are currently excluded from the provided services[15]. Such classification of reasons for non-participation would help to identify existing barriers to provision of telemonitoring services to patients with chronic conditions, and to work further to overcome the reasons which are not patient-related, such as logistic / technical limitations and clinician’s assessment decision.

Enrolment

Local Permissions (ethics and R&D) will be sought.

Potential participants are all patients hospitalised for exacerbation of COPD.

Enrolment will be carried out by a team experienced in COPD and TMon for each study site. Sequential patients admitted with AECOPD through EMRs (at least overnight) and any medical wards will be screened daily, aiming for consecutive recruitment just prior to hospital discharge, according to resources available (e.g. weekend admissions are likely to be approached Monday morning). Close collaboration with ward and EMR staff is therefore essential. Candidates are informed about the nature and the objectives of the intervention and the TMon equipment will be shown. Each patient will be supplied with a TMon briefcase and trained in the use of the telehealth system either on the ward, or within 24 hours of discharge once in their own home. Before deployment, they will demonstrate that they can complete symptom questions and use the peripherals technology; ideally a signal is tested.

Evaluation time points

Evaluation time points: at baseline and at the end of each of the three levels of intensity telemonitoring.

Demographic and clinical baseline characteristics

Demographic and clinical baseline characteristics are collected according to the common protocol. The following common data are collected at baseline for all patients in the intervention and comparator groups when available:

Demographic:

- Year of birth.
- Gender.
- Smoking status: never, ex, current.
- Social: lives alone Y/N; carers informal / formal.

Clinical

Previous 12 months:

- Number of admissions for exacerbation of COPD.
- Number of exacerbations needing oral steroids and/or antibiotics (self-reported and checked against primary care prescriptions- if available).
- Days in hospital (LOS) during last year for COPD.
- FEV1 (last available value and date to confirm diagnosis).
This admission (optional):

- Respiratory failure during admission: Y/N.
- Type 1, Type 2, Unknown.
- Lowest arterial pH during admission if known.
- Intubated: Yes / No.
- Needed acute NIV: Yes/No.
- Duration of stay in hospital (LOS).
- CAT (only intervention group).
- Medication on discharge (please circle):
  - LTOT, home NIV, SABA, SAMA, LAMA, LABA, ICS, nebs, Azithromycin, long term oral steroids, statins, beta blockers, PD4-inhibitor, Other.
- List of co-morbidities recorded with the ICD-10 classification.

In addition, the partners can collect the following optional data:

- PC user.
- Mobile phone user.
- Work status.
- Highest educational status (school, vocational, university).

### Intervention

A patient admitted with a COPD exacerbation is discharged from hospital and provided with a telemonitoring package including video conferencing, together with a pulse oximeter (Figure 4). Each day the patient will answer their symptom management questions, record their pulse oximetry reading and upload this data according to their agreed management plan before accessing a video consultation.

The intervention (provided service) represents three levels of intensity telemonitoring with specific duration for each level (Figure 5):

1. **High Level TMon:** daily teleconsultation (preferably via video-consultation or telephone if not possible); pulse oximetry and daily symptom questions are uploaded prior to the teleconsultation and will provide a partially standardised structure to the interview. This level of TMon will be targeted for 10 working days (but can be a minimum of 5, maximum of 30 days) after discharge to allow some pragmatism and better reflect a potential real-life clinical service.

2. **Moderate Level TMon:** daily pulse oximetry and symptom questions uploaded for up to 12 weeks (minimum of 4 weeks) after discharge.

3. **Low Level TMon:** optional symptom management questions and text message behaviour prompts or website links sent to a mobile phone for up to 12 months after discharge.

During the High level of TMon, a clinician (likely to be a specialist respiratory nurse) will make a scheduled teleconsultation (preferably video-consultation, otherwise telephone contact) with the patient after the receipt and review of the uploaded data (pulse and SpO2 and symptom questions) from the patient that day.
During the first 10 days, the clinician will determine a step down transition from the High Level to Moderate Level or continued High Level if needed. Those needing High Level TMon after 30 days or anyone with worrying clinical features or a combination of alerts (see below), will be referred for physician assessment. This should be to primary care or the hospital depending on clinical discretion. If readmitted to hospital, they remain within the study and are discharged again with High Level TMon.

After 10 working days, all patients deemed clinically stable will be reviewed by the specialist nurse with the specific intention to reduce the intensity of TMon to Moderate Level of TMon for up to a maximum of 12 week, with clinical discretion to step down earlier (minimum 4 weeks) or back to Higher Level.

Data recorded during High and Moderate TMon includes: pulse, oxygen saturation and answers to six pre-selected questions on symptoms:

2. How is your breathing? Usual, worse, much worse.
3. How is the amount of your sputum? Usual, worse, much worse.
4. How is your sputum colour? Clear/white, yellow, dark green or brown.
5. Are you using your reliever Inhalers/ nebs or oxygen? Same as usual, more than usual, much more than usual.
6. Are you taking any EXTRA antibiotics or steroids at the moment? Yes, No

An alert email/text will be sent to the respiratory nurse specialist if:

- Pulse rate <50 or >120 bpm,
- Oxygen saturations fall by 6% or more from their discharge baseline,
- Two from six questions are out of range (‘worse’ or ‘more than usual’) for two consecutive days.

The respiratory nurse will contact the patient for video / telephone review, or a home visit, or advise to attend hospital, according to their discretion. Criteria for hospital treatment will follow local protocols. Thereafter they will continue on Low level TMon (text prompts etc.) optionally for up to 12 months after last discharge.
Figure 4: COPD telemonitoring system architecture.

Figure 5: Three levels of intervention intensity (step-down COPD monitoring service)

Interventions in the comparator group

Patients in the comparator group receive usual care; retrospective anonymised data will be collected on each patient’s healthcare use.
Primary and secondary outcomes

Primary outcome:
- Number of (re)admissions for COPD exacerbations within one month between the Intervention and Comparator Groups.

Secondary outcomes:

a) Admission data
- Number of readmissions for COPD at 3, 6 and 12 months.
- Number of days in hospital for COPD over 12 months.
- Mean length of stay for re-admission for COPD.
- Mean/median time to first COPD readmission.

b) Health contacts
- Number ED visits.
- Number of visits to GPs and primary healthcare.
- Number of specialist nurse home visits.
- Number of clinic visits to secondary care.
- Mortality rate at 12 months.

Other Outcomes:
- Cost per avoided readmission.
- Qualitative reporting on the barriers to implementing TMon.
- Adverse events attributed to TMon.
- CAT score development at 3, 6 and 12 months’ follow-up (optional).

Economic evaluation

An economic evaluation will be performed according to the common protocol as described in section 5.1.

Evaluation of organisational changes

Assessment of the organisational changes will be done in accordance with the common protocol and the Renewing Health project methodology as described in section 5.2.

Evaluation of patient perception

The evaluation of patient satisfaction will be performed in accordance with the common methodology, using the WSD questionnaire, which was also used in the Renewing Health project (see section 5.3).
4.3 Pilot 3: Remote monitoring of Congestive Heart Failure

**WP8 Leader: Nekane Murga, Osakidetza – Basque Country**

**Members of the CHF Scientific Committee**

1. Nekane Murga (chair)
2. George Crooks
3. Iain Findlay
4. Milos Taborsky
5. Cirila Slemenik
6. Anna Kotzeva
7. Kristian Kidholm
8. Panagiotis Stafylas

**Study sites and local investigators**

Participants will be enrolled and the study will be conducted at the following health facilities:

**Scotland**
- NHS Ayrshire and Arran - East CHP, North CHP, South CHP
- NHS Lanarkshire - North CHP & South CHP
- NHS GGC – Renfrew CHP & East Renfrew CHP
- Principle Investigator: Dr Iain Findlay

**Basque Country**
- Basurto Hospital (Dr. Murga),
- Santa Marina Hospital (Dr. Ramirez) and
- Galdakao-Usansolo Hospital (Dr. Lekuona)
- Txagorритxu Hospital (Dr. Aros)
- Donostia Hospital (Dr. de la Cuesta)

**Northwest Moravia**
- University Hospital Olomouc
- Principal investigator: Prof. Milos Taborsky

**Slovenia**
- Slovenj Gradec General Hospital & Healthcare Centre of Ravne
- Principal investigator: Dr Cirila Slemenik

**Scientific background and rationale**

Congestive Heart Failure (CHF) is a complex syndrome characterised by the inability of the heart to expel sufficient amounts of blood needed for the metabolic requirements of different organs. As a result, the typical symptoms affecting patient with CHF are dyspnea and fatigue at rest or with reduced physical effort, and loss of
D3.1 Scientific study protocols for each of the three multicentre studies

appetite, which sometimes appear gradually over days or weeks. In addition, neurohormonal mechanisms produce liquid retention, resulting in a reduction of urine volume (occasionally not perceived by the patient) and the appearance of progressive oedemas, which frequently are not related to the disease by the patients and relatives due to ignorance[32].

Epidemiological studies indicate that the prevalence of CHF is considerably high, affecting 10% of the population older than 70 years old[33]. Over the last decade, the annual number of hospitalisations has increased from 800,000 to over a million for HF as a primary diagnosis and from 2.4 to 3.6 million for HF as a primary or secondary diagnosis[34]. Approximately 50% of HF patients are rehospitalised within six months of discharge; with the aging of the population, this trend will continue to rise[35,36]. Due to the ageing population and the increased survival of acute cardiac diseases, CHF is becoming more common, representing a public health problem. As the prevalence of CHF grows with the ageing of populations, it will become increasingly difficult to maintain the quality of care[32]. Recent trials have shown that the patients, after hospitalisation for HF, present 30-day, 1-year and 5-year mortality rates of 10.4%, 22% and 42.3% respectively[37].

Health care costs for CHF are at least two-fold higher than in the general population, mostly due to the high consumption of human resources caused predominantly by repeated and lengthy admissions to hospital[38]. Projections show that by 2030, the total cost of CHF will increase almost 120% (reaching $70 billion for USA)[39]. Despite advances in its treatment, CHF results in poor life expectancy, impaired quality of life, and repeated hospitalisations, so it is a considerable clinical, societal and economic burden[40,41].

Advances in treatment for CHF have resulted in reduced length of hospital stay and, in some cases, the avoidance of hospital visits, so the demand for home care services has increased. In this context, the design of new processes that improve the quality of life of patients with CHF and diminish clinical care burden is necessary. The current healthcare model is based on the management of acute destabilisation of chronic patients by hospitalisation, maintenance of a stable health state, and early diagnosis of decompensation[32,42]. These alternative models typically involve ICT, and may include self-monitoring and training delivered via standard telephone or more advanced telemonitoring technology. Home telemonitoring allows the clinical professional to follow up on the health status and biological constants of patients at home using ICTs[43,44,45,46,47]. Keeping the patient at home, the “white coat effect” is avoided, and the real-time assessment of monitored parameters is possible, pushing the patient to interact with the telemonitoring system, promoting self-care and enabling bi-directional communication between patient and professional more frequently than the conventional and periodic follow up. Home telemonitoring is not intended to replace health professional care or visits, but rather to enhance the level of care[46,48,49,50,51].

**Study Objectives**

The study aims to demonstrate that:

**Clinical**

• The provided service reduces hospitalisations for heart failure.
Organisational
- The required organisational changes result in a work load for the staff that is acceptable.
- The intervention can be successfully transferred to other regions and deployed at large scale.

Economic
- This intervention is cost-effective compared to usual care.

Other
- The new service is acceptable to patients.

Study Design
An observational study using as a comparator group the total population of the patients fulfilling the eligibility criteria who have been treated and followed for at least one year before the implementation of the telemedicine service, in the same health units as the intervention group, and whose data are available through EMR or other databases (retrospective collection of data for the comparator group).

Sample size of intervention group (Total N=1830 patients)

<table>
<thead>
<tr>
<th>Intervention group:</th>
<th>Total N=1830 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scotland</td>
<td>1250 patients (536 + 714 patients)</td>
</tr>
<tr>
<td>Basque Country</td>
<td>300 patients</td>
</tr>
<tr>
<td>Northwest Moravia</td>
<td>80 patients</td>
</tr>
<tr>
<td>Slovenia</td>
<td>200 patients</td>
</tr>
</tbody>
</table>

In the case of Scotland, 536 patients will be recruited and followed-up for one year in accordance with the study protocol, and 714 more patients will be recruited as part of the decision to deploy the service to the entire population who qualifies for it in Scotland till 30th September 2015. Clinical, organisational and economic outcomes will be assessed only for the first 536 patients completing follow-up.

Comparator group: the total population of patients fulfilling the eligibility criteria who have been treated and followed for at least one year before the implementation of the telemedicine service, in the same health units as the intervention group, and whose data are available through EMR or other databases. The final size of this population will have been defined before the implementation of the new service.

Study start and end dates, duration of the intervention and follow-up period

**Intervention group:** Study starts participant enrolment on 1st January 2014 and continues until 30th September 2014, or until they recruit the target population (whichever occurs first). The study duration for an individual participant is 12 months, identical to the follow-up period. However, there will be a sub-population comprised of patients recruited within the first three months of the study with an extended trial and monitoring of 18 months, in order to increase the sensitivity of the study to detect significant differences, given the chronic nature of the disease.
**Comparator group:** retrospective collection of the data of the patients in the comparator group will start on 1\textsuperscript{st} November 2013 and continue until 31\textsuperscript{st} December 2013 through EMR or other databases. The monitoring duration for an individual participant is 12 months.

**Eligibility criteria**

Hospitalisation or ED visit for decompensated HF (with need and administration of diuretics) in the previous six months, and at least one of the following three conditions:

- LVEF < 45% (at least once during the last year or in the last echocardiogram if older).
- LVEF > 45% but BNP > 400 (or plus NT-proBNP>1500) (at least once during the last year).
- Confirmed diagnosis of CHF by a cardiologist.

**Enrolment**

Potential participants are selected by screening electronic healthcare records or/hospital databases or/hospitalised patients. Candidates are informed about the nature and the objectives of the intervention. Once candidates have signed the informed consent form, they receive the telemonitoring devices and the appropriate education.

**Demographic and clinical baseline characteristics**

Demographic characteristics are collected during the recruitment according to the common protocol, and include:

- Year of birth.
- Gender.
- Smoking.
- Date of last hospitalisation/ED visit due to decompensated HF.
- If there is a carer (formal/informal), optional.
- Reason for non-participation, if not.
- Region/study site.
- Assessment of comorbidity using the ICD-10 International Classification of Diseases (including CHF aetiology, diabetes, COPD).

The selected clinical indicators and the time for assessment are:

- Heart rate: at recruitment and end of the study, and through telemonitoring.
- Oxygen saturation: at recruitment and the end of the study, and through telemonitoring.
- Blood pressure: at recruitment and the end of the study, and through telemonitoring.
- Weight: at recruitment and the end of the study, and through telemonitoring.
- Height: at recruitment.
- Left ventricular ejection fraction: at least once every 12 months.
- BNP or NT-proBNP and other laboratory exams, e.g. creatinine, urea, sodium etc. are optional.

**Description of the implemented telemedicine service**

The patient at his home uses the provided devices to measure his/her heart rate, blood pressure, pulse-oxymetry and weight (Figure 6) in accordance with the treating physician’s prescription, but at least once per week. Reminders will be sent if the centre does not receive any measurements for longer than a week, including a specific question: “Do you feel worse than last week?”

The telemonitoring devices used by the patient collect the data and send them to the gateway device wirelessly. The gateway device transmits data collected by the patient to the system server.

An operator checks the data sent by the patient, accessing them through the relevant portal. In case of clinical parameters out of normal range, as set by the treating physician for each patient, the system’s software detects the alert situation; the operator manages it following the standard protocol set by the physician.

In case of alert situation, the operator contacts the patient to verify the alert. If the alert is verified, depending to its severity, the operator contacts the reference clinician for that patient or follows the alert procedure. For the proper management of the alert situation, after the notification by the operator, the clinician accesses the relevant portal to check the patient data and take the appropriate actions.

Clinicians can access the portal to monitor patients’ health conditions any time they need, and not only in case of alert.

**Figure 6: CHF telemonitoring system architecture**
Description of necessary telemonitoring devices

- Pulse oximeter.
- Blood pressure monitor.
- Digital weight scale.

Primary and secondary outcomes

The primary outcome of the project should be an indicator able to demonstrate health, economic and organisational benefits. As such, the amount of health resources used seems to be appropriate.

**Primary clinical outcome:** HF related hospitalisations (readmissions).

**Secondary outcomes:** total days hospitalised for HF, all-cause admissions, ED visits, cardiovascular mortality, all-cause mortality, visits to GPs or primary healthcare.

Other indicators

For the treatment and follow-up of the patients and the evaluation of the provided services, the participating sites have the flexibility of, also, monitoring additional indicators too, adjusted to the local needs and experiences.

Evaluation time points

Data are collected at intervention initiation and end. For the sub-population with extended monitoring, there will be an assessment at study start, 12 months and 18 months.

Economic analysis is carried out throughout the study.

Economic evaluation

Economic evaluation will be performed according to the common protocol, as described in the section 5.1.

Evaluation of organisational changes

Assessment of the organisational changes will be done in accordance with the common protocol and the Renewing Health project methodology, as described in section 5.2.

Evaluation of patient perception

The evaluation of patient satisfaction will be performed in accordance with the common methodology, using the WSD questionnaire, which was also used in the Renewing Health project (see section 5.3).
5. COMMON EVALUATION METHODOLOGY

As described in section 3.2, United4Health will use a common evaluation methodology in the three studies. The methodology is based on MAST, and therefore includes a multidisciplinary assessment of safety and clinical outcomes, patient acceptability, economic aspects and organisational changes[3].

The outcomes and methods used in the common collection of data regarding patient acceptability, economic aspects, organisational changes and reasons for non-participation are described in the following sections. Hereafter the common database is presented.

5.1 Economic evaluation

In accordance with Drummond et al. (2005), the total costs per patient will be estimated in both the intervention and the control group. For the telemedicine patients, this will be estimated as the sum of the costs of producing the telemedicine intervention and the costs of the resources used in the healthcare sector in general (inpatient or outpatient care, ED, other healthcare contacts or medication). For the patients in the control group, the costs of the resources used in the healthcare sector in general will be estimated. Based on the estimated mean costs in the two groups, the difference will be identified and tested for statistical significance. If the telemedicine intervention reduces the patients’ use of healthcare in general during the period of 12 months, the hope is that these savings (S) will exceed the costs of the telemedicine interventions (C), and thereby result in a total reduction in the costs per patient.

Thereafter the estimated costs are compared with the estimated effect (E) on the primary outcomes in the cost-effectiveness analysis in each of the three studies. In practice this is done, as described by Drummond et al. (2005), by estimating the Incremental Cost-Effectiveness Ratio ICER = [(C - S) / E].

Thus, if, for example, the COPD study results in an increase in the costs per patient and reduction in the number of readmissions, the cost-effectiveness ratio will be equal to the cost of avoiding one readmission. In the CHF study, the primary outcome is the number of hospitalisations, thus the cost-effectiveness ratio will be the same. In the diabetes study, the primary outcome is the number of primary care face-to-face contacts. Therefore the cost-effectiveness ratio will be equal to the costs of avoiding one face-to-face contact.

In accordance with Drummond et al. (2015), the following tables will be produced as part of the economic evaluation describing the types of costs included, the prices, the use of resources and the average costs per patient.
Table 3: Types of resources included in the estimation of costs

<table>
<thead>
<tr>
<th>Type of costs</th>
<th>Method of data collection</th>
<th>Estimation at patient or group level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investment in the telemedicine application</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Physical change of buildings</td>
<td>Interview with staff</td>
<td>Group level</td>
</tr>
<tr>
<td>- Technical infrastructure</td>
<td>Interview with staff</td>
<td>Group level</td>
</tr>
<tr>
<td>- Education of the staff</td>
<td>Interview with staff</td>
<td>Group level</td>
</tr>
<tr>
<td>Running costs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Time used by staff on education of patients</td>
<td>Questionnaire to staff</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Time used by staff at the call centre</td>
<td>Questionnaire to staff</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Number of tele-consultations</td>
<td>Questionnaire to staff</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Rent of telemedicine device</td>
<td>Questionnaire to staff</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Staff time used by home care nurse</td>
<td>Questionnaire to staff</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Time used by patients</td>
<td>Questions to patient</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Time used by relatives</td>
<td>Questions to patient</td>
<td>Patient level</td>
</tr>
<tr>
<td>Effects on patients use of healthcare:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Number of readmissions</td>
<td>Register data</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Number of inpatient days</td>
<td>Register data</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Length of stay for each readmission</td>
<td>Register data</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Number of contacts to GP</td>
<td>Register data</td>
<td>Patient level</td>
</tr>
<tr>
<td>- Number of contacts to emergency doctor</td>
<td>Register data</td>
<td>Patient level</td>
</tr>
</tbody>
</table>

Table 4: Prices used in the calculation of costs

<table>
<thead>
<tr>
<th>Type of costs</th>
<th>Price per unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investment and running costs:</td>
<td></td>
</tr>
<tr>
<td>- Physical change of buildings</td>
<td>€€ in total</td>
</tr>
<tr>
<td>- Technical infrastructure</td>
<td>€€ in total</td>
</tr>
<tr>
<td>- Time used by staff:</td>
<td></td>
</tr>
<tr>
<td>- Nurses</td>
<td>€€ per hour</td>
</tr>
<tr>
<td>- Medical doctors</td>
<td>€€ per hour</td>
</tr>
<tr>
<td>- Secretary</td>
<td>€€ per hour</td>
</tr>
<tr>
<td>- Staff time used by home care nurse</td>
<td>€€ per hour</td>
</tr>
<tr>
<td>- Rent of telemedicine device</td>
<td>€€ per Briefcase</td>
</tr>
<tr>
<td>- Time used by patients</td>
<td>€€ per hour</td>
</tr>
<tr>
<td>- Time used by relatives</td>
<td>€€ per hour</td>
</tr>
<tr>
<td>- Transport</td>
<td>€€ per kilometre</td>
</tr>
<tr>
<td>Effects on patients use of healthcare:</td>
<td></td>
</tr>
<tr>
<td>- Readmissions</td>
<td>€€ per readmission</td>
</tr>
<tr>
<td>- Inpatient days</td>
<td>€€ per day</td>
</tr>
<tr>
<td>- Outpatient visits</td>
<td>€€ per visit</td>
</tr>
<tr>
<td>- GP visits</td>
<td>€€ per visit</td>
</tr>
<tr>
<td>- Emergency department visits</td>
<td>€€ per visit</td>
</tr>
</tbody>
</table>
Table 5: Average use of resources per patient in the intervention and comparison group

<table>
<thead>
<tr>
<th>Type of costs</th>
<th>Mean use per patient in the intervention group</th>
<th>Mean use per patient in the comparison group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Running costs of the telemedicine service and comparator:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Time used by staff on education of patients</td>
<td># min. ci: ##-##</td>
<td></td>
</tr>
<tr>
<td>- Time used by staff at the call centre</td>
<td># min. ci: ##-##</td>
<td></td>
</tr>
<tr>
<td>- Number of tele-consultations</td>
<td># cn: ##-##</td>
<td># days ci: ##-##</td>
</tr>
<tr>
<td>- Number of inpatient days</td>
<td># days ci: ##-##</td>
<td># days ci: ##-##</td>
</tr>
<tr>
<td>- Time used by patients</td>
<td># min ci: ##-##</td>
<td># min ci: ##-##</td>
</tr>
<tr>
<td>- Time used by relatives</td>
<td># min ci: ##-##</td>
<td># min ci: ##-##</td>
</tr>
<tr>
<td>Effects on patients’ use of healthcare:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Number of readmissions</td>
<td>#.# readmis. ci: ##-##</td>
<td>#.# readmis. ci: ##-##</td>
</tr>
<tr>
<td>- Length of stay for each readmission</td>
<td>#.# days ci: ##-##</td>
<td>#.# days ci: ##-##</td>
</tr>
<tr>
<td>- Staff time used by home care nurse</td>
<td>#.# min. ci: ##-##</td>
<td>#.# min. ci: ##-##</td>
</tr>
<tr>
<td>- Number of contacts to GP</td>
<td>#.# contacts ci: ##-##</td>
<td>#.# contacts ci: ##-##</td>
</tr>
<tr>
<td>- Number of contacts to emergency doctor</td>
<td>#.# contacts ci: ##-##</td>
<td>#.# contacts ci: ##-##</td>
</tr>
</tbody>
</table>

Table 6: Average costs of the treatment per patient in the intervention and comparison group

<table>
<thead>
<tr>
<th>Type of costs</th>
<th>Mean use per patient in the intervention group</th>
<th>Mean use per patient in the comparison group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investment in the telemedicine application</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Physical change of buildings</td>
<td>€ ######</td>
<td></td>
</tr>
<tr>
<td>- Technical infrastructure</td>
<td>€ ######</td>
<td></td>
</tr>
<tr>
<td>- Education of the staff</td>
<td>€ ######</td>
<td></td>
</tr>
<tr>
<td>Total investment costs</td>
<td>€ ######</td>
<td></td>
</tr>
<tr>
<td>Running costs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Staff</td>
<td>€#### ci: ##-##</td>
<td>€#### ci: ##-##</td>
</tr>
<tr>
<td>- Telemedicine devices</td>
<td>€ #### ci: ##-##</td>
<td>€#### ci: ##-##</td>
</tr>
<tr>
<td>- Inpatient days</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>- Readmissions</td>
<td>€#### ci: ##-##</td>
<td>€#### ci: ##-##</td>
</tr>
<tr>
<td>- Emergency department visits</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>- Home care nurse</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>- GP visits</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>- Transport</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>Total running costs</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>Time costs (lost productivity):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Time used by patients</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>- Time used by relatives</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>Total time costs</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
<tr>
<td>Total costs</td>
<td>€ #### ci: ##-##</td>
<td>€ #### ci: ##-##</td>
</tr>
</tbody>
</table>

5.2 Evaluation of organisational changes

Data on the organisational changes will be collected by focus group interviews with the healthcare professionals involved in delivering the telemedicine intervention to patients in the intervention group. A separate focus group interview will be held with the clinical managers involved in the implementation of the telemedicine service. All of them will be selected to make sure that they have experience with the services given to the patients both before and after the implementation of telemedicine. The
respondents will therefore have experience with both types of service, and be able to answer questions about their perception in a meaningful way.

As part of the evaluation of organisational changes, a narrative description of how the working routines and patient pathways have changed due to the introduction of telemedicine will be made. The figure below is an example of a simple illustration of the patient pathways for patients using telemedicine and patients treated by usual care[4].

![Patient Pathways Illustration]

**Figure 7: Illustration of patient pathways**

The following indicators will be collected [4]:

- **Effects on work processes:**
  - Workflow: Effects on number of patients treated, procedures performed, etc.
  - Staff: Changes in distribution of work (task shifting).
  - Resources: Changes in working hours for each profession.
  - Training: Time spent on training to learn to use the application.
  - Internal communication.
  - External communication.

- **Effects on structural outcomes:**
  - Description and number of units collaborating in the production of the service.
  - Changes in organisation of generalist and specialist tasks.
  - Changes in geographical spread.
  - Changes in time spent on travel.

- **Cultural outcomes:**
  - Staff attitudes towards the application.
  - Staff experiences with the use of the application.
    - The experiences of the clinical managers.
  - The clinical managers view of the barriers and facilitators to adoption of the telemedicine service.

With regard to the cultural outcomes and the attitudes of the staff towards the implementation of the telemedicine service, the following questions will be answered by the staff during the interview:
• Have you experienced technical difficulties which may affect the quality of care delivered by the telemedicine service? If so, please describe.
• Have you experienced difficulties in your collaboration with other professional groups in relation to the telemedicine service? If so, please describe.
• Have you experienced difficulties in your collaboration with staff at other institutions in relation to the telemedicine service? If so, please describe.
• How would you describe the usability of the telemedicine application for you?
• Has the use of the telemedicine application had any effect on your use of time? If so, please describe.
• Has the use of the telemedicine application had any effects on your tasks?
• Has the use of the telemedicine application had any effects on the communication within your institution? If so, please describe.
• Has the use of the telemedicine application had any effects on the communication with other institutions.
• Would you like to continue using the telemedicine service? Please elaborate.
• How would you describe your overall satisfaction with the use of the telemedicine service?

5.3 Evaluation of patient satisfaction

The WSD questionnaire[5,52] on patient acceptability is used in the study to assess the perception of the telemedicine service of the patients in the intervention group. This instrument was also used in the Renewing Health project, however the questionnaire has not been published yet, and the validity and reliability of this is still under consideration. The decision to use this questionnaire was based on the lack of a more appropriate and validated questionnaire, comparability reasons (comparison with WSD and RH projects), and the fact that the authors of the questionnaire have declared that it will be published by the end of 2013.

The questionnaire includes 22 items regarding:
• Utility of the “kit”.
• Effect on health status.
• Effect on health care/social care.
• Privacy.
• Suitability of the kit.
• Satisfaction with the kit.

These data will be collected for the first 100 patients in the intervention group in each region.

5.4 Reasons for non-participation

The number of patients who were screened but not included in the study and the underlying reasons will be registered and analysed with view to identify patient subgroup populations who are currently excluded from the provided services.
Such classification of reasons for non-participation (Table 7) would be of help to identify existing barriers to provision of telemonitoring services to patients with chronic conditions, and to work further to overcome the ones which are not patient-related[15].

Table 7: Reasons for non-participation

<table>
<thead>
<tr>
<th>A.</th>
<th>PATIENT REFUSAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient refuses the use of devices</td>
<td>☐</td>
</tr>
<tr>
<td>Patient refuses participation in the study in general (refuses to be monitored, to participate in an “experiment”, etc)</td>
<td>☐</td>
</tr>
<tr>
<td>Other reasons <em>please specify (open space)</em></td>
<td>☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B.</th>
<th>LOGISTIC/TECHNICAL LIMITATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No network coverage (broadband, 3G, 4G...)</td>
<td>☐</td>
</tr>
<tr>
<td>Patient not living in the area receiving healthcare coverage by the hospital, or about to leave this area during the study period</td>
<td>☐</td>
</tr>
<tr>
<td>Patient who is to be transferred in a different health centre (including nursing home) where the intervention (telemonitoring) cannot be carried on</td>
<td>☐</td>
</tr>
<tr>
<td>Other technical reasons <em>please specify (open space)</em></td>
<td>☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C.</th>
<th>CLINICIANS ASSESSMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient is unable to communicate (physical or cognitive condition).</td>
<td>☐</td>
</tr>
<tr>
<td>Patient not totally reliable for using the device (not meeting requirements for proper use and conservation of equipment and devices)</td>
<td>☐</td>
</tr>
<tr>
<td>Other: <em>please specify (open space)</em></td>
<td>☐</td>
</tr>
</tbody>
</table>

5.5 Database system

For each of the three studies, a web-based clinical database will be produced that includes all data at patient level for all patients in both the intervention and comparator groups.

Clinical data, data on patient perception, and economic data will be included in the database.

By use of the web-based databases, each region can enter data during the study. The databases can also be used to assess the status of recruitment of patients to the intervention group during the studies.
APPENDIX A - U4H project investigators and participating sites list

Scotland
- NHS24
- NHS Ayrshire and Arran - East CHP, North CHP, South CHP
- NHS Lanarkshire - North CHP & South CHP
- NHS GGC – Renfrew CHP & East Renfrew CHP
Principle Investigator for DM pilot: Dr Sandeep Thekkepat
Principle Investigator for COPD pilot: Dr Hugh Brown
Principle Investigator for CHF pilot: Dr Iain Findlay
Other investigators:

Wales
- Hywel Dda Health Board
- Prince Philip Hospital, Llanelli, Carmarthenshire,
- Glanegwil Hospital, Carmarthen, Carmarthenshire
- Withybush Hospital, Haverfordwest, Pembrokeshire
- Bronfains Hospital, Aberystwyth, Ceredigion
Principle Investigator for DM pilot: Dr Sam Rice
Principle Investigator for COPD pilot: Dr Keir Lewis
Other investigators:

Calabria
- Azienda Sanitaria Provinciale di Cosenza
- Distretto di Cosenza
- Via Milelli 23/A di Cosenza, Italy
Principal investigators for DM pilot: Dr Alfonso Longobucco and Dr Francesca Faggiano.
Other investigators:

South Karelia
- South Karelia Social and Health Care District
- Varto Käkelän katu 3, P.O.Box 24,
- 53101 Lappeenranta, Finland
Principal Investigator: Mira Pakanen MSc, Nurse

Central Greece
- General University Hospital of Larissa,
- Department of Endocrinology and Metabolic diseases
- Mezourlo area, 41110, Larissa, Greece
Principal investigators: Prof. Alexandra Mpargiota, with the collaboration of Dr George Dafoulas.

Northwest Moravia
- University Hospital Olomouc
Principal investigator for DM pilot: Dr Martin Hutyra
Other investigators for DM pilot: Dr. Jaronima Galdova, Dr Ivona Simkova.
Principal investigator for CHF pilot: Prof. Milos Taborsky
Other investigators for CHF pilot: Dr Marie Lazarova, Dr Marcela Skvanlova.

**Slovenia**
Slovenj Gradec General Hospital & Healthcare Centre of Ravne
Principal investigator for DM pilot: Dr Metka Epsek
Principal investigator for CHF pilot: Dr Cirila Slemenik

**Campania**
Agenzia Regionale Sanitaria Campania
Principal investigator: Dr Tiziana Spinosa

**Southern Norway**
Sorlandet Hospital.
Principal Investigator for COPD pilot: Dr Frode Gallefoss

**Northern Norway**
University Hospital North Norway (UNN)
Principal Investigator – Dr Audhild Hjalmarsen

**Galicia**
Galician Health Service – SERGAS
Principal Investigator: Dr Jose Alberto Fernandez Villar

**Berlin**
Pflegewerk
Principal Investigator: Dr Sebastian Gotzen

**Basque Country**
Principal investigator: Dr Nekane Murga.
Basurto Hospital (Dr. Murga),
Santa Marina Hospital (Dr. Ramirez) and
Galdakao-Usansolo Hospital (Dr. Lekuona)
Txagorritxu Hospital (Dr. Aros)
Donostia Hospital (Dr. de la Cuesta)
Appendix B - References


12. Campbell B, Stainthorpe AC, Longson CM. How can we get high quality routine data to monitor the safety of devices and procedures? *Bmj*. 2013;346:f2782


D3.1 Scientific study protocols for each of the three multicentre studies


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32 McMurray JJ, Adamopoulos S, Anker SD, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. European heart journal. Jul 2012;33(14):1787-1847.


