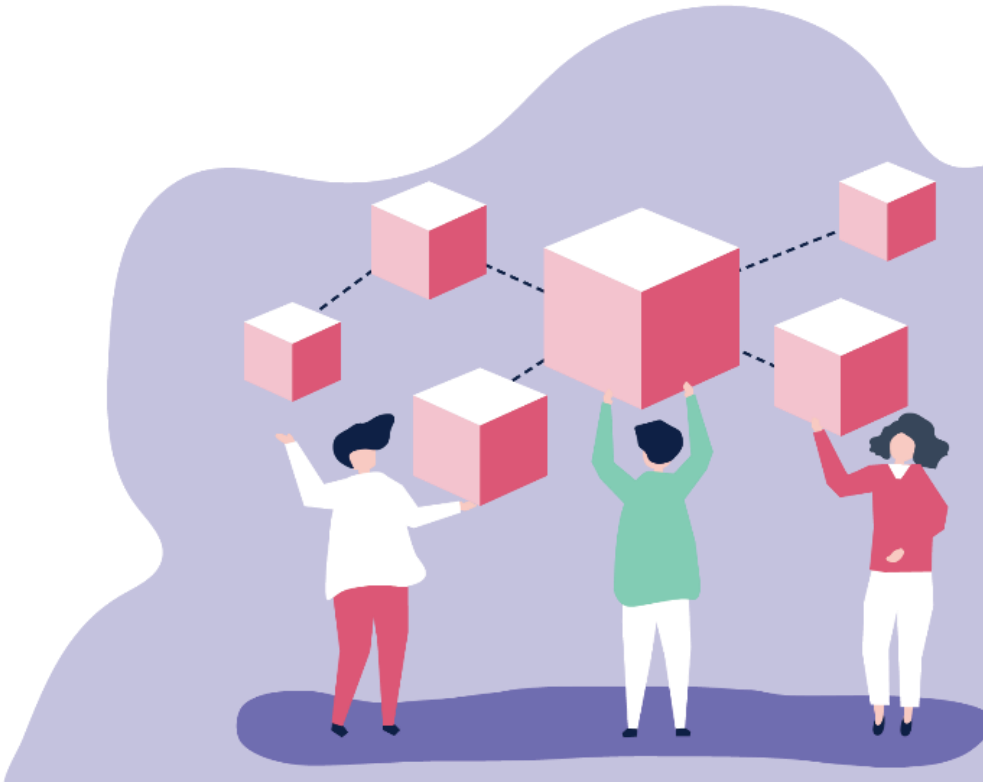
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement N° 857223

GATE KEEPER

D7.1 – Pilot Studies Use Case Definition and Key Performance Indicators (KPIs)

Deliverable No.	D7.1	**Due Date**	30/September/2020
Description	Report on pilots plans, KPIs for measuring and reporting, the training material and dissemination/communication plans.		
Type	Report	**Dissemination Level**	PU
Work Package No.	WP7	**Work Package Title**	Large Scale Pilot definition and execution
Version	1.0	**Status**	Final



Authors

Name and surname	Partner name	e-mail
Frans Folkvord	OE	ffolkvord@open-evidence.com
Nuria Febrer	OE	nfebrer@open-evidence.com
Laura Gunderson	OE	lgunderson@open-evidence.com
Francisco Lupiáñez-Villanueva	OE	flupianez@open-evidence.com
Alessio Antonini	OU	alessio.antonini@open.ac.uk
Przemyslaw Kardas	MUL	pkardas@csk.am.lodz.pl
Rosana Angles	SALUD	ranglesb@salud.aragon.es
Modesto Sierra	SALUD	msierrac@salud.aragon.es
Janire Orcajo	OSA	Janire.orcajolago@osakidetza.eus
Olatz Albaina	KG	oalbaina@kronikgune.org
Eleftheria Polychronidou	CERTH	epolyc@iti.gr
Ioanna Drympeta	CERTH	idrympeta@iti.gr
Eva Karaglani	HUA	ekaragl@hua.gr
Yannis Manios	HUA	manios@hua.gr
George Dafoulas	DCCG	gdafoulas@e-trikala.gr
Alexandra Bargiota	UTH	abargio@med.uth.gr
Laura Lopez	UPM	llopez@lst.tfo.upm.es
Gloria Cea Sanchchez	UPM	llopez@lst.tfo.upm.es
Giuseppe Fico	UPM	gfico@lst.tfo.upm.es
Maria Teresa Arredondo	UPM	mta@lst.tfo.upm.es

History

Date	Version	Change
10/05/2020	0.1	Creation of the Structure Content
29/05/2020	0.2	Integrating content
30/06/2020	0.3	Completion information Pilots
31/07/2020	0.4	Revisions information pilots
07/09/2020	0.5	Second round of iterations information
09/09/2020	0.6	Final version for peer review
21/09/2020	0.7	Final version for quality review
28/09/2020	1.0	Final version for submission

Key data

Keywords	Pilot Use Cases Definition; Key Performance Indicators
Lead Editor	Name: Frans Folkvord Partner: OE
Internal Reviewer(s)	Arik Eisenkraft (BIO), Pedro de la Peña Tejada, Pedro Maria (IBR)

Abstract

This document will report the detailed plan for the pilot use cases definition and the experimental design that will be conducted. The training strategy and material of the pilot sites are included and briefly discussed. In addition, this document focuses on determining and establishing Key Performance Indicators (KPIs) that will be used as measurable values that demonstrate (or refute) how effectively GATEKEEPER is achieving its key (business) objectives. The Key Performance Indicators (KPIs) will be described, including the scales and assessment tools that will be used that have been established in D6.4. Final, dissemination/communication plans will be discussed and some examples will be provided.

Statement of originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

Table of contents

List of Tables

List of Figures

1 About this document

This document focuses on determining Key Performance Indicators (KPIs) that will be used as measurable values that demonstrate (or refute) how effectively GATEKEEPER is achieving its key (business) objectives. More specifically, KPIs to be proposed will be those outcomes focused on testing the effectiveness and efficiency of the technical solutions, given the fact that this issue is of major importance for the GATEKEEPER evaluation framework. Patient development can occur as a result of the combination of several causes and circumstances and understanding the magnitude of the problem and the main contributing factors that lead to patient development is essential to devise effective and efficient solutions for the different contexts and environments, therefore experimental studies will be designed and conducted. We have defined the basic KPIs that will be assessed within this project, which will be developed in more detail in D7.2 and will be monitored and developed over the time period of the project.

The results described here is the outcome of task *T 7.2:* ***Detailed experiment and KPI definition***. Task 7.2 is part of *WP 7:* GATEKEEPER Large Scale Pilot definition and execution. Task 7.2 will identify and map the use cases with collected needs and requirements of WP2 with the current services and care programs, aligned with the experiment defined in WP6, specifically D6.4. It defines the different KPIs based on the specific measurement tools needed to indicate achievement of the specific goals; detailed definition and requirements for monitoring will be generated in D7.2. This task links the experiments defined to be done in each pilot site with the capabilities of the technology framework, KPIs, and will close the criteria to do the selection of the final users, of protocols, application workflow and integration needs. This task is in close coordination with T7.3 and T7.4 where evidence data aggregation is produced together with the QoL results and effectiveness reported in D7.5 and T9.2. In this document, it will be also presented an initial approach to the whole project evaluation framework and a first set of KPIs to be extended within WP6 and WP7, finally evaluated in WP 9.

1.1 Deliverable context

Table 1. Deliverable context

PROJECT ITEM	RELATIONSHIP
Objectives	Main objective: Detailed experimental design, use case definition (relating to the experimental design and impact assessment), and determining Key Performance Indicators (KPIs) that will be used as measurable values that demonstrate (or refute) how effectively GATEKEEPER is achieving its key (business) objectives
Exploitable results	N/A
Workplan	Part of the outcomes of Task 7.2 and it will feed future work within especially 7.5 and the 9.2 tasks.
Milestones	M10 Task 7.2 finished and M10 Deliverable 7.1 finished.
Deliverables	This deliverable is strongly related to D6.4, and will feed D6.6, D7.2, D7.4, D9.4 and D9.5
Risks	N/A

2 Training strategy and material to train the individuals or groups involved in the project pilots

GATEKEEPER will include a large number of user groups being representative of the respective population stratification within each large-scale pilot foreseen in seven European countries (Germany, Greece, Italy, Poland, Spain, UK and Cyprus). In this context the consortium is fully aware of the need to train the individuals and groups working in the pilots of the project on experimental designs, the development of the Key Performance Indicators (KPIs), the exact measurements, cost-effectiveness and impact assessment, and the execution of the studies, in order to align all the steps to conduct in an experimental study. Several steps were conducted to establish the experimental designs and KPIs together with the pilot sites, starting with a presentation in Milton Keynes, follow by bilateral meetings between the pilots and Open Evidence, the creation of a White Paper based on these meetings as a guideline for the experimental designs (see Appendix 1), followed by a webinar on experimental research and the development of KPIs. We will now outline the content of these meetings in more detail.

2.1 Presentations Milton Keynes

During the General Meeting in Milton Keynes, Open Evidence has conducted a presentation outlining the importance of using experimental designs to conduct impact assessment and cost-effectiveness evaluation. Central in this presentation was the use of impact assessment models, such as the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing (MAFEIP). As Prof. Dr. Guenther Jonitz, president of the Berlin Chamber of Physicians stated: "*"Medicine today resembles the church in the sixteenth century. What we need is a reformation. Few doctors are trained to judge and evaluate a scientific study. I myself chose to be trained as a surgeon to avoid two things: statistics and psychology. Now I realize that both are indispensable"*[1].

To improve the validity and reliability of the data that will be collected by the pilots in order to be able to conduct impact assessment with MAFEIP to show the effectiveness of the digital solution, a clear and straightforward experimental design is a key element of the studies that will be conducted, with validates scales to assess the outcomes. In addition, the assessment of quality of life with a validated scale (e.g., ED5Q) is essential to analyse the cost-effectiveness and take into account the importance of valuable years, therefore this presentation was mostly focused on these elements, see also Figure 1 and Figure 2.

[1] In Gigerenzer, Gerd. *Risk savvy: How to make good decisions*. Penguin, 2015.

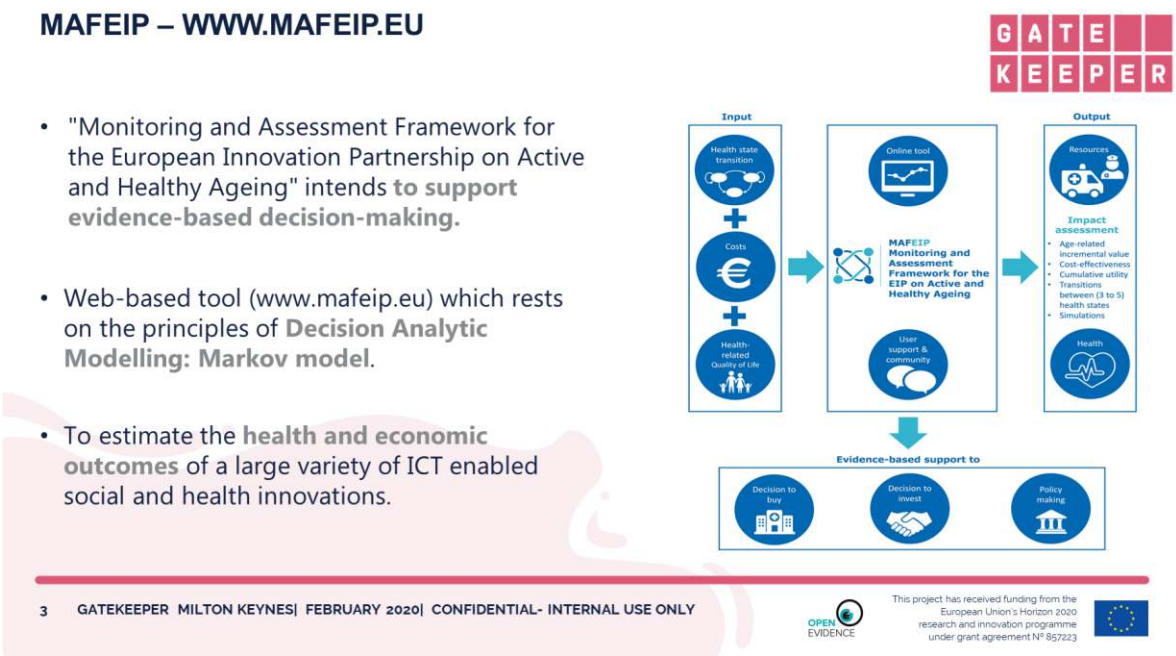


Figure 1: Slide presentation Milton Keynes

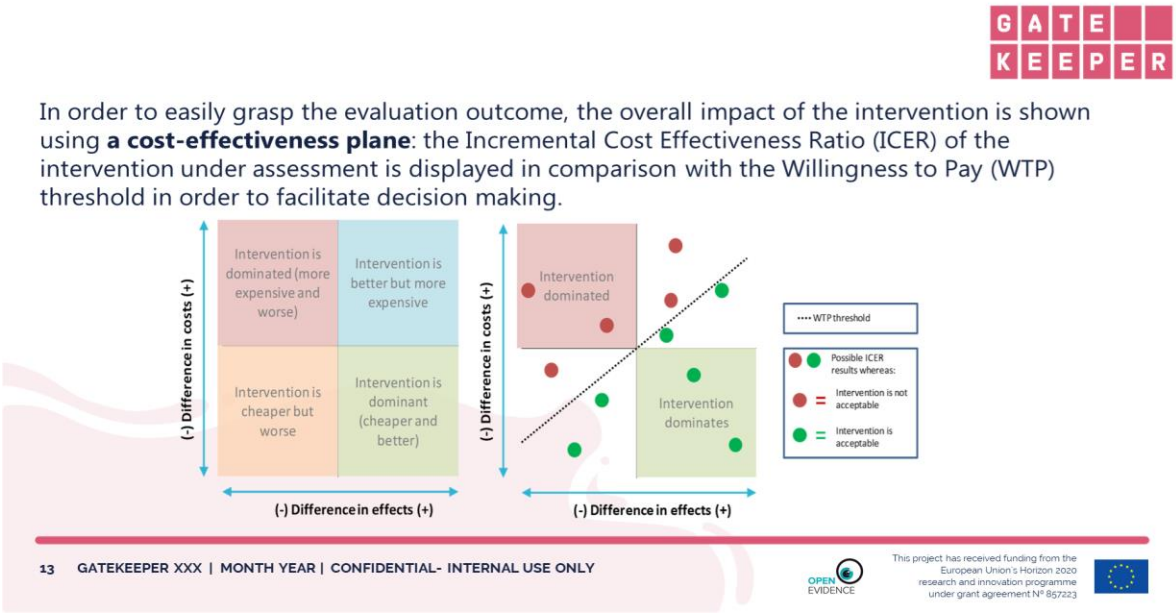


Figure 2: Slide presentation Milton Keynes

2.2 Bilateral Meetings

Subsequently, after the General Meeting in Milton Keynes where Open Evidence presented the general framework to conduct experimental designs and assess the impact with MAFEIP, Open Evidence has started organizing bilateral meetings with the pilot sites to discuss any potential questions or difficulties related the impact assessment. During these meetings individual questions were discussed and research plans developed. Between 3 and 10 bilateral (online) meetings were held with pilot sites, in order to explain experimental designs in more detail and to establish what kind of design would be feasible. In addition, KPIs were defined and in some cases scales and measurements were already established. Because some additional information on experimental designs was needed, a White Paper on this was created and shared with the pilots.

2.3 Experiment White Paper

In order to explain the importance/relevance of a control group in experimental designs to the pilot sites, we have developed a White Paper on this (see also Appendix 1).The document clearly describes different experimental designs, their advantage and limitations, and how to develop such an experimental design. This document was shared with the pilots in order to train them and align the work we are doing in this deliverable.

2.4 Webinars Experimental Research and Development KPIs

Final, during the remote meeting in May 2020 (due to Covid-19), progress was discussed with all partners, also from the other clusters, in order to align the work being conducted.

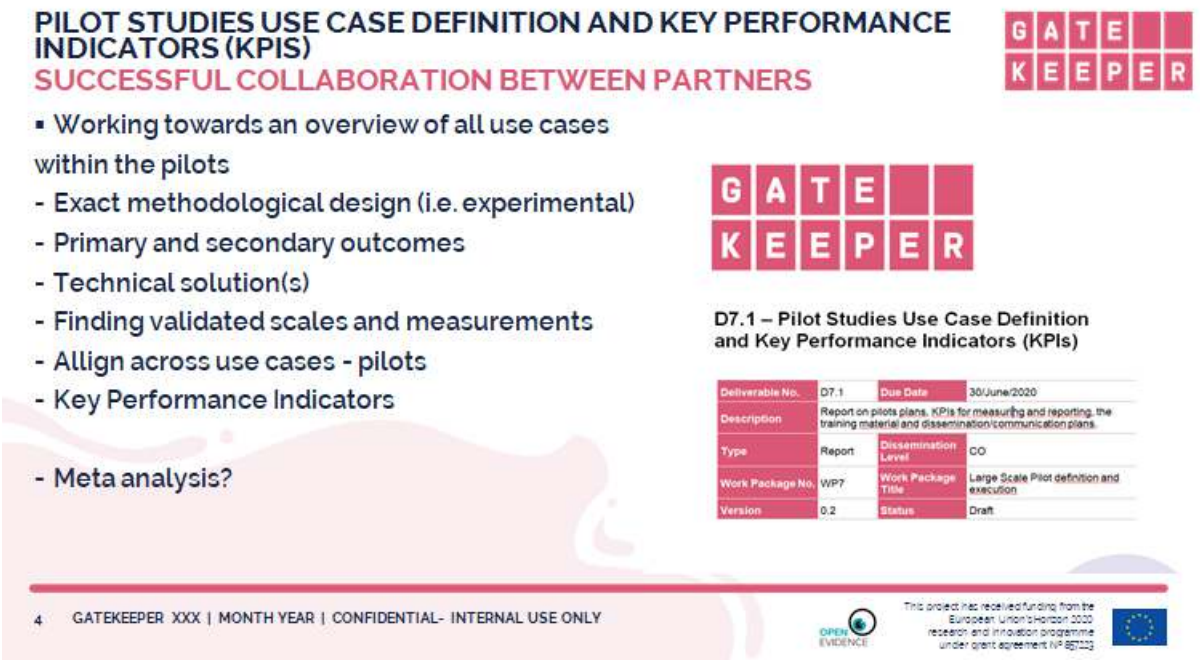


Figure 3: Slide presentation remote meeting

In addition, in close collaboration with partners from UPM and UoW we have developed plans to conduct a meta-analysis on all the outcomes that will be discussed in the sections hereafter, summarized in an extensive excel-file were all the different factors have been established, see Figure 4 and for a more extensive Appendix 2. This has been done in order to feed the general evaluation framework of the federated pilots to examine to what extent the GATEKEEPER is effective in improving the KPIs and to conduct the impact assessment for the socio-economic reports in D9.4. First, we differentiate all the information for all pilot sites and define the measurements for the use cases separately (see Appendix 2 for a full overview). Second, we have defined pilot details (e.g., technology adopted, intervention details, recruitment period), defined the differences in clinical variables at final follow-up (e.g., patients per group, proportion patients in baseline state, proportion patients in disease/impairment state), healthcare costs baseline (e.g., Markov model States, one-off costs, recurrent costs), and societal aspects (e.g., utility baseline, utility disease/impairment, technology acceptance).

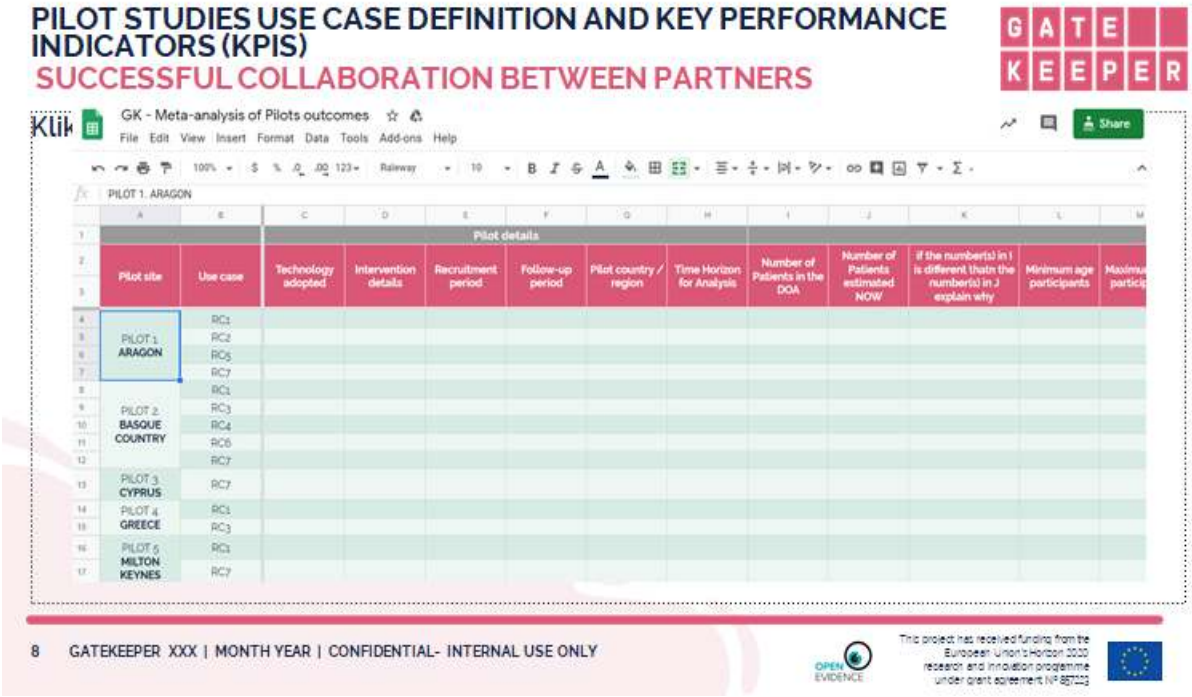


Figure 4: Slide presentation remote meeting

Hereafter we will describe the designs that will be conducted in the Use cases in all the different pilots and which factors have been established as primary and secondary outcomes, and which KPIs will be taken as measurements to assess effectiveness and impact. The exact measurements will be established in the D7.2, where the development of the KPIs and measurement will be conducted.

3 Experimental Designs Pilots and KPIs

In this chapter we will explain the different experimental studies and we will list the main outcomes and KPIs that will be assessed in the different Pilots and Use cases. All factors that will be established will feed the extensive excel file (see Appendix 2) that we have developed where we provide a clear overview of the Experimental Design of the Federated Pilots.

3.1.1 Basque

3.1.1.1 USE CASE 1

- Experimental Design: Between, Within, Mixed

Between subject design with an intervention group (prospective) and control group (retrospective)

- Technology adopted/used:

Questionnaire collector (Proms and online questionnaires), visualization, storage and data analytics infrastructure; virtual assistant and digital coach.

- Intervention details:

The intervention will focus on Lifestyle-Related Early Detection and Intervention. The intervention pretends to improve the provision of a multidimensional assessment and enabling of specific interventions according to the detected needs of elderly people, which includes different main/specific goals: to improve efficiency in data collection, visualisation, analysis and interventions. This includes:

- Facilitating risk stratification and multidimensional assessment
- Providing personalized care plans
- Preventing or delaying the appearance of disability/dependence
- Improving quality of life
- Avoiding undesired events as hospital admissions or visits to A&E department

- Recruitment period:

The recruitment will be carried out during 2-3 months approximately. It will commence once the technology is integrated in Osakidetza´s facilities

- Follow-up period:

12 months

- Time Horizon for Analysis (the longevity of the effect):

2 years

- Number of participants:

10.000 low complexity people aged 70 or older in a stable situation.

- Randomization procedure:

Participants will be randomized with a specific randomization program. The randomization unit most probably be the primary care centre not the individual to be included in the study.

- Groups: Control (N=5000) ; Intervention 1 (N=5000)
- Outcomes:

To improve quality of life, to delay the appearance of frailty and to prevent undesired events as hospital admissions or visits to A&E department.

- KPIs

  Quality of life

  Functionality of the technical solutions

  Utilities

  Patient visits and time spent

  Resources use of Primary Care

  Resources use of Hospital Care

  Technology acceptance

3.1.1.2 USE CASE 3

- Experimental Design:

  A between subject design: Intervention Group / Control Group

- Technology adopted/used:

  Glycaemia continuous monitoring system

  IoT data collection: ACTIVAGE platform, Samsung

  Patients' resources

  Clinician's management

- Intervention details:

  The intervention will focus on Patients with Diabetes Type II from the Endocrinology Service of Cruces University Hospital, ≥ 65 years, on treatment with basal insulin and / or any type of added oral antidiabetic that also presents some type of cardiovascular event and vascular risk factors.

- Recruitment period:

  The recruitment period will be continuous during 12 months.

- Follow-up period:

  12 months

- Time Horizon for Analysis(the longevity of the effect):

  2 years

- Number of participants:

  n = 100

- Randomization procedure:

  All patients who meet the inclusion criteria and who have signed and registered the informed consent approved by the local ethics committee will be included.

Patients will be recruited in the Endocrinology Unit of Cruces University Hospital. Randomization will be conducted using randomization program.

- Groups:

  Control (N=50), Intervention (N=50).

  We will include the patient's primary caregiver in the study.

- Outcomes:

  Primary outcomes:

  To learn and analyse the state of metabolic control based on the treatment, in relation to the risk of cardiovascular events of the patients of the Cruces University Hospital over 65 who suffer from DM2.

- Secondary outcomes:

  To improve the self-management of the disease.

  To improve independence in activities of daily living (ADL).

  To improve the quality of life of patients and their caregivers.

  To improve adherence to pharmacological and non-pharmacological treatment.

  To decrease the need for your caregivers.

  To reduce disease complications.

  To reduce the number of outpatient visits to hospital and primary care centers.

  To know the comorbidities associated with a poor evolution of DM2.

  To evaluate possible adverse events of the system created in the study participants.

  To establish an evidence-based management protocol for patient management.

  To evaluate the impact in terms of efficiency of the implementation of said protocol in relation to cardiovascular risk factors in patients with T2DM.

- KPIs

Clinical KPIs:

Hospital admissions / health deteriorations

Patient visits and time spent

Patient adherence to treatment

Quality of life

Adverse events

Societal KPIs

Technology acceptance

Patient empowerment / health literacy

Cultural discomfort alleviation

Return on investment

Adoption Potential:

Integrability with current infrastructure

Compatibility with clinical workflows/protocols

Usability issues

3.1.1.3 USE CASE 4

- Experimental Design:

  A between subject design: Intervention Group / Control Group

- Technology adopted/used:

  STAT-ON Parkinson's holter, Sense4Care

  IoT data collection: ACTIVAGE platform, Samsung

  Patients' resources

  Clinician's management

- Intervention details:

  The intervention will focus on Patients with Parkinson Disease (PD) from the Neurology Service of Cruces University Hospital, ≥ 65 years. The strategic objective of the present Medical Use Case aims to find greater sensitivity in the early detection of these diagnostic criteria of an Advanced stage of the Parkinson Disease (APD), with respect to the conventional approach to the disease (diaries and interviews with patients, video recordings of family members, neuropsychological scales, etc.). This will help to detect earlier the presence of fluctuations, dyskinesias, cognitive decline and non-motor symptoms and, so, to slow down motor disability progression, reduce incidence of motor complication and improve medication adherence.

- Recruitment period:

  The recruitment period will be continuous during 12 months.

- Follow-up period:

  12 months

- Time Horizon for Analysis:

  15 months

- Number of participants:

  n = 100

- Randomization procedure:

  All patients who meet the inclusion criteria and who have signed and registered the informed consent approved by the local ethics committee will be included. Patients will be recruited in the Movement Disorders Unit of Cruces University Hospital.

  Based on the registered pharmacological treatments specific for Parkinson's disease, the equivalent dose of levodopa is calculated. It is important that the patients to be evaluated have a stable treatment of their disease in the last months. Patients will be randomly allocated using a randomization program.

- Groups:

  Control (N=50), Intervention (N=50).

  We will include the patient's primary caregiver in the study.

- Outcomes:

  Primary outcomes:

  To show that sensors used in conjunction with the ACTIVAGE platform are more effective in detecting Advanced Parkinson Disease (APD) criteria. The approved criteria for this classification will be used, specifically the presence of cognitive impairment, motor fluctuations with an ON period greater than 20 %, and falls to the ground. As a support criterion, the presence of orthostatic hypotension and dyskinesias in a period of 25 % of ON time will be used.

  The ultimate goal is to create alarm tools that detect these phases of the disease and help implement therapeutic measures in the patient that reduce the risk of falls and dependency.

  Secondary outcomes:

  To develop an evidence-based management protocol for the management of patients at risk of EPA.

  To evaluate the impact in terms of efficiency of the implementation of said protocol in relation to the risks associated with the disease.

  To improve the self-management of the disease.

  To improve independence in activities of daily living (ADL).

  To improve the quality of life of patients and their caregivers.

  To improve adherence to pharmacological and non-pharmacological treatment.

  To decrease the need for your caregivers.

  To reduce complications of the disease.

  To reduce the number of outpatient visits to hospital and primary care centres.

  To evaluate the accessibility of the created system.

  To evaluate possible adverse events of the system created in the study participants.

- KPIs

Clinical KPIs:

Physical activity increase

Hospital admissions / health deteriorations

Patient visits and time spent

Patient adherence to treatment

Better quality of life patients and caregivers

Adverse events

Societal KPIs

Technology acceptance

Patient empowerment / health literacy

Cultural discomfort alleviation

Return on investment

Adoption Potential:

Integrability with current infrastructure

Compatibility with clinical workflows/protocols

Usability issues

3.1.1.4 USE CASE 6

- Experimental Design:

  A between subject design: Intervention Group / Control Group

- Technology adopted/used:

  Virtual reality glasses, Tecnalia

  IoT data collection: ACTIVAGE platform, Samsung

  Patients' resources

  Clinician's management

- Intervention details:

  The intervention will focus on: Stroke Prevention in patients ≥ 65 years with risk factors. The purpose of this project is twofold:

  1. To increase awareness of stroke in patients over 65 years by an orientation program in the improvement of lifestyles in the prevention of cerebrovascular diseases, and the early identification of symptoms for a rapid activation of the Stroke Code.

  2. To increase the amount of stroke education provided by the primary care provider.

- Recruitment period:

  The recruitment period will be continuous during 12 months.

- Follow-up period:

  12 months

- Time Horizon for Analysis:

  15 months

- Number of participants:

  $N_T = 100$

- Randomization procedure:

All patients who meet the inclusion criteria and who have signed and registered the informed consent approved by the local ethics committee will be included. Patients will be recruited in the Neurology Service of Cruces University Hospital.

- Groups:

  Study Phase 1 (N = 50):

  Group A (Control), N = 20

  Group B (Intervention 1), N = 20

  Group C (Intervention 2), N = 10

  Study Phase 2 (N = 50):

  Group A (Control), N = 25

  Group B (Intervention), N = 25

- Outcomes:

  Primary outcomes:

  To evaluate virtual reality as an educational medium on strokes and the impact of this education on the usability of the ACTIVAGE platform as a follow-up and monitoring system that will measure the relationship between control over the daily activities and the risks of having a stroke.

  Secondary outcomes:

  To present a new experience in the development of stroke health education programs.

  To evaluate the impact of health education on strokes using virtual reality technology with animated videos versus staged videos with actors.

  To educate in the early identification of the symptoms of a stroke.

  To reduce the time between the start of a stroke and the performance of the medical service.

  To increase the number of patients with cerebral infarction treated with thrombolysis thanks to education in rapid action in the event of a stroke.

  To increase the number of patients accessing care in an acute stroke unit.

  To reduce the complications of the disease.

  To provide knowledge about what a stroke is.

  To improve self-management.

  To improve independence in activities of daily living (ADL).

  To improve Life Quality.

  To improve adherence to pharmacological and non-pharmacological treatment.

  To decrease the need for caregivers.

  To reduce the number of hospital admissions, urgent care and outpatient visits to hospital and primary care centres.

  To evaluate the accessibility of the created system.

To evaluate the profitability of the created system.

To evaluate the sustainability of the system created.

To evaluate the satisfaction of users, caregivers and professionals related to the created system.

To evaluate possible adverse events of the system created in the study participants.

- KPIs

Clinical KPIs:

Physical activity increase

Hospital admissions / health deteriorations

Patient visits and time spent

Patient adherence to treatment

Better quality of life patients and caregivers

Adverse events

Societal KPIs

Technology acceptance

Patient empowerment / health literacy

Cultural discomfort alleviation

Return on investment

Adoption Potential:

Integrability with current infrastructure

Compatibility with clinical workflows/protocols

Usability issues

3.1.1.5 USE CASE 7

- Experimental Design: Between, Within, Mixed

Intervention Group (prospective) and Control Group (retrospective)

- Technology adopted/used:

Electronic pill dispenser; virtual assistant; digital coaching (to improve adherence to medication).

- Intervention details:

The intervention will focus on: Multi-Chronic Elderly Patients under polymedication. The intervention aims to improve treatment adherence, control and monitor drug intake and avoid adverse events resulting from polypharmacy. The objectives of the present Medical Use Case are the following:

- To improve patient safety
- To guarantee the prescription of the necessary drugs for the active diseases

- To avoid adverse drug events, interactions and duplication
- To eliminate unnecessary medication
- To increase adherence in order to improve health outcomes and control of pathologies
- To improve quality of life

- Recruitment period:

The recruitment will be carried out during 2-3 months approximately. It will commence once the technology is integrated in Osakidetza´s facilities.

- Follow-up period:

12 months

- Time Horizon for Analysis:

2 years

- Number of participants:

1000 moderate complexity patients, with more than one chronic condition, under polymedication and in a stable situation.

- Randomization procedure:

Participants will be randomized with a specific program. The randomization unit most probably be the primary care centre not the individual to be included in the study.

- Groups

Control (N=500), Intervention (N=500).

- Outcomes:

To improve quality of life, to reduce of adverse events.

- KPIs

Quality of life

Adverse events

Adherence to treatment

Functionality

Utilities

Resources use of Primary Care

Resources use of Hospital Care

Technology acceptance

3.1.2 Aragon

3.1.2.1 USE CASE 1

- Experimental Design: Between, Within, Mixed

Between subject design, with one intervention group and one control.

- Technology adopted/used:

Health promotion APP / Contents

Collection of PROMS

Information on Health

Data federation Engine

Big Data Analytics

Professional Dashboard

- Intervention details:

The intervention will focus on: Lifestyle-related early detection of chronic diseases. The generic description of the intervention in Aragon is health promotion, which includes different main/specific goals, namely; (I) to avoid/delay/prevent the appearance of chronic disease, (II) to empower patients on the self-management of their disease, and (III) to promote healthy habits.

- Recruitment period:

The recruitment will be performed on a continuous phase, starting as soon as the application is ready to test until the end of the project trial.

- Follow-up period:

6 months

- Time Horizon for Analysis:

2 year

- Number of participants:

2000 including: Citizens (> 50) and primary care professionals

- Randomization procedure:

No randomization as we will use only descriptive analysis.

- Outcomes

Primary outcomes:

- Use of application
- Walk a minimum of steps
- Doing minimum of exercises
- Follow the health programs
- Answer the PROMs required

- Knowing how to self-manage their disease (by looking/following advices/videos etc..)
- Follow or see nutrition tips.
- Secondary outcomes:

Users satisfaction

empowerment of patients on the self-management of their diseases.

Early assessment of the deterioration and death risk for hospitalized COPD patients.

24-hour admission to hospital for COPD,

24-hour initiation of oral corticosteroid treatment

Predict the presence of an exacerbation

Exacerbation identification

Exacerbation prediction (2-class problem, Stable period / Prodromal period)

Joint prediction of the rate and severity of COPD exacerbations over one year

- KPIs

Users satisfaction (Measured with a questionnaire)

Sustainability (Measured with an analysis of service(s))

Avoid/prevent appearance of chronic diseases (Measured with questionnaires before/after based on healthy lifestyles)

Empower citizens (Measured with standard questionnaire (PAM))

Promote healthy habits (Measured with PROMS completion, use of the APP)

- **List of information to be collected in low complexity patients:**
  - Questionnaires: quality of life, healthy habits (food intake, exercise, smoking, alcohol), depression / anxiety, level of dependency
  - BMI (Body Mass Index)
  - Steps / Physical activity
  - Sleep

3.1.2.2 USE CASE 2

3.1.2.2.1 Use case 2: Mid complexity

- Experimental Design: Between, Within, Mixed

A **between subject design**: Intervention / control group

- Technology adopted/used:

Monitoring devices

Patient app

Collection of Vital Signs

Telemonitoring platform

Data federation Engine

Big Data Analytics

Professional Dashboard

HF and COPD predictive models

- Intervention details:

The intervention will focus on COPD early detection of exacerbations. The generic description of the intervention in Aragon is enhanced integrated care, which includes integrated care management of people with chronic diseases for an early detection of the appearance of exacerbations

- Recruitment period:

The recruitment period will be continuous during the GATEKEEPER project.

- Follow-up period:

6 months

- Time Horizon for Analysis:

2 years

- Number of participants:

50 including: Chronic patients 65+ and health and social care professionals.

- Randomization procedure:

Participants will be randomly allocated through an assignment procedure (dice, coin or similar).

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

Control (N=25), Intervention (N=25)

- Outcomes:

Primary outcomes: early detection of symptoms of exacerbations, reduce activity in healthcare centres, avoid hospitalizations and decrease length of stays.

Secondary outcomes: Increase quality of life and satisfaction of users.

- KPIs

Users satisfaction (Measured with a questionnaire)

Sustainability (Measured with an analysis of service(s))

Prevent the appearance of exacerbations (Measured with the number of alarms that generate a consultation)

Decrease number of consultations (Measured with the number of consultations performed by other agents (social/relatives) as a result of transfer of competences, and the destiny of an alarm)

Increase QoL (Measured with a questionnaire)

- **List of information to be collected:**
  - Low complexity patients information +
  - Heart Rate
  - Blood Pressure

- Oxygen Saturation
- Respiratory Rate
- Weight.
- Body Temperature
- Dyspnoea
- ECG
- Other (Systemic vascular resistance, Sweat level, FEV – Forced Expiratory Volume, Peak Expiratory Flow, Glucose)

3.1.2.2.2 Use case 2: High complexity

- Experimental Design: Between, Within, Mixed

A between subject design, with an intervention and control group

- Technology adopted/used:

Monitoring devices

Collection of Vital Signs

Telemonitoring platform

Data federation Engine

Big Data Analytics

Professional Dashboard

HF and COPD predictive models

- Intervention details:

The intervention will focus on: COPD exacerbations management. The generic description of the intervention in Aragon is integrated care management of exacerbations, which aims at reducing adverse effects improving the quality of life and optimizing resources during the recovery period and decreasing the number of hospitalizations and length of stays.

- Recruitment period:

The recruitment period will be continuous during the GATEKEEPER project. Potential participants will come from hospitalizations at emergencies rooms, specific specialities, etc. when suffering an exacerbation. We cannot preview when participants exactly will participate. Probably the enrolment will be scaled. In winter we may identify and enrol more patients, but also in spring. That is that during the 2 years of duration of the GK project, we will include patients staggered over that period.

- Follow-up period:

We will follow-up until stabilization objective defined by the healthcare specialist is reached (approx. 2 -4 weeks)

- Time Horizon for Analysis:

2 years

- Number of participants:

10 including chronic patients 65+ suffering and exacerbation and health and social care professionals.

- Randomization procedure:

Participants will be randomly posed at each group through a random assignment procedure (dice, coin or similar).

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

Control (N=5), intervention (N=5)

- Outcomes:

Primary outcomes: Reduce number of hospitalisation, length of stays

Secondary outcomes: Increase Quality of life

- KPIs

Users satisfaction (Measured with a questionnaire)

Sustainability (Measured with an analysis of service(s))

Reduce number of hospitalisations (Measured in interventions that might have required traditional hospitalisations)

Reduce length of stays (Measured in early discharges thanks to intervention)

Increase quality of life (Measured with a questionnaire such as E5Qd)

- **List of information to be collected:**
  - Low complexity patients information +
  - Heart Rate
  - Blood Pressure
  - Oxygen Saturation
  - Respiratory Rate
  - Weight.
  - Body Temperature
  - Dyspnoea
  - ECG
  - Other (Systemic vascular resistance, Sweat level, FEV – Forced Expiratory Volume, Peak Expiratory Flow, Glucose)

3.1.2.3 USE CASE 5

3.1.2.3.1 Use case 5: Mid complexity

- Experimental Design: Between, Within, Mixed

a **between subject design** with an intervention and control group

- Technology adopted/used:

Monitoring devices

Patient app

Collection of Vital Signs

Telemonitoring platform

Data federation Engine

Big Data Analytics

Professional Dashboard

HF and COPD predictive models

- Intervention details:

The intervention will focus on: Predicting readmissions and decompensations in Heart Failure/early detection of exacerbations. The generic description of the intervention in Aragon is enhanced integrated care, which includes Integrated care management of people with chronic diseases for an early detection of the appearance of exacerbations

- Recruitment period:

The recruitment period will be continuous during the GATEKEEPER project.

- Follow-up period:

6 months

- Time Horizon for Analysis:

2 years

- Number of participants:

50 including: Chronic patients 65+ and health and social care professionals.

- Randomization procedure:

Participants will be randomly exposed to one of the conditions through random assignment procedure (dice, coin or similar).

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

Control (N=25), Intervention 1 (N=25),

- Outcomes:

Primary outcomes: early detection of symptoms of exacerbations, reduced activity in healthcare centres, avoid hospitalizations and decrease length of stays.

Secondary outcomes: Increase quality of life and satisfaction of users.

- KPIs

Users satisfaction (Measured with a questionnaire)

Sustainability (Measured with an analysis of service(s))

Prevent the appearance of exacerbations (Measured with the number of alarms that generate a consultation)

Decrease number of consultations (Measured with the number of consultations performed by other agents (social/relatives) as a result of transfer of competences, and the destiny of an alarm)

Increase quality of life (Measured with a questionnaire)

- **List of information to be collected:**
  - Low complexity patients information +
  - Heart Rate
  - Blood Pressure
  - Oxygen Saturation
  - Respiratory Rate
  - Weight.

- Body Temperature
- Dyspnoea
- ECG
- Other (Systemic vascular resistance, Sweat level, FEV – Forced Expiratory Volume, Peak Expiratory Flow, Glucose)

3.1.2.3.2 Use case 5: High complexity

- Experimental Design: Between, Within, Mixed

a **between subject design** with an Intervention / control group

- Technology adopted/used:

Monitoring devices

Patient app

Collection of PROMS

Collection of Vital Signs

Telemonitoring platform

Data federation Engine

Big Data Analytics

Professional Dashboard

HF and COPD predictive models

- Intervention details:

The intervention will focus on: Predicting readmissions and decompositions in heart failure. The generic description of the intervention in Aragon is integrated care management of exacerbations, which aims at reducing adverse effects, improving the quality of life, optimizing resources during the recovery period and decreasing the number of hospitalizations and length of stays.

- Recruitment period:

The recruitment period will be continuous during the GATEKEEPER project.

- Follow-up period:

Until the objective defined by the healthcare specialist is reached (approx. 2 -4 weeks)

- Time Horizon for Analysis:

2 years

- Number of participants:

10 chronic patients 65+ suffering and exacerbation and health and social care professionals.

- Randomization procedure:

Participants will be randomly posed at each group through a random assignment procedure (dice, coin or similar).

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

Control (N=5), intervention (N=5)

- Outcomes:

Primary outcomes: Reduce number of hospitalisation, length of stays

Secondary outcomes: Increase QoL

- KPIs

Users satisfaction (Measured with a questionnaire)

Sustainability (Measured with an analysis of service(s))

Reduce number of hospitalisations (Measured in interventions that might have required traditional hospitalisations)

Reduce length of stays (Measured in early discharges thanks to intervention)

Increase QoL (Measured with a questionnaire)

- **List of information to be collected:**
  - Low complexity patients information +
  - Heart Rate
  - Blood Pressure
  - Oxygen Saturation
  - Respiratory Rate
  - Weight.
  - Body Temperature
  - Dyspnoea
  - ECG
  - Other (Systemic vascular resistance, Sweat level, FEV – Forced Expiratory Volume, Peak Expiratory Flow, Glucose)

3.1.2.4 USE CASE 7

3.1.2.4.1 Use case 7: Mid complexity

- Experimental Design: Between, Within, Mixed

A between subject design with an intervention and control group

- Technology adopted/used:

Monitoring devices

Patient app

Collection of Vital Signs

Telemonitoring platform

Data federation Engine

Big Data Analytics

Professional Dashboard

HF and COPD predictive models

- Intervention details:

The intervention will focus on: Predicting exacerbations in Multi-chronic elderly patient management including polymedication. The generic description of the intervention in

Aragon is enhanced integrated care, which includes Integrated care management of people with chronic diseases for an early detection of the appearance of exacerbations

- Recruitment period:

  The recruitment period will be continuous during the GATEKEEPER project

- Follow-up period:

6 months

- Time Horizon for Analysis:

2 years

- Number of participants:

70 including: Chronic patients 65+ and health and social care professionals.

- Randomization procedure:

Participants will be randomly posed at each group through a random assignment procedure (dice, coin or similar).

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

Control (N=35), Intervention 1 (N=35)

- Outcomes:

Primary outcomes: early detection of symptoms of exacerbations, reduce activity in healthcare centres, avoid hospitalizations and decrease length of stays.

Secondary outcomes: Increase quality of life and satisfaction of users.

- KPIs

Users satisfaction (Measured with a questionnaire)

Sustainability (Measured with an analysis of service(s))

Prevent the appearance of exacerbations (Measured with the number of alarms that generate a consultation)

Decrease number of consultations (Measured with the number of consultations performed by other agents (social/relatives) as a result of transfer of competences, and the destiny of an alarm)

Increase quality of life (Measured with a questionnaire such as E5Qd)

- **List of information to be collected:**
  - Low complexity patients information +
  - Heart Rate
  - Blood Pressure
  - Oxygen Saturation
  - Respiratory Rate
  - Weight.
  - Body Temperature
  - Dyspnoea
  - ECG
  - Other (Systemic vascular resistance, Sweat level, FEV – Forced Expiratory Volume, Peak Expiratory Flow, Glucose)

3.1.2.4.2 Use case 7: High complexity

- Experimental Design: Between, Within, Mixed

a between subject design with an intervention and control group

- Technology adopted/used:

Monitoring devices

Patient app

Collection of PROMS

Collection of Vital Signs

Telemonitoring platform

Data federation Engine

Big Data Analytics

Professional Dashboard

HF and COPD predictive models

- Intervention details:

The intervention will focus on: Multi-chronic elderly patient management including polymedication. The generic description of the intervention in Aragon is integrated care management of exacerbations, which aims at reducing adverse effects, improving the quality of life, optimizing resources during the recovery period and decreasing the number of hospitalizations and length of stays.

- Recruitment period:

The recruitment period will be continuous during the GATEKEEPER project.

- Follow-up period:

until stabilization objective defined by the healthcare specialist is reached (aprox 2 -4 weeks)

- Time Horizon for Analysis:

2 years

- Number of participants:

10 including chronic patients 65+ suffering and exacerbation and health and social care professionals.

- Randomization procedure:

Participants will be randomly allocated to the intervention or control group (dice, coin or similar).

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

Control (N=5), intervention (N=5)

- Outcomes:

Primary outcomes: Reduce number of hospitalisation, length of stays

Secondary outcomes: Increase quality of life

- KPIs

Users satisfaction (Measured with a questionnaire)

Sustainability (Measured with an analysis of service(s))

Reduce number of hospitalisations (Measured in interventions that might have required traditional hospitalisations)

Reduce length of stays (Measured in early discharges thanks to intervention)

Increase quality of life (Measured with a questionnaire such as E5Qd)

- **List of information to be collected:**
  - Low complexity patients information +
  - Heart Rate
  - Blood Pressure
  - Oxygen Saturation
  - Respiratory Rate
  - Weight.
  - Body Temperature
  - Dyspnoea
  - ECG
  - Other (Systemic vascular resistance, Sweat level, FEV – Forced Expiratory Volume, Peak Expiratory Flow, Glucose)

3.1.3 Saxony

3.1.3.1 USE CASE 1

- Experimental Design: Between, Within, Mixed

Cross section design and if agreed within usage design (pre and post questionnaire in the app)

- Technology adopted/used:

Available from Saxony site: Telemedical tools "TeleNePs" (DgApp, CompanionApp, Online Writing Therapy) and Coach PTBS.

Samsung technology suggestions: Overall needed technologies include smartwatch, smartphone, web-based platform, secure storage.

- Intervention details:

UC-1-A: Prevention of mental health disorders:

Information and psychoeducation

Lifestyle-related exercises for well-being

Additional: for COVID-19 pandemic related burden

Increase socialization and building of networks (e.g., local senior counselling networks)

UC-1-B:

Screening and early detection of mental health symptoms

Assessment via screening questionnaires

Assessment-driven psychoeducation and suggestions for self-management

Helping networks

- Recruitment period:

November/December 2020 - May 2022

- Follow-up period:

If agreed six to eight weeks

- Time Horizon for Analysis:

June 2022-December 2022

- Number of participants:

Up to 10,000.

- Randomization procedure:

No Randomization procedure will be applied.

- Groups: Intervention 1 (N=XX)

No control group, if agreed pre-post usage within design

Mild intervention complexity will involve 1 predefined use case (up to 10.000 participants).

- Outcomes:

Detect and track mental health symptoms, improve self-management for prevention or better daily coping, facilitate mental healthcare use, enhance daily activity and social participation.

- KPIs:

MAFEIP

Validated questionnaires

UC-1-A: Demographic data, age, basic health parameters (weight, height), temperature, blood pressure, heart rate, medication, allergy

UC-1-B: Mental health symptoms

- EFB (short screening questionnaire with demographics and PHQ4, PC-PCL5, and addiction questions)
- GPS (International questionnaire on PTSD) + special questions on COVID-19 burden
- ITQ (Complex PTSD)
- LEC-5 (List of traumatic events)
- PCL-5 (PTSD)
- PHQ-D (Depression, anxiety and somatization)
- RS-13 (Resilience)
- MoCA (Montreal cognitive assessment)
- QMCI (Quick Mind Cognitive Impairment - Italy) or MMST (Hogrefe)

Usability and applicability

PROMs in the beginning/end of the pilot (for users)

Clinical Benefits (Hospital admissions and health deteriorations)

Societal Aspects (technology acceptance, cultural discomfort, patient empowerment, mental health literacy)

Advances in clinical practice/effectiveness and user satisfaction

Certification as medical devices for prevention and detection, and accompanying treatments

Prescriptions

3.1.3.2 USE CASE 2

- Experimental Design: Between, Within, Mixed

Mixed Design (Within and Between) within: pre and post usage. Between: with and without collaboration with practitioners

- Technology adopted/used:

Available from Saxony site: Telemedical tools "TeleNePs" (DgApp, CompanionApp, Online Writing Therapy) and Coach PTBS.

Samsung technology suggestions: Overall needed technologies include smartwatch, smartphone, web-based platform, secure storage and possibilities of ActiveAge.

- Intervention details:

UC-2: Neurophysiological assessment and self-management interventions

- Ecological Momentary Assessment (EMA)
- Assessment-driven psychoeducation and suggestions for self-management
- Measurement of physiological parameters, e.g., heart rate
- Exercises with biofeedback
- Sleep patterns for sleep improvement
- Measurement data exchange with health care providers in one group
- Additional: for COVID-19 pandemic related burden

- Recruitment period:

November/December 2020/- May 2022

- Follow-up period:

Six to eight weeks

- Time Horizon for Analysis:

June 2022-December 2022

- Number of participants:

Up to 200.

- Randomization procedure:

Participants will be randomly allocated through an assignment procedure (randomcode or similar)

- Groups: Intervention supervised by practitioner (N=100) Intervention non supervised (N=100),

Moderate intervention complexity will involve the use case from previous level, as well as two predefined use cases (up to 200 participants will be included together with UC3)

- Outcomes:

Detect and track mental health symptoms, improve self-management for prevention or better daily coping, facilitate mental healthcare use, enhance daily activity and social participation, create a safe environment, enable secure contact and sharing between users and healthcare providers, secure data management within the healthcare network and the helping alliance.

- KPIs:

Cost-effectiveness

Validated questionnaires

- Demographic data and medication
- Physiological measures (heart rate, blood pressure)
- Sleep patterns
- Quality of life
    - Global Assessment of Functioning (GAF)
    - EQ-5D or SF-36 or SF-8 or SF-12 or SF-6D (to be determined)
- Level of irritability and mental health symptoms
        - PHQ-15, LEC-5, PCL-5, BDI II, FDS-20, BSI-18, HAQ, RS-13, SWE.
- Social support

The Multidimensional of Perceived Social Support

Usability and applicability

PROMs in the beginning/end of the pilot (for users)

RCT – intervention (practitioner supervised group) compared to intervention non supervised group

Clinical Benefits (Hospital admissions and health deteriorations)

Societal Aspects (technology acceptance, cultural discomfort, patient empowerment, mental health literacy)

Advances in clinical practice/effectiveness and user satisfaction

Certification as medical devices for prevention and detection, and accompanying treatments

Prescriptions

3.1.3.3 USE CASE 3

- Experimental Design: Between, Within, Mixed

Mixed Design (Within and Between) within: pre and post usage. Between: Between with and without supervision of practitioners

- Technology adopted/used:

Available from Saxony site: Telemedical tools "TeleNePs" (DgApp, CompanionApp, Online Writing Therapy) and Coach PTBS.

Samsung technology suggestions: Overall needed technologies include smartwatch, smartphone, web-based platform, secure storage, movement/fall sensors

- Intervention details:

UC-3: Inactivity and mobility detection

Relief dissociative states: Stimulation in multiple ways, in order to reduce habituation to the same stimuli

Personal diary for symptoms tracking (dissociation and mild cognitive impairment)

Increase activity to improve mood

Personalized symptoms constellation for more effective and personalized health care

Measurement data exchange with health care providers

- Recruitment period:

November/December 2020 - May 2022

- Follow-up period:

Six to eight weeks

- Time Horizon for Analysis:

June 2022-December 2022

- Number of participants:

up to 200

- Randomization procedure:

Participants will be randomly allocated through an assignment procedure (randomcode or similar)

Groups: Intervention supervised by practitioner (N=100) Intervention non supervised (N=100),

Moderate intervention complexity will involve the use case from previous level, as well as three predefined use cases (up to 200 participants will be included together with UC2)

- Outcomes:

Detect and track mental health symptoms, improve self-management for prevention or better daily coping, facilitate mental healthcare use, enhance daily activity and social participation, , create a safe environment, enable secure contact and sharing between users and healthcare providers, secure data management within the healthcare network and the helping alliance.

- KPIs:

Cost-effectiveness

Validated questionnaires

Usability and applicability

PROMs in the beginning/end of the pilot (for users)

RCT – intervention compared to control groups

Clinical Benefits (Hospital admissions and health deteriorations)

Societal Aspects (technology acceptance, cultural discomfort, patient empowerment, mental health literacy)

Advances in clinical practice/effectiveness and user satisfaction

Certification as medical devices for prevention and detection, and accompanying treatments

Prescriptions

3.1.3.4 USE CASE 4

- Experimental Design: Between, Within, Mixed

Between as RCT

- Technology adopted/used:

Available from Saxony site: Telemedical tools "TeleNePs" (DgApp, CompanionApp, Online Writing Therapy) and Coach PTBS.

Samsung technology suggestions: Overall needed technologies include smartwatch, smartphone, web-based platform, secure storage, movement/fall sensors and eventually home sensors/and devices.

- Intervention details:

UC-4: Fall detection

Due to dissociation, neurological or other physical conditions

Emergency contacts to be notified in order to get immediate help and prevent further injury

Differential diagnosis of falls

- Recruitment period:

November/December 2020- May 2022

- Follow-up period:

Six to eight weeks

- Time Horizon for Analysis:

June 2022-December 2022

- Number of participants:

Up to 100

- Randomization procedure:

Stratified subgroups are created (subgroups based on gender and age range) within which randomization will be performed through an assignment procedure (e.g. randomcodes). Treatment groups are comparable in terms of these factors

- Groups: Control (N=50), Intervention (N=50).

High intervention complexity will involve the four use cases from previous levels, as well as three predefined use cases (up to 100 participants. Controls: 50, Intervention: 50, will be included together with UC5).

- Outcomes:

Detect and track mental health symptoms, improve self-management for prevention or better daily coping, facilitate mental healthcare use, enhance daily activity and social participation, create a safe environment, enable secure contact and sharing between users and healthcare providers, secure data management within the healthcare network and the helping alliance.

- KPIs:

MAFEIP

Validated questionnaires

- Demographic data and medication
- Level of irritability and mental health symptoms questionnaires (see level above)
- DERS (Difficulties and emotional relation Scale), BriefCOPE, PANAS (Positive and negative affective schedule)

Usability and applicability

PROMs in the beginning/end of the pilot (for users)

RCT – intervention compared to control groups

Clinical Benefits (Hospital admissions and health deteriorations)

Societal Aspects (technology acceptance, cultural discomfort, patient empowerment, mental health literacy)

Advances in clinical practice/effectiveness and user satisfaction

Certification as medical devices for prevention and detection, and accompanying treatments

Prescriptions

3.1.3.5 USE CASE 5

- Experimental Design: Between, Within, Mixed

as UC-4 between as RCT

- Technology adopted/used:

Available from Saxony site: Telemedical tools "TeleNePs" (DgApp, CompanionApp, Online Writing Therapy) and Coach PTBS.

Samsung technology suggestions: Overall needed technologies include smartwatch, smartphone, web-based platform, secure storage, movement/fall sensors, home sensors/and devices.

- Intervention details:

UC-5-A: Violence reporting

Mid-, and long-term assessment and reporting of experienced violence

Additional: for COVID-19 pandemic related burden

UC-5-B: Activation of personal emergency network in case of violence

Emergency or immediate reporting

Geo-detection

Notification of trusted persons

Additional: for COVID-19 pandemic related burden

- Recruitment period:

November/December 2020 - May 2022

- Follow-up period:

Six to eight weeks

- Time Horizon for Analysis:

June 2022-December 2022

- Number of participants

Up to 100

- Randomization procedure:

Stratified subgroups are created (subgroups based on gender and age range) within which randomization will be performed through an assignment procedure (e.g. randomcodes). Treatment groups are comparable in terms of these factors.

- Groups: Control (N=50), Intervention (N=50).

High intervention complexity will involve the four use cases from previous levels, as well as three predefined use cases (up to 100 participants. Controls: 50, Intervention: 50, will be included together with UC4).

- Outcomes:

Detect and track mental health symptoms, improve self-management for prevention or better daily coping, facilitate mental healthcare use, enhance daily activity and social participation, detect signs of violence and prevent violence, create a safe environment, enable secure contact and sharing between users and healthcare providers, secure data management within the heartcare network and the helping alliance.

- KPIs:

MAFEIP

Validated questionnaires

UC-5-A: Violence reporting:

- Violence screening
  - Childhood Trauma Screener (CTS), and Conflict Tactics Scale (CTS2S). The frequency of usage will be decided by the user
- Falls detection: diagnosis of falls

Physiological measures: heart rate, blood pressure

Usability and applicability

PROMs in the beginning/end of the pilot (for users)

RCT – intervention compared to control groups

Clinical Benefits (Hospital admissions and health deteriorations)

Societal Aspects (technology acceptance, cultural discomfort, patient empowerment, mental health literacy)

Advances in clinical practice/effectiveness and user satisfaction

Certification as medical devices for prevention and detection, and accompanying treatments

Prescriptions

3.1.3.6 USE CASE 6

- Experimental Design: Between, Within, Mixed

Cross section design

- Technology adopted/used:

Available from Saxony site: Telemedical tools "TeleNePs" (DgApp, CompanionApp, Online Writing Therapy) and Coach PTBS.

Samsung technology suggestions: Overall needed technologies include smartwatch, smartphone, web-based platform, secure storage, movement/fall sensors, home sensors/and devices. As an option, and machine learning and linguistic features in the detection of possible mental health disorders with possible involvement of voice signal processing (audio recordings), or without voice signal processing (typed input) in assessment of mild cognitive impairment, depression and stress.

Structured interviews or scripts for text and language recognition e.g. Adult Attachment Projective Picture System (AAP) or self registered texts or texts for diagnosing mild cognitive impairment

- Intervention details:

UC-6: (optional) Machine learning and linguistic features in the detection of possible mental health disorders

- Health-Voice-on Device: Automatic Speech Recognition (ASR) and Natural Language Processing (NLP)
- Addressing German Language
- Audio recordings and typed input in assessment of mild cognitive impairment, depression and stress
- In cooperation with Samsung

- Recruitment period:

January 2021 - May 2022

- Follow-up period:

None

- Time Horizon for Analysis:

June 2022-December 2022

- Number of participants:

up to 100

- Randomization procedure:

No randomisation will be applied.

- Groups: needs to be discussed with Samsung depending on the targeted topic (depression, stress, mild cognitive impairment)

High intervention complexity will involve the four use cases from previous levels, as well as three predefined use cases (up to 100 participants. Controls: 50, Intervention: 50.

- Outcomes:

Detect and track mental health symptoms, enable secure contact and sharing between users and healthcare providers, secure data management within the healthcare network and the helping alliance.

- KPIs:

Cost-effectiveness

Validated questionnaires

Usability and applicability

Advances in clinical practice/effectiveness and user satisfaction

Certification as medical devices for prevention and detection, and accompanying treatments

Prescriptions

Further specified together with Samsung

3.1.4 Greece

3.1.4.1 USE CASE 1

- Experimental Design: Between, Within, Mixed

Between subject design

- Technology Adopted:

Per healthcare professional (clinician / nutritionist / nurse): Management Platform

Per patient in Intervention Group 1: Lifestyle app

Per patient in Intervention Group 2: Smart tracker, Weight scale, Lifestyle app (mobile device)

- Intervention details:

The intervention will focus on: **Lifestyle-related early detection and interventions – Risk Level #1.** Big Data Analytics techniques will be exploited to address risk stratification and early detection, based on lifestyles analysis including: pattern recognition for the improvement of public health surveillance and for the early detection of cognitive decline and frailty; data mining for inductive reasoning and exploratory data analysis; Cluster Analysis for identifying high-risk groups among elder citizens. In the above cases timely intervention is provided by through AI-based, digital coaches developed e.g. on top of Samsung AI assistant, Bixby through Natural Language Processing techniques, based structured conversations, consultation and education. The main target group (N=1000) is the ageing population with risk factors of metabolic syndrome.

Health promotion is the cornerstone of RUC1. Therefore, all sites aim at avoiding, delaying, or preventing the appearance or worsening of chronic conditions that would impact the citizen's functionality and quality of life. It is planned to measure a set of clinical outcomes which would be preserved or improved by the intervention (e.g. waist circumference, fasting glucose, or blood pressure) as well as general measure of quality of life. The intervention will take 3 months in total and there will be no follow-up measurement.

- Recruitment period:

First subject in: November 2020 (M14)

Last subject in: May 2022 (M32)

Last subject out: August 2022 (M35)

- Follow-up period:

The intervention will last 3 months. There will be no follow-up measurement in the deliverable.

- Time Horizon for Analysis:

We expect that the intervention will have an effect for around 1 year.

- Number of participants:

The total number of participants is N=1000.

Healthcare professionals: N=40

Control group: N=320

Intervention group 1: N=320

Intervention group 2: N= 320

- Randomization procedure:

Cluster-randomization will be used to allocate participants to "intervention" and "control" groups, using municipalities as the cluster unit. Therefore, the target end-users living within the same municipality will be automatically allocated to the intervention or control group. The end-users will be allocated at a 70:30 ratio between Attica region (site partner: Harokopio University) and Central Greece (site partner: Digital Cities of Central Greece and its subcontractor University of Thessaly).

- Groups: Control (N=320), Intervention 1 (N=320), Intervention 2 (N=320).
- Primary outcome

Change in waist circumference (in cm).

- Secondary outcomes
  - Changes in body mass index (BMI), %body fat
  - Patient-reported outcome measures (PROMs)
  - Physical activity increase and sedentary time decrease
  - Sleep duration
- KPIs

Clinical KPIs:

Waist circumference reduction

Reduction of BMI, % body fat

Proper sleep duration

Physical activity increase and sedentary time decrease

Vital signs' values improvement

Risk assessment of diabetes: FPG <126 mg/dl (7.0 mmol/l), 2-h PG < 200 mg/dl (11.1 mmol/l)

Better quality of life

Societal KPIs

- Technology acceptance
- Patient empowerment
- User satisfaction
- Return on Investment
- Monthly/Annual health care costs: inpatient, outpatient, emergency room, pharmaceutical costs
- Adoption Potential:
- Integrability with current infrastructure

- Compatibility with clinical workflows/protocols
- Usability issues

3.1.4.2 USE CASE 3

- Experimental Design: Between, Within, Mixed

Between (randomized trial, in which patients enrolled in an intervention trial receive the non-obtrusive physiological signal monitoring via short-term prediction of glucose concentration for the prospective 2nd phase of the trial, since the 1st phase includes a retrospective AI algorithm development and validation).

Control group of the prospective study receives standard care, via follow up from the outpatient department.

- Technology Adopted:
  - Diabetes technology – Real-Time Continuous Glucose Monitoring (RT-CGM)
  - Non-obtrusive physiological signal monitoring
  - Short-term prediction of glucose concentration in the interstitial fluid (UOI)
  - Diabetes management platform (CERTH)
  - Localised nutrition database
- Intervention details:

The Use Case 3 in Central Greece will develop and provide services for individuals with type 2 diabetes over the age of 65 years belonging in Groups 2 and 3 according to the "Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline – 2019" (Table 2).

The inclusion and exclusion criteria will also be included in the D6.4. Clinical study and CRF [Report]–v1.

Target number is 195 volunteer patients recruited (80 in the retrospective study and 75 in intervention group of the prospective study and 40 in the control group: 2-1 randomisation).

Table 2 Conceptual Framework for Considering Overall Health and Patient Values in Determining Clinical Targets in Adults Aged 65 years and Older

Overall Health Category		Group 1: Good Health	Group 2: Intermediate Health	Group 3: Poor Health
Patient characteristics		No comorbidities **or** 1-2 non-diabetes chronic illnesses* **and** No ADL[ε] impairments and ≤1 IADL impairment	3 or more non-diabetes chronic illnesses* **and/or** Any one of the following: mild cognitive impairment or early dementia; ≥2 IADL impairments	Any **one** of the following: End-stage medical condition(s)**; Moderate to severe dementia; ≥2 ADL impairments; Residence in a long-term nursing facility
		Reasonable glucose target ranges and HbA1c by group		
		Shared decision-making: individualized goal may be lower or higher		
Use of drugs that may cause hypoglycemia (e.g., insulin, sulfonylurea, glinides)	No	Fasting: 90-130 mg/dL Bedtime: 90-150 mg/dL <7.5%	Fasting: 90-150 mg/dL Bedtime: 100-180 mg/dL <8%	Fasting: 100-180 mg/dL Bedtime: 110-200 mg/dL <8.5%[¥]
	Yes[ε]	Fasting: 90-150 mg/dL Bedtime: 100-180 mg/dL ≥7.0 and <7.5%	Fasting: 100-150 mg/dL Bedtime: 150-180 mg/dL ≥7.5 and <8.0%	Fasting: 100-180 mg/dL Bedtime: 150-250 mg/dL ≥8.0 and <8.5%[¥]

Note: While glucose targets are highlighted for each group in this framework, overall health categories can also be considered for other treatment goals such as blood pressure and dyslipidemia. See Appendix A on "How to use the conceptual framework."

* Coexisting chronic illnesses may include osteoarthritis, hypertension, chronic kidney disease stages 1-3, or stroke, among others.

**One or more chronic illnesses with limited treatments and reduced life expectancy. These include metastatic cancer, oxygen-dependent lung disease, end-stage kidney disease requiring dialysis, and advanced heart failure.

[ε] As long as achievable without clinically significant hypoglycemia; otherwise, higher glucose targets may be appropriate. Note also that the lower HbA1c boundary was included as data suggesting increased hypoglycemia and mortality risk at lower HbA1c levels are strongest in the setting of insulin use. However, the lower boundary should not reduce vigilance for detailed hypoglycemia assessment.

[¥] HbA1c of 8.5% correlates with an average glucose level of approximately 200 mg/dL. Higher targets than this may result in glycosuria, dehydration, hyperglycemic crisis and poor wound healing.

[ε] ADLs include bathing, dressing, eating, toileting, and transferring, and IADLs include preparing meals, shopping, managing money, using the telephone, and managing medications.

Includes data from Cigolle CT, Kabeto MU, Lee PG, Blaum CS. Clinical complexity and mortality in middle-aged and older adults with diabetes. J Gerontol A Biol Sci Med Sci 2012; 67(12):1313-1320 (39); and from Kirkman MS, Jones Briscoe V, Clark N, et al. Diabetes in older adults. Diabetes Care 2012; 35(12): 2650-2664 (40).

Abbreviations: IADL, instrumental activity of daily living; ADL, activity of daily living; SU, sulfonylurea.

The intervention will focus on: **Diabetes: predictive modelling of glycaemic status – Risk Level #2.** Short-term prediction of glycaemic dynamics is essential to improve diabetes self-management. GATEKEEPER will provide a personalized, adaptive, real-time data driven computational solution based on data federation in the Healthcare Space, identifying the different modes of the underlying glucose metabolism and, eventually, the prevention of hypoglycaemic events. Advanced GK "things" will collect clinical data at

home such as bio- and physiological signals (i.e. blood glucose concentration data or continuous glucose monitoring data, physical activity, galvanic skin response, heart rate variability), whose input-output dynamics with respect to the short-term prediction of the interstitial glucose concentration will be represented via an adaptive machine-learning-based regression model[2,3,4,5]. The main target group (N=195) is elderly diabetes patients with comorbidities. More specifically, individuals with type 2 diabetes over the age of 65 years belonging in Groups 2 and 3 according to the "Treatment of Diabetes in Older Adults: An Endocrine Society* Clinical Practice Guideline – 2019".

The system will focus on monitoring patients' adherence to medical treatment as well as their physiological and environmental variables and it will provide a personalised guidance platform for the users. Finally, alarms and early detection signs will be assessed by professionals. The intervention will take 28 days per patient, in monthly batches of about 10 patients.

- Recruitment period:

A. Retrospective study (80 patients):

M14 (Nov 2020) to M22 (Jul 2021) in monthly batches

M23 (Aug 2021) to M25 (Oct 2021) ML model fine tuning and validation

Retrospective Phase											
Experiment Running									ML Model Fine-Tuning & Validation		
M14	M15	M16	M17	M18	M19	M20	M21	M22	M23	M24	M25
Nov-20	Dec-20	Jan-21	Feb-21	Mar-21	Apr-21	May-21	Jun-21	Jul-21	Aug-21	Sep-21	Oct-21
Batch 1	Batch 2	Batch 3	Batch 4	Batch 5	Batch 6	Batch 7	Batch 8	Spare	–	–	–

B. Prospective study (75 in intervention group of the prospective study and 40 in the control group: 2-1 randomisation)

M26 (Nov 2021) to M36 (Sep 2022) in monthly batches

[2] Georga, E. I., Príncipe, J. C., & Fotiadis, D. I. (2019). Short-term prediction of glucose in type 1 diabetes using kernel adaptive filters. *Medical & biological engineering & computing*, *57*(1), 27-46.

[3] Georga, E. I., Principe, J. C., Polyzos, D., & Fotiadis, D. I. (2016, August). Non-linear dynamic modeling of glucose in type 1 diabetes with kernel adaptive filters. In *2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* (pp. 5897-5900). IEEE.

[4] Georga, E. I., Protopappas, V. C., Ardigò, D., Marina, M., Zavaroni, I., Polyzos, D., & Fotiadis, D. I. (2012). Multivariate prediction of subcutaneous glucose concentration in type 1 diabetes patients based on support vector regression. *IEEE journal of biomedical and health informatics*, *17*(1), 71-81.

[5] Georga, E. I., Protopappas, V. C., Polyzos, D., & Fotiadis, D. I. (2015). Evaluation of short-term predictors of glucose concentration in type 1 diabetes combining feature ranking with regression models. *Medical & biological engineering & computing*, *53*(12), 1305-1318.

Prospective Phase										
Experiment Running										
M26	M27	M28	M29	M30	M31	M32	M33	M34	M35	M36
Nov-21	Dec-21	Jan-22	Feb-22	Mar-22	Apr-22	May-22	Jun-22	Jul-22	Aug-22	Sep-22
Batch 1	Batch 2	Batch 3	Batch 4	Batch 5	Batch 6	Batch 7	Batch 8	Spare	–	Spare

The recruitment will take place at the Regional University Hospital of Larisa, in Thessaly, Central Greece http://www.uhl.gr/uhlen/index.html

- Follow-up period:

28 days per patient

- Time Horizon for Analysis:

Retrospective Study: M23 (Aug 2021) to M25 (Oct 2021) ML model fine tuning and validation

Prospective Study: M37 (Oct 2022) – M39 (Dec 2022)

- Number of participants:

In total 155 participants will participate, 80 in the retrospective study and 75 in the prospective study.

- Randomization procedure:

Target number is 195 volunteer patients recruited (80 in the retrospective study and 75 in intervention group of the prospective study and 40 in the control group: 2-1 randomisation)

Randomisation will be performed following standard procedures (PC based generation of random integer sequences and allocation based on the alphabetical order of coded initials). Randomisation will be performed separately by dedicated personnel not involved in trial conduct (statistical external consultant of the study). Allocation concealment will take place via opale envelopes.

- Groups:

Target number is 195 volunteer patients recruited (80 in the retrospective study, 75 in intervention group of the prospective study and 40 in the control group: 2-1 randomisation)

- Primary Outcome

Minimization of hypoglycaemic events

- Secondary Outcomes

Glycaemic control

Health Related Quality of Life (measured via Patient-reported outcome measures - PROMs)

- KPIs

Clinical KPIs:

- Minimisation of hypoglycaemic events – Questionnaire based on Reference: Seaquist, E. R., Anderson, J., Childs, B., Cryer, P., Dagogo-Jack, S., Fish, L., …

Vigersky, R. (2013). Hypoglycemia and diabetes: A report of a workgroup of the American diabetes association and the endocrine society. *Diabetes Care*, 36(5), 1384–1395. http://doi.org/10.2337/dc12-2480

- Glycaemic control (Time in Range)

PROMs KPIs

- **EQ5D** (Generic HRQL)
- Problem Areas in Diabetes scale - **PAID** (Disease specific HRQL)
- **HSF-II** (Hypoglycaemia Fear Survey-II)
- Glucose Monitoring System Satisfaction Survey (**GMSS**).

Return on investment:

The Health Technology Assessment of the UC services , will take place based on MAFEIP tools. The ICER and QALYs will be calculated[6], based on the outcomes of the prospective study phase.

[6] Wan, W., Skandari, M. R., Minc, A., Nathan, A. G., Winn, A., Zarei, P., … Huang, E. S. (2018). Cost-effectiveness of continuous glucose monitoring for adults with type 1 diabetes compared with self-monitoring of blood glucose: The DIAMOND randomized trial. *Diabetes Care*, *41*(6), 1227–1234. http://doi.org/10.2337/dc17-1821)

3.1.5 Puglia

The Puglia Pilot Medical Use Cases that will be experimented in WP7 are described in detail in deliverable D6.1 (*Medical use cases specification and implementation guide*). They can be summarized as follows:

- Medical Use Case "Low Complexity": it targets elderly citizens who are healthy but at risk of health decay, due to conditions typical of aging such as frailty and Mild Cognitive Impairment (MCI). The main objective of this Medical Use Case is to assess the cost-effectiveness of early detection and intervention technologies when used to prevent the transition of such subjects to higher health risk classes. In particular, the case focusses on lifestyle related monitoring and intervention, based on the usage of (i) unobtrusive Key Enabling Technologies (KETs) for detecting unhealthy behaviours and the onset of potential health decays, and (ii) one-way message delivery for e-coaching and self-empowerment. With respect to DoA, this case covers Reference Use Case #1.
- Medical Use Case "Moderate Complexity": it targets elderly citizens affected by chronic conditions and enrolled in the Puglia Region's Chronic Care Model (named "Care Puglia"). The main objective of this Medical Use Case is similar to the previous one (assess the cost-effectiveness of early detection and intervention technologies) but when technology is applied to managing chronic patients, including multimorbid ones. With respect to DoA, this case covers Reference Use Case #2 (COPD patients), Reference Use Case #3 (Type 2 Diabetes patients), Reference Use Case #5 (Heart Failure patients) and Reference Use Case #7 (multimorbid patients). In addition, it addresses patients affected by High Blood Pressure, an important condition addressed in the frame of the Care Puglia CCM, for which there is no specific Reference Use Case described in the DoA (although Reference Use Case #6, on stroke prevention, is close).

Before describing the experimental set-up of these Use Cases in details, a couple of introductory notes are necessary.

A first note regards the number of subjects to be involved in each Case.

According to the initial plan, reported in the DoA, 10,000 subjects are to be involved in the Low Complexity Use Case, while 500 subjects are to be involved in the Moderate Complexity Use Case. The lower number of participants in the second Case is due to the higher costs of equipping them with appropriate KETs.

On the other hand, further elaboration conducted by partners involved in the Puglia Pilot while drafting D6.1, led to the conclusion that – if possible – a better balancing of the total number of participants among the Low and Moderate Use Cases would be beneficial. In fact, this would lead to both (a) more statistical robustness for the Moderate Use Case and (b) better comparison among the results of the two Cases. For this reason, a shift in participants' numbers, as reported in the table below, has been proposed to try to achieve such balancing. On the other hand, since the possibility of implementing this shift strongly depends on the availability of a sufficient number of KETs instances to be deployed to participants, and since this element is still uncertain at the time of this writing, because discussions with KET providing partners are still ongoing, the proposal has to be considered as an ambition to aim to, while maintaining commitment to the numbers initially planned in the project's DoA (reported in the table's second column). A final decision will be made when discussions with KET providing partners, under the supervision from the Coordination team, will be concluded.

Table 3. Participants' numbers: DoA commitment and a more ambitious plan

Medical Use Case	Participant numbers: DoA committment	Participant numbers: Pilot ambition
Low Complexity	At least 10,000	At least 7,000
Moderate Complexity	At least 500	Up to 3,500
Total	10,500	10,500

A second introductory note regards the experimentation of predictive models, based on big data analytics and Artificial Intelligence (AI), addressed in task T6.3 (*Big data and data analytics strategies for early detection and intervention*). In deliverable D6.1, with respect to the Puglia Pilot case, the application of such models has been proposed for both Low Complexity and Moderate Complexity Use Cases. In particular:

- Low Complexity Use Case: possibility to detect robustness[7] decay in healthy elderly subjects (i.e. onset of frailty and/or MCI)
- Moderate Complexity Use Case: possibility of predicting adverse events and health risks linked to COPD, T2D, HF, HBP

Starting from next May 2021, when the new EU Medical Device Regulation (MDR, EU Regulation 2017/745[8]) will come into full force, such models will be generally considered as Class IIa medical devices (MDR's Classification Rule 11) and will need an appropriate certification[9] to be used in interventional studies. As the models investigated in the GATEKEEPER project are likely not to possess such certification, by implication they cannot be used in the experimental designs that will be implemented in the Puglia Pilot.

To address this issue, the Puglia Pilot team plans to implement a separate, observational study design, where the performance of the predictive models will be assessed on the datasets that will be collected from the interventional experiments, but without involving such models in the clinical pathway. Cost-effectiveness can still be reasonably estimated, according to approaches proposed in the frame of the MAFEIP users' community[10] (more details are provided in the relevant subsection below).

Given the above introductory remarks, the following subsections illustrate four different study designs that are planned for the Puglia Pilot, as follows:

[7] Intended as a progression towards frailty, as per Dapp, U., Minder, C.E., Anders, J. et al. Long-term prediction of changes in health status, frailty, nursing care and mortality in community-dwelling senior citizens - results from the longitudinal urban cohort ageing study (LUCAS). BMC Geriatr 14, 141 (2014). https://doi.org/10.1186/1471-2318-14-141

[8] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31993L0042:EN:HTML

[9] Or, at least, authorization to be used as investigational devices, as per MDR's article 15

[10] https://www.mafeip.eu/the-mafeip-community

- Experimental study design for the cost effectiveness assessment of the Moderate Complexity Medical Use Case
- Experimental study design for the cost effectiveness assessment of the Low Complexity Medical Use Case
- Observational study design for assessing the effectiveness of models predicting the influence of physical activity on health risk trajectories in T2D patients. This study is aimed at covering an example of management of hospitalized chronic patients and related follow up after discharge, in the frame of the Moderate Complexity Use Case
- A design template for observational studies aimed at assessing the effectiveness of models for the prediction of adverse events related to conditions addressed in Low Complexity (e.g. onset of pre-frailty, frailty, or MCI) and Moderate Complexity (exacerbations, decompensations, hypoglycaemic events, etc.) Use Cases. Since at the time of this writing the exact KETs that could be deployed to study participants - and, consequently, the variables that can be fed as input into the models - are not known and the models themselves are still under investigation in T6.3, only a template is provided for this case, which will be consequently instantiated when relevant information will become available.

3.1.5.1 Moderate Complexity Medical Use Case interventional experiment

- Rationale

In the frame of the overall objective of the GATEKEEPER project – which aims to facilitate the deployment of novel KETs to support active and heathy aging – the Puglia Pilot Moderate Complexity Use Case experiment aims to deploy a combination of patient monitoring, data analysis and e-coaching technologies for enacting a patient centred, early detection and intervention scheme, conducive to better management of elderly, chronic patients in the frame of Puglia's CCM "Care Puglia"
Literature, including reports produced in the context of Care Puglia[11], has shown that patient centred management schemes are effective in improving health outcomes, particularly by reducing acute events and consequent recourse to emergency care. On the other side, it has also been shown that achieving these advantages could imply the usage of additional healthcare resources since, although costs related to unplanned hospitalization are significantly reduced[11], other costs (planned hospitalizations, drugs, specialist visits) may increase because of the need to deploy multi-specialist pathways

[11] Robusto F, Bisceglia L, Petrarolo V, et al. The effects of the introduction of a chronic care model-based program on utilization of healthcare resources: the results of the Puglia care program. BMC Health Serv Res. 2018;18(1):377. Published 2018 May 25. doi:10.1186/s12913-018-3075-0

of care and more appropriate pharmacological therapies[11] and because of extra resource usage associated with prolonged life[12]

We expect that the deployment of the Puglia Pilot Moderate Complexity Medical Use Case intervention will generate a similar pattern, with concomitant improvement in patient outcomes and increased usage of healthcare resources, making it necessary to assess the cost-effectiveness of the intervention, in order to decide on its viability, following a Value Based HealthCare (VBHC) paradigm. This is the rationale to undertake this study.

- Experimental Design: Between, Within, Mixed

This study will use the same design applied by Robusto et al 2018[11], in a previous evaluation of the Puglia Care CCM, combining "within-subjects" and "between-subjects" approaches. In particular, (i) we will divide the study population into two arms, A and B, and (ii) we will divide the 24-month experiment duration into two consecutive 12-months periods. Arm A will use the GATEKEEPER solution in the second period. In this way, we will obtain (i) a within-subjects (before-after) approach by comparing the first (control) and second (intervention) periods in arm A; (ii) a between-subjects approach by comparing arm B (control) and A (intervention) in the second period.

The design is necessarily not blinded, as both patients and HCPs are aware of the usage of GATEKEEPER KETs

- Technology adopted/used:

Although, at the time of this writing, the exact number of devices that will be deployed to each participants is still not established, as it depends on ongoing work jointly conducted with KET providing partners and under the supervision of the project Coordination Team, the categories of devices to be used have been mostly determined, based on the Medical Use Case description reported in D6.1 and subsequent KET presentation webinars and discussions with KET providing partners (in particular, SAM, ENG, Medisanté, BB). They are reported in the table below, subdivided along the chronic conditions addressed in the Care Puglia CCM

Table 4. Technologies to be used for the Moderate Complexity Use Case

Disease	Early detection / intervention	Key Enabling Technologies
COPD	• Unobtrusive measurement of oxygen saturation	• Biobeat wrist device (if appropriate, depending the participant's comorbidity profile, since this device measures a large number of other parameters, beyond oxygen saturation) • Possible alternative: less expensive, market available, MDR certified oxygen saturation meter, e.g. in case COPD is the only morbidity (Note: this KET is not included in the current

[12] Lundqvist M, Alwin J, Henriksson M, Husberg M, Carlsson P, Ekdahl AW. Cost-effectiveness of comprehensive geriatric assessment at an ambulatory geriatric unit based on the AGe-FIT trial. BMC Geriatr. 2018;18(1):32. Published 2018 Jan 31. doi:10.1186/s12877-017-0703-1

		version of the GATEKEEPER KET catalogue and should be added)
T2D	• Flash measurement of glycemia	• A market available, MDR certified, Google Fit compatible meter for flash measurement of glycaemia (Note 1: this KET is not included in the current version of the GATEKEEPER KET catalogue and should be added; Note 2: Google Fit compatibility is necessary for integration with ENG's DMCoach solution, as per below)
	• Conventional measurement of glycaemia	• Medisanté BP800 3G, which combines blood pressure and glucose meters • Possible alternative: separate, less expensive, market available, MDR certified conventional glucometer and blood pressure meter, e.g. in case measurements (of glycaemia and blood pressure) are not needed at the same time, given the subject comorbidity profile (Note: these KETs are not included in the current version of the GATEKEEPER KET catalogue and should be added)
	• Type 2 Diabetes management solution	• ENG's DMCoach solution, including patient monitoring and promotion of healthy lifestyles; the solution requires the usage of a Google Fit compatible glucometer, as above mentioned, and the usage of the patient's own smartphone, to run the related app; the DMCoach HCP-facing UI will be adapted by ENG to integrate, with the support of the GATEKEEPER platform, data visualization related to other possible patient's comorbidities, based on other devices mentioned in this table (as long as they comply to standards-based GATEKEEPER rules).
HF	• Unobtrusive measurement of oxygen saturation • Unobtrusive measurement of HR/HRV	• Biobeat wrist device
	• Unobtrusive measurement of body weight and composition	• Medisanté BC800 3G (scale for measuring weight and body composition)
HBP	• Unobtrusive measurement of Blood Pressure/BP Variability	• Biobeat wrist device (if appropriate, depending the participant's comorbidity profile, since this device measures a large number of other parameters, beyond blood pressure)
	• Conventional measurement of Blood Pressure/BP Variability	• Medisanté BP800 3G, which combines blood pressure and glucose meters • Possible alternative: less expensive, market available, MDR certified blood pressure

		meter, e.g. if the Medisanté glucose meter is not needed at the same time
For all patients (CVD protection scheme)	• Unobtrusive measurement of physical activity • Unobtrusive measurement of sleep quality	• Samsung Gear Fit-e (Note: this device is not MDR certified; pending additional investigation with support from expert partners, this implies that, in principle, data detected with this device cannot be shown to HCPs and cannot be used for medical purposes)
	• Measurement of blood pressure	• Biobeat wrist device (if appropriate, depending the participant's comorbidity profile, since this device measures a large number of other parameters, beyond blood pressure) • Medisanté BP800 3G, which combines blood pressure and glucose meters (if appropriate, depending the participant's comorbidity profile, since this device also provides glycemic measurement which is needed only if the subject is affected by T2D) • Possible alternative: less expensive, market available, MDR certified blood pressure meter, if the full capabilities of the above mentioned devices are not warranted, given the patient comorbidity profile
	• Nutrition diaries collected through Samsung Bixby capsules • Validated geriatric or specific disease scales collected through Samsung Bixby capsules	• Samsung J6, Bixby compliant smartphone (Note: this device is not MDR certified; pending additional investigation with support from expert partners, this implies that, in principle, data detected with this device cannot be shown to HCPs and cannot be used for medical purposes)
For COPD, HF, HBP patients (data visualization for HCPs)	• Data visualization dashboard for Care Puglia GPs, Care Managers and Specialists	• T5.5 Authoring tool, to design data-model based visualization layers and UIs (Note: this technology is to be used for those patients whose comorbidity profile does not include T2D, since for the latter case the DMCoach data visualization layer will be extended as needed, as previously mentioned)

- Intervention details:

The intervention for the Moderate Complexity Medical Use Case consists of the prescription of unobtrusive early detection and intervention technologies to patients enrolled in the Care Puglia programme (see also details in deliverable D6.2, *Early detection and interventions operational planning*). In particular:

Patients will be prescribed by their GPs an unobtrusive remote monitoring equipment, depending on their diseases and comorbidity profiles (COPD, T2D, HF, HBP) as illustrated in the previous item. In general, comorbid patients will be possibly given the union of KETs needed for each of their conditions. However, as discussed in the introductory notes, this must be balanced against the actual availability of KETs and related budget limits

HCPs will be given a dashboard to visualize, analyse and interpret data collected by the above equipment, as also illustrated under the previous item. Through such dashboard, Care Puglia GPs, Care Managers and Specialists will be able to monitor relevant clinical measurements longitudinally and continuously, in addition to the measurements which are currently obtained during scheduled Care Puglia visits (usually, with 4-6 months periodicity). This is expected to improve the assessment of the individual status of each patient and lead to better adjustment of Individual Care Plans

T2D patients will also be provided with the DMCoach self-empowerment support, oversighted by HCPs. This is expected to improve the way these patients will manage their condition

- Recruitment period:

Current planning envisions:

  - Start of recruitment in October 2020
  - End of recruitment accrual in December 2021
  - End of first period and start of second period for the before-after (within-subjects) study in December 2021
  - End of second period and end of experiment in December 2022

It has to be noted that the above planning is to be considered as provisional at the time of this writing, since some uncertainties have still to be accounted for, such as the evolution of the Covid-19 crisis in autumn and the potential related impact on Ethics Approval and recruitment process timing

- Follow-up period:

See previous item and item on experimental design above: the overall follow up period will by 24 months, subdivided into two consecutive periods of 12 months each, to implement both a before-after (within-subjects) and a between-subjects approach

- Time Horizon for Analysis:

The MAFEIP analysis will be conducted with respect to two different time horizons:

For the primary outcome, a time horizon sufficient for convergence (due to the absorbing state "dead") will be selected (several tens of years)

In order to separately assess the effects of potentially reduced recourse to emergency care (an exploratory objective, see relevant item below), a shorter time horizon (3 years) will also be examined

- Target population:

65+ patients enrolled in the Care Puglia CCM, with a DDCI risk score under a predetermined threshold (to be defined at the time of this writing, as previously mentioned; this is needed to ensure that all patients in the MAFEIP analysis start from the baseline state)

- Number of participants:

A number of participants between 500 and 3,500 will be selected, according to the availability of devices deployable for this Medical Use Case (see introductory notes)

- Randomization procedure:

Perfect randomization (both in the selection of participants and in subsequent assignment to study arms) would be difficult to achieve, and some forms of volunteer or convenience sampling will be necessarily applied (e.g. patients selected by cooperative GPs, patients responding to communication in the media, etc.). To reduce risks of bias, quota sampling will be applied, i.e. choosing patients with predefined comorbidity profiles and other characteristics, in line with the proportions in the target population (i.e. the population of chronic patients enrolled in the Care Puglia programme).

Some types of bias (e.g. consenting participants differing from non-consenting ones) seems to be unavoidable.

- Groups:

As illustrated under the experimental design item, enrolled patients will be divided in two groups of equal size, followed up for two consecutive periods of 12 months each:

    - A first group will receive the standard of care in the first period and the GATEKEEPER intervention in the second period. This group will act as both control group (first period) and intervention group (second period) of the within-subjects analysis. It will also act as intervention group (second period) for the between-subject analysis
    - A second group will receive the standard of care. This group will act as a control group (second period) for the between-subjects analysis

- Outcomes:
    - Primary outcome: cost-utility of the GATEKEEPER solution compared to usual care, for elderly chronic patients enrolled in the Care Puglia CCM
    - Secondary outcomes (providing insights on how selected characteristics of the GATEKEEPER solution may influence the primary outcome):
        - To determine the level of adherence to the usage of the GATEKEEPER solution by patients and HCPs
        - To determine the level of patients' and HCPs acceptability, usability, and trust in relation to the GATEKEEPER solution
    - Exploratory outcomes:
        - Explore the influence of different diseases and comorbidity profiles on the cost-utility assessment of the GATEKEEPER solution (providing insights on the suitability of the GATEKEEPER solution for different diseases and comorbidity profiles)
        - Explore the influence of the GATEKEEPER solution on the number and duration of unplanned hospitalizations (providing insights on the effects of the GATEKEEPER solution on emergency care usage)
        - Explore the associations among the number and duration of unplanned hospitalization and:
            - Acceptability, usability, and trust in relation to the GATEKEEPER solution (providing insights on the influence of selected GATEKEEPER characteristic on emergency care usage)
            - Patients' HRQoL levels (providing insights on the influence of emergency care usage on HRQoL in the Care Puglia

population, a factor which is relevant to put the cost-utility assessment of the GATEKEEPER solution in context)

- KPIs
  - For primary objective:
    - Variation in HRQoL after a 12-month usage period (the denominator of ICER)
    - Healthcare expenditure disbursed along a 12-month usage period (the numerator of ICER) for:
      - Unplanned hospitalizations
      - Planned hospitalizations
      - Drugs
      - Specialist visits
  - For secondary objectives:
    - Patients' and HCPs usage logs related to GATEKEEPER solution's components
    - Acceptability scales (patients and HCPs)
    - Usability scales (patients and HCPs)
    - Trust scales (patients and HCPs)
  - For exploratory objectives:
    - Variation of patients' HRQoL level (in the above mentioned 12 months period), per diseases and comorbidity profiles
    - Variation of healthcare expenditure (during the above mentioned 12 months period), per diseases and comorbidity profiles
    - Number of unplanned hospitalizations
    - Duration of unplanned hospitalizations
- eCRF
  - Demographics
    - Age
    - Sex
    - Local Healthcare Authority
  - DDCI at enrollment, after 12 months (end of the first period) and after 24 months (end of the second period)
  - Hospitalization data during each 12-month period (for both periods)
    - # unplanned hospitalizations
    - Duration of unplanned hospitalizations
    - Costs of unplanned hospitalizations
    - Costs of planned hospitalizations

- Drug usage data during a 12-month period (for both periods)
  - Costs of drugs
- Specialist visits data during a 12-month period (for both periods)
  - Costs of specialist visits
- HRQoL at enrollment, after 12 months (end of the first period) and after 24 months (end of the second period)
  - EQ5D scale
- Data on usage of the GATEKEEPER solution
  - Usage logs from HCPs (for the specific patient under consideration)
  - Usage logs from patients
- Acceptability
  - TAM scale[13]
- Usability
  - SUS scale[14]
- Truts
  - PATAT scale[15]

3.1.5.2 Low Complexity Medical Use Case interventional experiment

- Rationale

As illustrated in deliverable D6.1, and as typical for most Italian and European regions, a large part of healthcare expenditure (almost 80% for the Puglia Region[16]) is disbursed for caring chronic patients

In such context it appears advantageous to support healthy elderly patients into adopting appropriate lifestyles, that can reduce the risk of transitions to less robust health states (e.g. pre-frailty, frailty or MCI)

The market has already produced applications which – by building on the rapid adoption of mobile devices that allow continuous unobtrusive monitoring of behaviour and lifestyle and timely delivery of coaching strategies – provide effective fitness/wellness support, mostly targeting the younger segments of the population

[13] "Technology Acceptance Model – an overview | ScienceDirect Topics." [Online]. Available at: https://www.sciencedirect.com/topics/social-sciences/technology-acceptance-model

[14] "System Usability Scale (SUS) | Usability.gov." [Online]. Available at: https://www.usability.gov/how-to-and-tools/methods/system-usability-scale.html

[15] Van Velsen et al. Measuring patient trust in telemedicine services: Development of a survey instrument and its validation for an anticoagulation web-service, International Journal of Medical Informatics, 2017. https://doi.org/10.1016/j.ijmedinf.2016.09.009

[16] See deliverable D6.1, Annex A6

It is expected that the GATEKEEPER platform – in particular, the GATEKEEPER Consumer Space components – would enable businesses to effectively implement and deploy similar non-medical, fitness/wellness applications, that specifically target the aging population segment and support healthy elderly citizens in maintaining their good fitness status for longer

In order to provide evidence for this claim and to encourage businesses to design and produce such new class of applications for active and healthy aging, it is important to assess the cost-utility ratio that can be achieved when the GATEKEEPER platform is applied to this endeavour

- Experimental Design: Between, Within, Mixed

The same type of design as for the previous Medical Use Case will be applied. To avoid repetition, the reader is referred to the relevant description above.

- Technology adopted/used:

The main device that will be used in the Low Complexity Use Case will be the own smartphone of the participant, equipped with an extended version of Samsung Health application[17] and a one-way message-based coaching technology, from partner FPM. Depending on agreements with partner SAM, which are undergoing at the time of this writing, the Samsung Health application will be possibly extended, through the application of its relevant SDK, in order to include novel trackers aimed at the collection of behavioural and lifestyle measures that are of specific interest to assess the robustness status of elderly citizens. Given the above, the following table summarizes the technologies to be used for this Use Case.

[17] https://www.samsung.com/global/galaxy/apps/samsung-health/

Table 5. Technologies to be used for the Low Complexity Use Case

Condition	Early detection / intervention	Key Enabling Technologies
Robustness[7]	• Measurement of physical activity	• Samsung Health application, measuring step count, walk distance, walk time, walk speed, walk calories
	• Measurement of active and healthy aging parameters	• New Samsung Health trackers, to measure socialization (e.g. through anonymized phone call log measures) and IADLs (e.g. Google Activity Recognition API, detection of visits to relevant Points of Interest through anonymized semantic location tracking)
	• Delivery of one-way coaching messages, aimed at supporting healthy behaviors and health literacy	• Technology for coaching message planning and delivery, experimented by FPM in the frame of the H2020 City4Age Project[18]. The user-facing part of this technology can be attached to any common messaging application, including popular ones such as WhatsApp or Facebook Messenger (in the City4Age Project, WhatsApp was used).

- Intervention details:

The intervention for the Low Complexity Medical Use Case consists in the implementation of a "community-based" scheme for the prevention of robustness decays in elderly subjects, based on (i) unobtrusive monitoring of behaviour and habits, (ii) sharing such data with the patient herself and with other people who she trusts, and (iii) delivery of one-way coaching messages to encourage subjects to maintain an active and healthy lifestyle (see also details deliverable D6.2, *Early detection and interventions operational planning*). In particular:

- The (possibly extended, as above mentioned) Samsung Health app will be downloaded by participants and installed on their own smartphones and it will unobtrusively monitor deviations in daily habits and activities, in order to early detect signs of decay in robustness and/or unhealthy conducts
- The FPM coaching technology will send relevant, timely messages to promote healthy behaviours and countering risks detected as per previous item. Content for such messages will include e.g. information, education, suggestions, etc. linked to the local context in which the elderly subject lives
- The user will be able to both (i) see her monitored data and (ii) share it with other people she trusts (e.g. family members, neighbours, her

[18] https://cordis.europa.eu/project/id/689731/it

pharmacist, etc.) implementing a "community care" scheme that involves all actors that have an interest in the wellbeing of the elderly subject

- Recruitment period:

The same recruitment period as for the previous Medical Use Case will be applied. To avoid repetition, the reader is referred to the relevant description above.

- Follow-up period:

The same follow-up period as for the previous Medical Use Case will be applied. To avoid repetition, the reader is referred to the relevant description above.

- Time Horizon for Analysis:

A time horizon sufficient for convergence (due to the absorbing state "dead") will be selected (say, several tens of years) for the MAFEIP analysis

- Target population

65+ healthy elderly citizens living in the Puglia Region, at risk of robustness decay (to be defined according to scales and cut-off thresholds currently under determination, as mentioned in the data analysis item above)

- Number of participants:

A number of participants between 7,000 and 10,000 will be selected, in relation to the availability of devices deployable for the previous Medical Use Case (see introductory notes)

- Randomization procedure:

The same considerations made for the previous Medical Use Case also apply in this one. To avoid repetition, the reader is referred to the relevant description above. Note that, in this case, quota sapling will aim at recruiting subjects that have demographic and socioeconomic characteristics in line with the proportions in the overall elderly population in the Puglia Region.

Like the previous Medical Use Case, some types of bias (e.g. consenting participants differing from non-consenting ones) seems to be unavoidable.

- Groups:

Like the previous Medical Use Case, enrolled patients will be divided in two groups of equal size, followed up for two consecutive periods of 12 months each. To avoid repetition, the reader is referred to the relevant description above.

- Outcomes:
    - Primary outcome: cost-utility of the GATEKEEPER solution compared to usual care, for healthy elderly subjects living in the Puglia Region
    - Secondary outcomes:
        - Increasing the engagement of the elderly population in the Puglia Region in maintaining healthy lifestyles
        - Increasing the health literacy of the elderly population in the Puglia Region

        - To determine the level of users acceptability, usability, and trust in relation to the GATEKEEPER solution
        - Increasing the involvement of multiple "community actors" in ensuring the active and healthy aging of the elderly population in the Puglia Region

- KPIs
    - For primary objective:
        - Variation in HRQoL after a 12-month usage period (the denominator of ICER)
        - Healthcare expenditure disbursed along a 12-month usage period (the numerator of ICER) for:
            - Drugs
            - Specialist visits
            - Hospitalizations
    - For secondary objectives
        - Engagement with mHealth apps scales
        - Usage logs related to GATEKEEPER solution's components
        - Health literacy scales
        - Acceptability scales
        - Usability scales
        - Trust scales
        - Number and of actors with which elderly subjects decided to share data with
- eCRF
    - Demographics
        - Age
        - Sex
        - Local Healthcare Authority
    - Healthcare expenditure
        - Costs of drugs
        - Costs of specialist visits
        - Costs of hospitalizations
    - HRQoL at enrollment, after 12 months (end of the first period) and after 24 months (end of the second period)
        - EQ5D scale
    - Data on usage of the GATEKEEPER solution
        - Samsung Health and FPM message delivery technology usage logs

- Engagement
- Health literacy
- Acceptability
  - TAM scale[13]
- Usability
  - SUS scale[14]
- Trust
  - PATAT scale[15]

3.1.5.3 Moderate Complexity Medical Use Case: observational study on the effects of physical activity and other behavioural changes in Type 2 Diabetes management

- Rationale

The study intends to leverage GATEKEEPER Consumer Space technologies to produce new evidence on the positive effects of physical activity and other behavioural changes in Type 2 Diabetes management. The improvement of patients' outcomes will be measured through lab exams and standardized validated risk scores, like the ENFORCE calculator[19,20] developed by CSS, that evaluates diabetes chronic complications

The main foreseen result will be that the patients with better adherence to physical activity prescriptions, as measured with GATEKEEPER Consumer Space technologies, will end in an improvement of diabetes control and a lower risk of developing Type 2 Diabetes complications, as expected according to the present guidelines on disease management.

A second endpoint to be investigated will be the possible role of the quality of the performed physical activities (duration, intensity, specific patterns, etc.) in improving the patients' health conditions. According to this principle, similar investigations will be performed considering all the variables measured with GATEKEEPER Consumer Space technologies, in search for novel variables or combination of variables that can be highly correlated with the evolution of the disease. The newly found correlations can be incorporated in future guidelines that can also be implemented as coaching features in future consumer apps.

As a consequence, a third endpoint will be the design of new disease progression prediction models that will take into account both the data derived from the patient's Electronic Medical Records (conventional clinical variables) and the data obtained from

[19] Massimiliano Copetti, Hetal Shah, Andrea Fontana, Maria Giovanna Scarale, Claudia Menzaghi, Salvatore De Cosmo, Monia Garofolo, Maria Rosaria Sorrentino, Olga Lamacchia, Giuseppe Penno, Alessandro Doria, Vincenzo Trischitta, Estimation of Mortality Risk in Type 2 Diabetic Patients (ENFORCE): An Inexpensive and Parsimonious Prediction Model, The Journal of Clinical Endocrinology & Metabolism, Volume 104, Issue 10, October 2019, Pages 4900–4908, https://doi.org/10.1210/jc.2019-00215

[20] http://www.operapadrepio.it/enforce/enforce.php

the patient's Personal Health Record (unconventional data or combination of data gathered by GATEKEEPER Consumer Space technologies).

These models can also be specialized to assess Type 2 Diabetes onset in not- or pre-diabetic individuals. This result can easily be obtained by combining EMR and PHR data, as above defined, with the answers to simple questions which are part of validated questionnaires like the FINDRISC (Finnish Diabetes Risk Score)[21].

As an exploratory objective, an estimation of the cost-effectiveness ratio that could be obtained if the above models were to be integrated in clinical practice will be also conducted

- Experimental Design: Between, Within, Mixed

This study will follow an observational design. As illustrated in the introductory notes, the reason is that the models that will be investigated in the frame of the study will not possess certification as medical devices, that will be mandatory for clinical usage when the new EU's MDR will enter into full force, in May 2021

- Technology adopted/used:

A Samsung smartwatch device, to be delivered to the participating patients, will be used as an instance of GATEKEEPER Consumer Space technologies. This device will collect PHR variables that will be merged with EMR variables coming from the CSS hospital and given as input to the predictive models, developed in the frame of the GATEKEEPER AI framework component

Table 6. Technologies to be used for the study on the effects of physical activity and other behavioural changes in Type 2 Diabetes management

Condition	Early detection / intervention	Key Enabling Technologies
T2D progression	• Measurement of physical activity and other variables	• Samsung smartwatch, measuring step count, walk distance, walk time, walk speed, walk calories • In addition, the smartwatch will also measure sleep quality, HR/HRV and, based on this, stress level. These variables can also be considered in the development of the predictive models
	• Predictive models based on both EMR (conventional data) and PHR (unconventional data)	• Models will be investigated with the support of the GATEKEEPER AI framework component

[21] https://www.mdcalc.com/findrisc-finnish-diabetes-risk-score

- Intervention details:
    - Patients will be enrolled if they agree to comply with a physical activity program and an initial assessment of their disease stage will be performed according to lab examinations and the computation of the risk of developing complications based on the most widely used and clinically validated risk calculation engines
    - Depending on the results of the prior evaluation, above mentioned, the physical activity program will be prescribed, according to current established standards (e.g. from The American Heart Association, the American Diabetes Association, and the American College of Sports Medicine)
    - A Samsung smartwatch will be assigned to each patient enrolled in the study, to monitor physical activity. The device will also measure additional variables, such as sleep, HR/HRV and stress level that can be used when developing models for the secondary endpoints
- Recruitment period:

Current planning envisions:

- Start of recruitment in October 2020
- End of recruitment accrual March 2021

- Follow-up period:

Patients will be followed up for 12 months

- Time Horizon for Analysis:

Time horizon for model predictions will be 6 years

A time horizon sufficient for convergence (due to the absorbing state "dead") will be selected (say, several tens of years) for the MAFEIP analysis

- Target population:

Patients with Type 2 Diabetes, which required hospitalization and are followed up by CSS hospital

- Number of participants:

A cohort of 100 patients will be enrolled in the study

- Randomization procedure:

Being the study design observational, there will be no randomization

- Groups:

Being the study design observational, there will be no control/intervention groups; these will be estimated to conduct an exploratory cost-utility analysis, as mentioned in the data analysis item above

- Outcomes:
    - Primary outcome: determine the association between physical activity measured with GATEKEEPER Consumer Space technologies and T2D outcomes

    - Secondary outcomes:
        - Determine the association between quality of physical activity measured with GATEKEEPER Consumer Space technologies and T2D outcomes
        - Investigate if unconventional data, measured with GATEKEEPER Consumer Space technologies, and conventional data, extracted from CSS EMRs, can jointly improve prediction of disease progression in T2D patients as compared to current standards
    - Exploratory outcomes:
        - Estimate the potential cost-utility of the integration of the above models in the clinical practice
- KPIs
    - Specificity, sensitivity and AUC of models
    - Estimated ICER resulting from the integration of the models in the clinical practice
- eCRF
    - Demographics
        - Age
        - Sex
    - ENFORCE score at enrollment and after 12 months of follow up
    - Clinical parameters needed for ENFORCE computation
        - Antihypertensive therapy
        - Insulin Therapy
        - Body Mass Index
        - High Density Lipoprotein
        - Low Density Lipoprotein
        - Diastolic Blood Pressure
        - Urinary Albumin Creatinine Ratio
    - Unconventional data from GATEKEEPER Consumer Space technologies
        - Step count
        - Walk distance
        - Walk time
        - Walk speed
        - Walk calories
        - HR/HRV
        - Sleep quality
        - Stress level

3.1.5.4 Moderate and Low Complexity Medical Use Cases: template for observational studies on prediction of adverse events

- Rationale

Patients affected by chronic diseases addressed in the Care Puglia CCM (T2D, HF, HBP, COPD) are subject to adverse events – such as hypoglycaemic events, decompensations, exacerbations, etc. – which imply higher health risks and likely recourse to emergency healthcare, that negatively impacts HRQoL and may cause overuse of resources

Algorithms able to predict such events, so that timely risk mitigation interventions can be effectively applied, carry the promise to improve the situation

The GATEKEEPER AI framework aims to promote the development of such algorithms, to support the enactment of related early detection and intervention strategies

In this subsection a template is proposed to develop relevant observational studies aimed at assessing the performance of predictive models that can early detect risks of adverse events linked to the chronic conditions addressed in the Care Puglia CCM, in the frame of the Moderate Complexity Medical Use Case interventional experiment presented in subsection 3.1.5.1 above.

A similar objective can also be pursued with respect to prediction of robustness decays in healthy elderly subjects, to mitigate related health risks, as addressed in the Low Complexity Medical Use Case interventional experiment presented in subsection 3.1.5.2 above.

In addition, as an exploratory objective, an estimation of the cost-utility ratio that could be obtained if the above models were to be integrated in clinical practice can be also conducted.

The exact models to be investigated are currently under consideration in the frame of ongoing work in task T6.3 (*Big Data and Data analytics strategies for early detection and intervention*), which is specifically dedicated to this purpose. They will be finally determined as soon as such work will be completed.

The observational studies outlined in this subsection can be performed by leveraging the same datasets collected in the respective interventional experiments previously mentioned, for Moderate and Low Complexity Use Cases

- Experimental Design: Between, Within, Mixed

This template is based on an observational design, for the same reason illustrated for the preceding study in subsection 3.1.5.3 above, and linked to the entry into force of the new EU Medical Device Regulation. To avoid repetition, the reader is referred to the experimental design item in such subsection for details.

- Technology adopted/used:

Model input comes from the technologies deployed for the Moderate and Low Complexity interventional experiments, as described in previous subsections 3.1.5.1 and 3.1.5.2

- Intervention details:

Data will be collected from patients enrolled in the Moderate and Low Complexity interventional experiments, as described in previous subsections 3.1.5.1 and 3.1.5.2

- Recruitment period:

The studies will be conducted on the same patients enrolled in the Moderate and Low Complexity interventional experiments, as described in previous subsections 3.1.5.1 and 3.1.5.2

- Follow-up period:

The studies will be conducted on the same patients enrolled in the Moderate and Low Complexity interventional experiments, as described in previous subsections 3.1.5.1 and 3.1.5.2

- Time Horizon for Analysis:

Time horizons for predictions will depend on the specific models that will be investigated (e.g. time horizons for predicting COPD exacerbations will be short term, while those for predicting onset of pre-frailty will be medium term)

A time horizon sufficient for convergence (due to the absorbing state "dead") will be selected (say, several tens of years) for the MAFEIP analysis

- Target population:

The same populations addressed, respectively, in the Moderate and Low Complexity interventional experiments, as described in previous subsections 3.1.5.1 and 3.1.5.2, will be targeted.

- Number of participants:

For models regarding the prediction of adverse events linked to Care Puglia CCM diseases (T2D, HF, HBP, COPD), data will come from participants enrolled in the Moderate Complexity Use Case interventional experiment (i.e. between 500 and 3,500 subjects, depending on factors mentioned in the introductory notes). However, it has to be noted that, depending on costs of devices and budget limits, not all these patients can be provided with all the hypothesized technologies and, by implication, not all patients will have all the detected variables available for the investigation of predictive models

For models regarding the prediction of robustness decay in healthy elderly subjects, data will come from participants enrolled in the Low Complexity Use Case interventional experiment (i.e. between 7,000 and 10,000, depending on factors mentioned in the introductory notes)

- Randomization procedure:

Being the study design observational, there will be no randomization

- Groups:

Being the study design observational, there will be no control/intervention groups; these will be estimated as mentioned in the data analysis item above

- Outcomes:
    - Primary outcome: assess the performance of predictive models for relevant adverse events, in the frame of the Moderate and Low Complexity interventional experiments
    - Exploratory outcomes:
        - Estimate the potential cost-utility of the integration of the above models in the clinical practice

- KPIs
    - Specificity, sensitivity and AUC of models
    - Estimated ICER resulting from the integration of the models in the clinical practice
- eCRF
    - Demographics
        - Age
        - Sex
        - Local Healthcare Authority
    - For T2D (hypothesizing the application of the technologies mentioned in the experimental study for Moderate Complexity, in subsection 3.1.5.1):
        - Parameters collected by the Medisanté BP800 3G device
            - Blood pressure
            - Glycaemia
        - Parameters collected by a fitness band such as Samsung Gear Fit-e:
            - Physical activity
            - Sleep quality
    - For HF (hypothesizing the application of the technologies mentioned in the experimental study for Moderate Complexity, in subsection 3.1.5.1):
        - Parameters collected by the Biobeat wrist device:
            - Blood pressure
            - Respiratory rate
            - Blood oxygen saturation
            - Pulse rate
            - Heart rate variability
            - Stroke volume
            - Cardiac output
            - Cardiac index
            - Pulse pressure
            - Systemic vascular resistance
            - Mean arterial pressure
            - Sweat level
            - Temperature
        - Body composition, collected by the Medisanté BC800 3G bioimpedance scale

        - Parameters collected by a fitness band such as Samsung Gear Fit-e:
            - Physical activity
            - Sleep quality
    - For HBP (hypothesizing the application of the technologies mentioned in the experimental study for Moderate Complexity, in subsection 3.1.5.1):
        - Blood pressure, collected by the Medisanté BP800 3G device or other similar market available device, yet to be determined at the time of this writing
        - Parameters collected by a fitness band such as Samsung Gear Fit-e:
            - Physical activity
            - Sleep quality
    - For COPD (hypothesizing the application of the technologies mentioned in the experimental study for Moderate Complexity, in subsection 3.1.5.1):
        - Blood oxygen saturation, to be collected with a market available device, yet to be determined at the time of this writing
        - Blood pressure, collected by the Medisanté BP800 3G device or other similar market available device, yet to be determined at the time of this writing
        - Parameters collected by a fitness band such as Samsung Gear Fit-e:
            - Physical activity
            - Sleep quality
    - For healthy elderly subjects (hypothesizing the application of the technologies mentioned in the experimental study for Low Complexity, in subsection 3.1.5.2):
        - From Samsung Health:
            - Step count
            - Walk distance
            - Walk time
            - Walk speed
            - Walk calories
        - Possibly, through new Samsung Health trackers, under discussion with SAM:
            - Phone call log (in, out and missed calls)
            - Activities from Google Activity Recognition API:
                - IN_VEHICLE
                - ON_BICYCLE

  - RUNNING
  - STILL
  - WALKING
- Points of Interest visited (see City4Age proof-of-concept[22])

In addition to the above variables, that come from KETs deployed for Moderate and Low Complexity interventional experiments, other conventional clinical data may become available from the EHRs of the Puglia Region's healthcare system and, for patients that needed hospitalization, from the EMRs of the CSS hospital. This availability is still under discussion at the time of this writing, in the frame of T6.3 work

[22] City4Age Consortium, public deliverable D2.11 City4Age frailty and MCI risk model, 2018

3.1.6 Milton Keynes

3.1.6.1 USE CASE 1

- Experimental Design: Between, Within, Mixed

Mixed subject design

- Technology adopted/used:

ActiveAge for monitoring and support social intervention

Smartphone/tablet

Connectivity

Smart home devices (controlled by family)

- Intervention details:

The main issue of Woughton elder population is the insurgence of mental health conditions, as consequence of years of social isolation in deprived conditions. Even though presence and effort of the WCC is significant, the population numbers and the isolation of elders from their families still result in many cases of self-isolation and mental health that are daily reported by all local authorities, such as police, fire police, social services, GPs, community services and pharmacies.

The RUC1 intervention is based on the use of an app to coordinate the monitoring and mutual support within a community. Using a common app, elder participants will be supported in self-monitoring and managing their health and wellbeing. Furthermore, the application will support the monitoring of the whole community by social and community workers, merging the effort of family, friends and neighbours in keeping track and support the elder members of the community. This intervention aims to prevent social isolation by increasing the cohesion of the community and by sharing the responsibility of monitoring and care dynamically among all community members.

- Recruitment period:

September 2020 – July 2022

- Follow-up period:

Six months

- Time Horizon for Analysis:

Three months between the end of the last batch of participants and the analysis

- Number of participants:

The UC1 concerns a total population of 400:
100 primary participants, age 65+ in good health
300 secondary participants in the network of the primary participants.

- Randomization procedure: randomly selection
- Groups: Control (N=70), Intervention (N=100).

During the period between the recruitment and start of the trial, each batch will be monitored as a control group.

- Primary outcomes

Context and status factors

- Primary Outcomes
  - Health – Cognitive
    - Mood
- Secondary Outcomes
  - Dependence
  - Health – Physical
    - Visit to doctors
    - Visit to health-related places

Primary Outcomes

- **Behavioural factors**
  - Instrumental Activities
    - Phone usage
    - New media communication
  - Socialization
    - Visits (remote)
    - Attending events (remote)
- **Contest and status factors**
  - Health – Cognitive
    - Mood

Secondary Outcomes

- **Behavioural factors**
  - Dependence
  - Basic Activities of Daily Living
    - Going out
- **Context and status factors**
  - Environment
    - Quality of neighbourhood

KPIs

Clinical KPIs:

- Social activity increase
- Better quality of life

Societal KPIs

- Technology acceptance
- Patient empowerment
- Social discomfort alleviation
- Return on investment

Adoption Potential:

- Privacy / data issues
- Usability issues

3.1.6.2 USE CASE 7

- Experimental Design: Between, Within, Mixed

Mixed-subject design.

- Technology adopted/used:

ActiveAge for monitoring physical and mental conditions

Smartwatch

Robotic platform

- Intervention details:

The main issue of Simpson elder population is the timely access to care services, as the village is physically isolated and ill connected from the rest of MK. The isolation with the rest of the city is mitigated by a strong presence of the community and small area of the village. Nevertheless, living with more than one conditions requires periodical access to care services and implies multiple constraints that could hard to follow on a daily base. The hardship experienced in accessing to care services combined with a demanding organization of life and self-care can result in elders losing their confidence in an independent living. This can further cause self-isolation, lack of adherence with the medial guidelines and a healthy active lifestyle, and ultimately the exacerbation or emergence of new conditions that will actually impede the independent living.

The RUC7 intervention is based on the use of personal devices, such as smartwatch, and tracking app. These devices should provide support to the adherence of an active healthy lifestyle, including social activities, physical activity and self-care. Furthermore, the technological solutions should support the elder's sense of safety and confidence in an independent living by providing a continuous monitoring of their condition and emergency response mechanisms.

- Recruitment period:

September 2020 – July 2022. Participants will be split in two batches and begin the pilot at six months of distance.

Community workers, small batches and mutual support among participants is important.

- Follow-up period:

Six months

- Time Horizon for Analysis:

Three months between the end of the last batch of participants and the analysis

- Number of participants:

The RUC7 intervention involve elder participants, and family members and neighbours as secondary participants:

- Primary participants will use the provided technologies - app and smart watch - for self-monitoring and self-managing their daily routine and general condition. This is the main facet of the intervention and it should result in mitigating the negative effects of living in a rural area, far from care services, and therefore mitigating both real and perception of risks concerning self-managing multiple conditions.

- Secondary participants will use the app to monitor and being engaged in specific interventions:
    - Family members can check the status of primary participants, building and sustaining a sense of trust in general, and provide timely support both in case of an event or general deterioration of the elder condition and lifestyle
    - Neighbours similarly can be engaged for a face-to-face periodical monitoring of elders and to provide support in daily activities, such as errands and socialization.
- Randomization procedure: randomly allocating participants
- Groups: Control (N=30), Intervention (N=30).

During the period between the recruitment and start of the trial, each batch will be monitored as a control group.

Primary outcomes

- **Behavioural factors**
    - Basic Activities of Daily Living
        - Going out
    - Socialization
        - Visits (remote)
- **Context and status factors**
    - Health – Cognitive
        - Mood

Secondary Outcomes

- **Behavioural factors**
    - Mobility
        - Moving across rooms
    - Physical activity
    - Instrumental Activities
        - Housekeeping
        - Phone usage
        - New media communication
        - Medication
- **Context and status factors**
    - Dependence
    - Health – Physical
        - Visit to doctors
        - Visit to health-related places
- KPIs

Clinical KPIs:

- Physical activity increase
- Social activity increase
- Patient visits and time spent

- Better quality of life
- Adverse events

Societal KPIs

- Technology acceptance
- Patient empowerment
- Isolation alleviation
- Return on investment

Adoption Potential:

- Usability issues
- Privacy / data sharing issues

3.1.7 Poland

3.1.7.1 USE CASE 1 (Lodz-1)

- Experimental Design: Between, Within, Mixed

Within-subject design

- Technology adopted/used:

Health promotion app for adherence promotion

Set of PROMS related to adherence, polypharmacy, and QoL

Big Data Analytics

- Intervention details:

Prevention of non-adherence to medication in community-dwelling older adults

Unobtrusive behaviour monitoring for early detecting the risk of non-adherence,

Enacting e-coaching interventions to promote healthy behaviour.

Elderly Citizens (1.000), age ≥50 years, GPs and the GP practice teams, Local community (family, informal and formal caregivers, etc.)

Living at home (either alone or with relatives) / non-institutionalized

Self-reported IT literacy

Self-reported ability and responsibility for managing their medications

Having at least 1 out of these asymptomatic / low symptomatic conditions:

- Hypertension
- Congestive heart failure
- Hyperlipidaemia
- Type 2 diabetes
- Hypothyroidism
- COPD
- Chronic kidney disease

At least **1 prescribed drug** taken on a typical day

Exclusion:

1. Mental condition
2. Any condition seriously lowering expected life duration
3. Hospitalisation due to any indicator condition (see above) within last 12 months

- Recruitment period:

October 2020 – March 2022

- Follow-up period:

Up to 6 months

- Time Horizon for Analysis:

Full effect of intervention is expected to last at least 6 months; some effects will stay lifelong

- Number of participants:

1,000 elderly citizens;

- Randomization procedure:

N/A

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

N/A

- Primary outcome:

Patient adherence, as assessed with validated tool (8-item Morisky Medication Adherence Scale, MMAS-8)

- Secondary outcome:

Health related quality of life

Increased health literacy and awareness

Increased skills in employing coping strategies to assure patient adherence

Cost-effectiveness of employed intervention

- KPIs
    - Increase in self-assessed health literacy and awareness of non-adherence by 25%
    - Reduction of the risk of non-adherence by 20%
    - Statistically significant increase of quality of life
    - Increase of self-assessed skills in polypharmacy management by 20% (in Lodz-2)

3.1.7.2 USE CASE 2 (Lodz-2)

- Experimental Design: Between, Within, Mixed
- Within-subject design
- Technology adopted/used:
- Health promotion app for adherence promotion
- Set of PROMS related to adherence, polypharmacy, and QoL
- Remote adherence monitoring
- Big Data Analytics
- Intervention details:

Prevention of non-adherence to medication in community-dwelling older adults

Unobtrusive behaviour monitoring for early detecting the risk of non-adherence-related problems

Multimorbidity and related polypharmacy management

Prevention of drug-related problems

Ageing population (age ≥50 years) with ≥2 asymptomatic chronic conditions

Individuals prescribed chronic medication (≥5 a day)

Multimorbid polymedicated elderly citizens (180)

GPs and the GP practice teams

Local community (family, informal and formal caregivers, pharmacists, etc.)

Age ≥50 years

Living at home (either alone or with relatives) / non-institutionalized

Self-reported IT literacy

Self-reported ability and responsibility for managing their medications

Having at least 1 out of these asymptomatic / low symptomatic conditions:

- Hypertension
- Congestive heart failure
- Hyperlipidaemia
- Type 2 diabetes
- Hypothyroidism
- COPD
- Chronic kidney disease

1. At least **5 prescribed drugs** taken on a typical day
2. At least **2 chronic conditions** from the list provided above (see p.5g above) present
3. For **high intensity group** only: hospitalisation due to any indicator condition within last 12 months

Exclusion:

1. Mental condition
2. Any condition seriously lowering expected life duration

- Recruitment period:

October 2020 – March 2022

- Follow-up period:

Up to 6 months

- Time Horizon for Analysis:

Full effect of intervention is expected to last at least 6 months; some effects will stay lifelong

- Number of participants:

180 (of which 130 will be of moderate complexity, and 50 of high complexity).

- Randomization procedure:

N/A

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

N/A

- Primary outcome:

Patient adherence, as assessed with validated tool (8-item Morisky Medication Adherence Scale, MMAS-8) and digital monitoring (for high-complexity stratum only)

- Secondary outcome:

Patient adherence, as measured with remote monitoring

Health related quality of life

Increased health literacy and awareness

Increased skills in employing coping strategies to assure patient adherence

Rate of drug-related problems

Self-rated ability to cope with polypharmacy management (as assessed with dedicated tool, for high-complexity stratum only)

Cost-effectiveness of employed intervention

- KPIs
    - Increase in self-assessed health literacy and awareness of non-adherence by 25%
    - Reduction of the risk of non-adherence by 20%
    - Statistically significant increase of quality of life
    - Increase of self-assessed skills in polypharmacy management by 20% (in Lodz-2)
    - Risk of drug-related problems lowered by 10%

3.1.8 Cyprus

3.1.8.1 USE CASE 7

- Experimental Design: Between, Within, Mixed

Within Subject Design

- Technology adopted/used:

Digital coach interaction applications

User friendly digital questionnaires

Smart-home devices

Multiparameter wearables

Virtual Reality – Avatar : The proposed avatar-based virtual reality intervention for women with breast cancer is based on the fact that in clinical practise hormone therapy-related side-effects appear to generally impact the quality of life of women with breast cancer to a greater extent than the mastectomy operation.

- Intervention details:

The intervention will focus on: Multi-chronic elderly patient management including polimedication. Both organizations (AMEN and PASYKAF) will adopt a holistic health assessment and intervention program integrated into an app or wearables or both. The main objective set by AMEN and PASYKAF will be addressed by:

- Gain a more holistic picture of the difficulties and needs of patients (medical, psychological, social, and financial) to be able to provide earlier and more targeted interventions that will improve their quality of life.

- Promotion of sleep hygiene and improvement in sleep problems.

- Increase committed action towards important values. This includes behavioural activation.

- Manage the pain the patients encounter efficiently.

- Recruitment period:

September 2020 - June 2022

- Follow-up period: (face to face, telephone based approaches, web-based)

As it concerns the cancer patients, the follow-up period depends on the hardness of the signs that frequently occur in the patients (ECOG PS). Therefore, we will not be able to follow up on the intervention if the patient, for example, has a worsening of the disease or if he starts any treatment or if he dies within the period after the intervention. In that reason, we propose to follow up at 4 weeks, 8 weeks and 12 weeks;

- Time Horizon for Analysis:

September 2022 – December 2022

- Number of participants:

1,400 patients will be involved, from both sites Archangelos Michael Elderly People Nursing Home / Rehabilitation Centre for patients with Alzheimer (AMEN) and the Pancyprian Association of Cancer Patients and Friends (PASYKAF). AMEN patients are 60+

age, able to use digital services and face dementia. PASYKAF patients are 50+ age, able to use digital services, face difficulties with co-morbidities and have cancer.

- Randomization procedure:

Stratified Random Sampling (create subgroups based on gender, age range, type of cancer, phase of illness.)

- Groups: Control (N=XX), Intervention 1 (N=XX), Intervention 2 (N=XX).

PASYKAF

Sample size (1000 target population in total):

1. Standard Health Care (Control group) - 350 patients
2. Standard Health Care + platform/system (Intervention group) - 350 patients
3. 250 Caregivers
4. 50 HCPs

AMEN

Sample size (400 target population in total)

5. Standard Health Care (Control group) – 175 patients
6. Standard Health Care + platform/system (Intervention group) - 175 patients
7. 50 HCPs

- Outcomes:

Primary outcomes:

The **primary objective** will be the early detection of condition worsening.

Secondary objectives include the self-reported patient's Quality of life (QoL) and satisfaction with treatment.

More specifically, the following outcomes will be assessed:

Primary outcomes: By monitoring patients can trigger appropriate management, thereby reducing the need for higher acuity care, and even, at times, improving survival.

Secondary outcomes: sleep hygiene, pain management, Hospital Anxiety and Depression Scale.

Other secondary outcomes:

Patient: Compliance with medical therapy, lifestyle changes, motivation, self-efficacy, quality of life, satisfaction with treatment,

Healthcare professionals: Content accuracy, confidence in decision making, support in medical counselling, cost-effectiveness, clinical inertia.

Caregivers:

- Supporting informal caregivers providing devices and essential training to manage the common problems and emergencies that have to deal with, ease their strain, as they often feel unprepared for the tasks they are required to perform.
- Reducing physical burden
- Improving communication with health professionals

- Accessibility and availability of information and advice, provision of equipment on time and adequate support networks will be the key actors useful in minimizing the disorders that informal caregivers reveal.
- Amelioration of their quality of life (IPOS, Integrated Palliative Outcome Scale)
- Improvement of psychopathology symptoms (rumination, depression, anxiety, panic attacks, trauma). Some items from interviews that are considered as the 'gold standard' will be used, which can assess the aforementioned symptoms [i.e., items from the Structured Clinical Interview of the DSM-5 (SCID-5, American Psychiatric Association, 2015)].
- Improvement of sleep problems. This can be assessed with simple questions regarding difficulty with the start and maintenance of sleep on a Likert scale (0 to 5; 0= no difficulty, 5= extreme difficulty).
- Increase in social engagement and in activities that give them meaning in life (values work). This can be assessed using the Valued Living Questionnaire (VLQ). Reminders/ prompts can be also used to assess whether the person has completed the goal he/she set (Did you complete this goal, which is in line with your value of family? Yes/No answers, if Yes, a positive reinforcement can be offered (i.e., a phrase that can encourage the patient to repeat the behaviour) If No, the app can ask the patient 'would you be willing to do it along with your pain and/or difficult emotions?').
- KPIs

Clinical KPIs: Better quality of life based on:

- IPOS
- Pain Diary
- QLQ-C30
- EORTC Quality of Life – Core Questionnaire
- The Hospital Anxiety and Depression Scale (HADS)
- Behavioral activation (BA)
- Sleep Hygiene
- Physical activity increase
- Patient visits and time spent
- Patient adherence to treatment
- Adverse events
- Standardized questionnaires: https://www.ichom.org/portfolio

Societal KPIs

- Technology acceptance
- Patient empowerment / health literacy
- Informal Caregivers empowerment
- Health Professionals quality of life in relation to technology adopted

Adoption Potential:

- Compatibility with clinical workflows/protocols
- Usability,
- Acceptability,
- Effectiveness

Technology Adopted:

- Software/Hardware
- Prediction features

4 Conclusions

Following the information in this deliverable, we can conclude that the training we have provided to the pilots has resulted in a better understanding of experimental designs and the definition of the KPIs. Considering the work that has been done in task 7.2, summarized in this deliverable, to plan the exact pilot use cases definition and the experimental design that will be conducted. Together with partners working in work package 6 and 9 we have developed a large excel file to collect all the information that will lead to a meta-analysis assessing the overall outcome. In D7.2 we will continue the work presented here, together with University of Warwick, to describe the exact measurements of the KPIs and which scales will be used, to align as much as possible between the pilots across GATEKEEPER.

The innovative element of GATEKEEPER is that we are able to actively involve different stakeholders in the co-creation of the evaluation framework, whereby all partners, together with the pilot-sites (from Basque country, Aragon, Saxony, Puglia, Poland, Milton Keynes, Greece and Cyprus), have worked on establishing the evaluation framework and therefore can deliver higher qualities of research..

Designing a methodological sound evaluation framework with valid and reliable key performance indicators is necessary to effectively test the outcomes of digital solutions in the healthcare sector, taking into account methodological aspects such as validity and reliability for the results.. Subsequently, it provides the opportunity to conduct cost-effectiveness analyses to support evidence-based decision-making processes for stakeholders with the MAFEIP tool, part of WP9.

Appendix A Introduction to Experimental Designs

This white paper has been established by Open Evidence in order to support the development of the Evaluation Framework, the detailed experiment and KPI definition (T7.2), and for the harmonization, coordination and socio-economic assessment (T9.2) and local impact assessment (T7.8). In addition, it is important to make sure the deployment of the detection and intervention use cases are of high clinical and scientific standards (WP6). In this introduction we will briefly explain what experimental designs are and which are the necessary elements needed to conduct a valid and reliable study design to ensure it is a useful experiment. In the current introduction we mean with pretest the baseline test/measurements (in GATEKEEPER) and with treatment we mean the technical solutions used as an intervention (in GATEKEEPER). Next, we will explain some methodological designs that can be used in the GATEKEEPER project.

Experiment

An **experiment** is a methodological procedure and design carried out to support, refute, or validate a hypothesis. Experimental research is the only methodological design existing that is able to detect whether there is an actual effect between one factor and the outcome factor(s) of interest. Well-conducted experiments, such as high quality randomized controlled trials (RCTs), are considered to have the highest reliability and validity of all scientific forms of research (see also **Figure 5**). Experiments provide outcomes into **cause-and-effect** by demonstrating what the results are when a particular factor is manipulated, controlling for other factors that might affect the outcome through different procedures. Experiments vary greatly in their research goals and scales, but always use controlled procedures and direct analysis of the results.

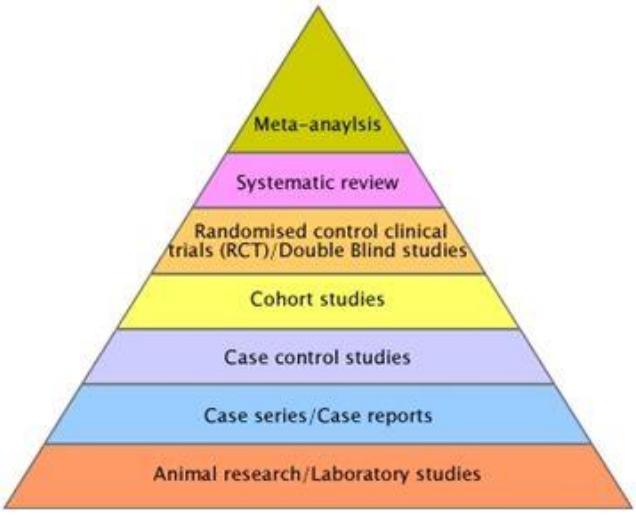


Figure 5. The pyramid of scientific evidence

In general, experiments typically include **control groups**, which are designed to **minimize** the effects of variables other than the single independent variable. This increases the reliability and validity of the results, through a **comparison between control groups and intervention group on the specified outcomes**. Ideally, all variables in an experiment are

controlled through **randomization processes** and the number of participants in every group. **Randomization** means that a participant in the study is randomly allocated to one of the conditions (see **Figure 6)**. Participants cannot choose themselves in which condition they want to participate. If participants do not know in which condition they are allocated, because they are not aware that there are other conditions or what the content of the conditions is, this is called **single blinded**. If the experimenter also does not know in which condition participants are allocated, this is called **double blinded**. If randomization was not successful, or participants are aware of the allocation of the conditions, it is no longer an experiment but quasi-experiment, which means that other factors than the manipulation can be the factor that explains the results.

Randomization is a method based on chance alone by which study participants are assigned to a treatment group and to the control group. If you have more than one treatment group, you will randomly allocate participants to one of the treatment groups (and control). Randomization can be done by allocating the participants on alphabetical order, by numbering them and then use a coin or dice to establish the conditions. **Randomization** minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms, also over time. If all controls work as expected, it is possible to conclude that the experiment works as intended, and that results are due to the effect of the tested variable. Because within the GATEKEEPER project we are interested in the effects of the digital solutions, experimental designs are a prerequisite of the research being conducted.

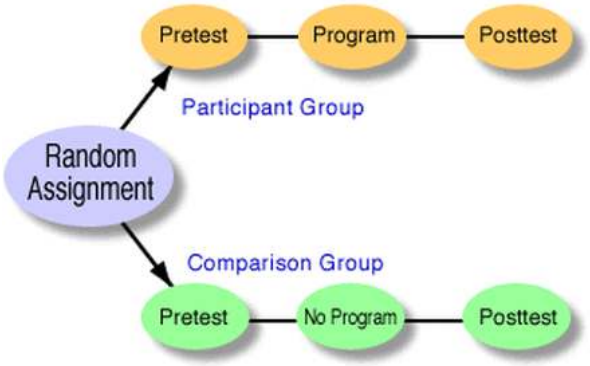


Figure 6. A visualization of an experimental design with one treatment (program) and one control group

Experimental Designs:

In general, there are three different study designs; (1) a **between subject design,** (2) a **within-subject** design, and (3) a **mixed-method design**. The different designs will be briefly explained below.

Between-subjects is a type of experimental design in which the subjects of an experiment are randomly assigned to different conditions, with each subject experiencing only one of the experimental conditions. In Figure 3 you see that Subject 1 and 2 are assigned to treatment A (for example technical solution X), Subject 3 and 4 to treatment B (for example technical solution Y), and subject 5 and 6 to the control treatment. All subjects are pretested (in Gatekeeper Baseline measurements) before the treatment and after the treatment to test the effects. The most important advantage of this design is that it is straightforward and easy to understand, analyse, and report, and participants are only measured twice. The most important disadvantage is that the participants in the control treatment do not get any of the treatments.

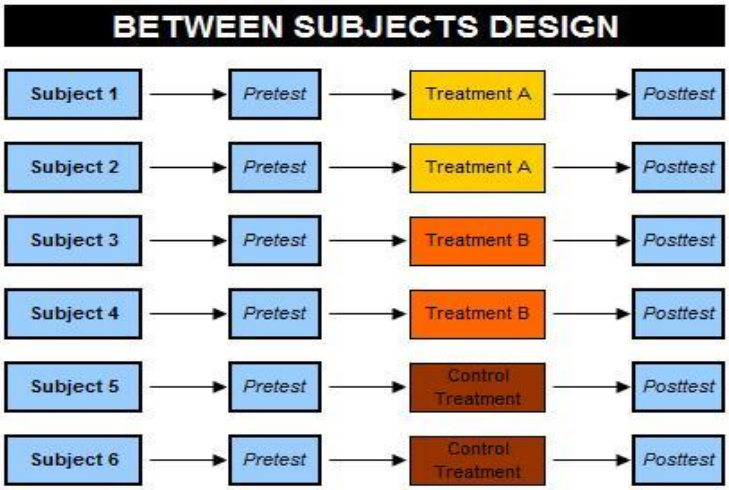


Figure 7. A visualization of a between subject design with two treatment groups and one control

A **within-subject design** is a type of experimental **design** in which all participants are exposed to every treatment or condition, always in the same order. In Figure 8 you see that all subjects are allocated to all treatments, starting with the control and followed by the other treatments. All subjects are pretested before the treatment and after all the treatments, to test the effects. The most important advantage of this design is that it all participants receive all treatments. The most important disadvantage is that it has to be tested multiple times creating a test-effect, for example people remember their previous answers, people want to improve to provide more positive answers, people learn how to do the test, etc. Another disadvantage is that the order of the conditions presented can have an effect as well.

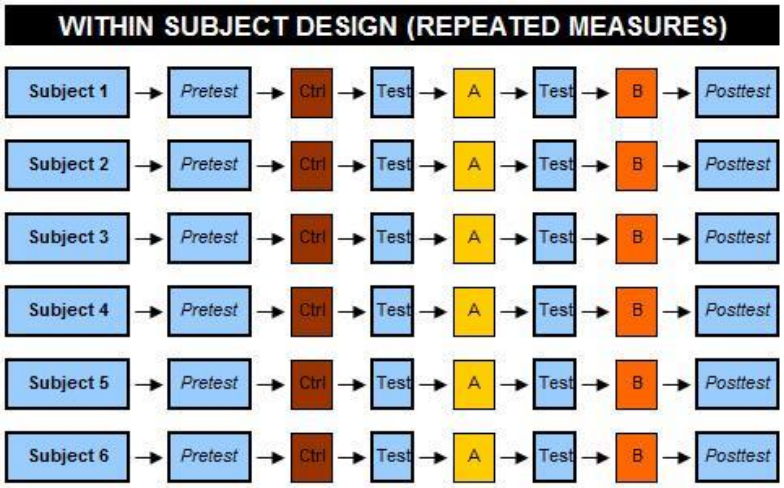


Figure 8. A visualization of a within subject design with two treatment groups and one control

A **mixed-method design** is a type of experimental **design** in which all participants are exposed to every treatment or condition, and the order is counterbalanced (for example randomly selected) to overcome the order effect. In Figure 9 you see that all subjects (now in groups) are allocated to all treatments, starting with one of the conditions randomly. All subjects are pretested before the treatment and after all the treatments, to test the effects of every individual treatment. The most important advantage of this design is that it all

participants receive all treatments. The most important disadvantage is that you have to test multiple times, creating also a test-effect. For example, people remember their previous answers, people want to improve to provide more positive answers, people learn how to do the test, etc.

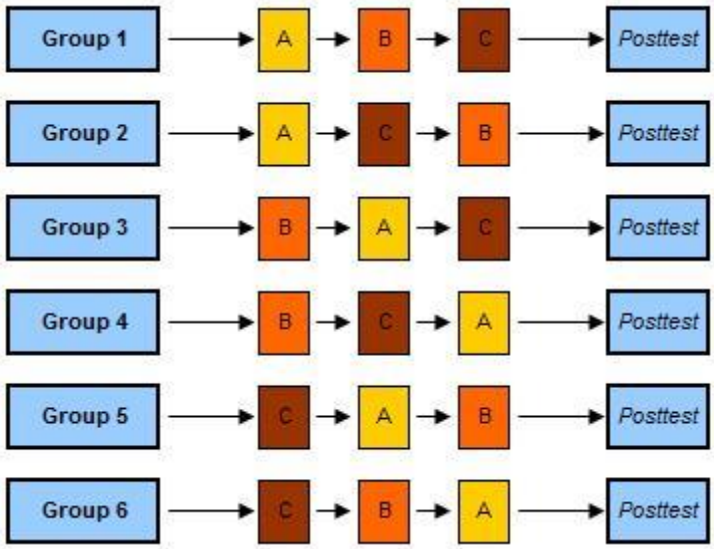


Figure 9. A visualization of a mixed method design with two treatment groups and one control (there is also a pretest and after all treatments there is a test)

Appendix B Table of factors

In this appendix we have visualized the different factors that are needed to conduct a meta-analysis to test the effectiveness of the GATEKEEPER evaluation framework of the federated pilots and to conduct the impact assessment for the socio-economic reports in D9.4. In Figure 10-13 you see the different factors that we aim to collect, hereby we provide a list of factors we have established as important. Because this is a working document, we might add more variables that we think are needed for an effective evaluation framework.

- Pilot Details
- Technology adopted
- Intervention details
- Recruitment period
- Follow-up period
- Pilot country/region
- Time Horizon for Analysis

- Differences in Clinical Variables at Final Follow-Up
- Number of patients in the DoA
- Number of patients estimated now
- If the number(s) in I is different than the number(s) in J explain why
- Minimum age participants
- Maximum age participants
- Patients per group [intervention, control]
- Proportion patients in baseline state [intervention, control]
- Proportion patients in disease/impairment state [intervention, control]
- Transitions probabilities – incidence rate [intervention, control]
- Transition probabilities – recovery rate [intervention, control]
- Patient information and frequency of monitoring [daily, weekly, monthly]
- Gender [general, intervention, control]
- Comorbidities/conditions/risk factors Baseline [type, intervention, control]
- Dementia/Cognitive Functioning Baseline [intervention, control)
- IT Literacy Baseline [intervention, control]
- Other characteristics to be added [intervention, control]
- Planned patients visits [intervention, control]
- Unplanned patients visits [intervention, control]
- Unplanned hospitalizations [intervention, control]
- Lenght of visits [intervention, control]
- Adherence to treatment [intervention, control]
- Improving healthy habits [intervention, control]
- Transitions to higher risk strata [intervention, control]
- Health related quality of life [intervention, control]
- Other clinical outcomes to be added [intervention, control]

- Healthcare costs baseline
- Markov Model [number of states]
- One-off costs [intervention, control]
- Recurrent costs [intervention, control]
- Healthtcare costs baseline [intervention, control]
- Healthcare costs disease/impairment [intervention, control]
- Societal costs baseline [intervention, control]

- Societal costs disease/impairment [intervention, control]

- Societal aspects
- Utility baseline [intervention, control]
- Utility disease/impairment [intervention, control]
- Technology acceptance [intervention, control]
- Other societal outcomes to be added [intervention, control]

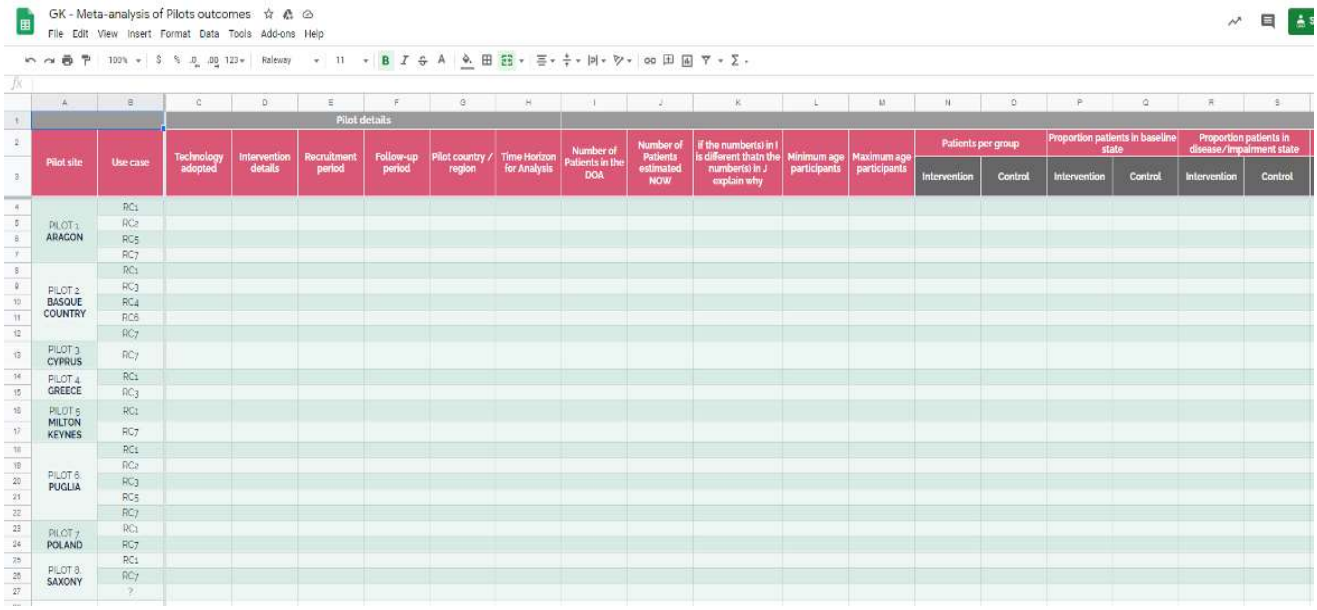


Figure 10. Part I of the excel-file created to collect and organize all information collected

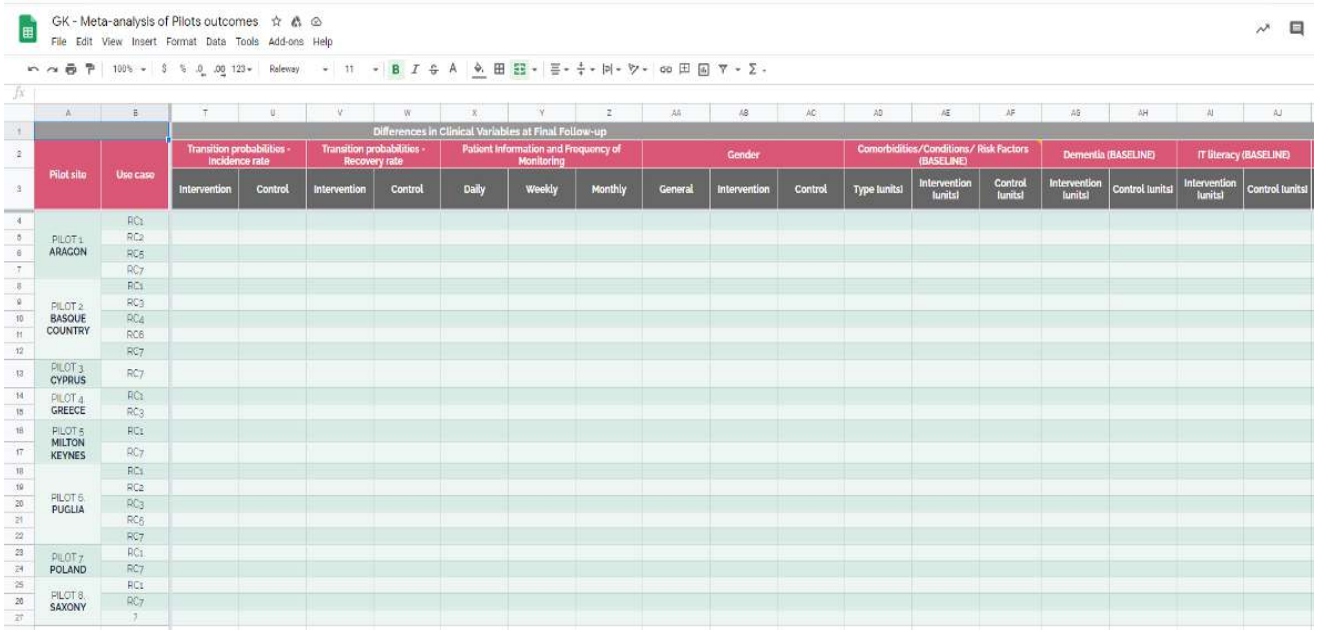


Figure 11. Part II of the excel-file created to collect and organize all information collected

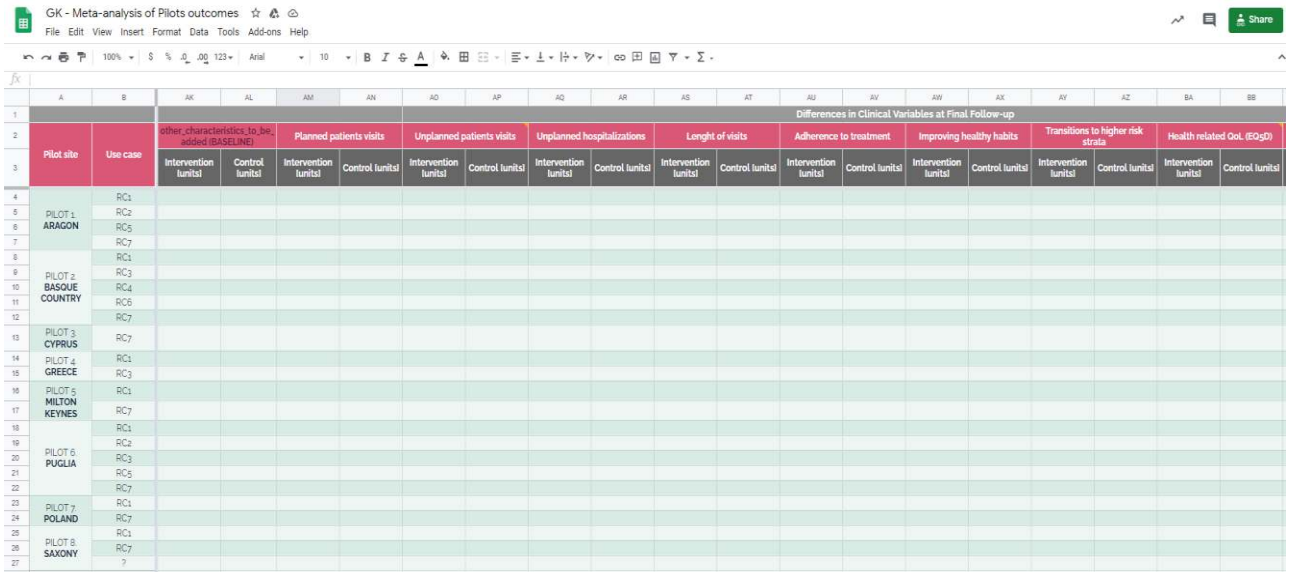


Figure 12. Part III of the excel-file created to collect and organize all information collected

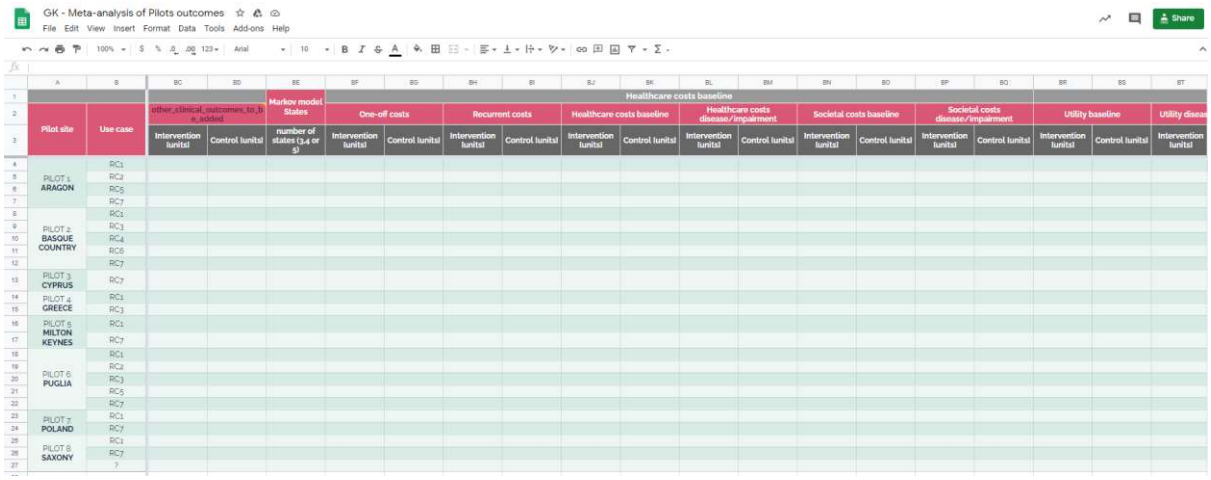


Figure 13. Part IV of the excel-file created to collect and organize all information collected

Appendix C Communication and Dissemination

The following news article was published (on May 15th, 2020) based on the work we have been doing.

Evaluation as starting point to capture Gatekeeper value across Europe

Currently, **Open Evidence** is actively involved in the co-creation of the **evaluation framework** together with the pilot-sites (from Basque country, Aragon, Saxony, Puglia, Poland, Milton Keynes, Greece and Cyprus). The evaluation framework is designed to systematically assess the application of Gatekeeper platform services, with the aim of improving the quality of life of citizens while demonstrating its significant efficiency gains in health and care delivery across Europe. To start with, the experimental design and key performance indicators are being established in order to structurally examine the outcomes and show the effectiveness of the deployment of technical solutions that will involve around 40,000 elderly citizens in 8 regional communities from 7 EU member states. It is of great importance to establish the experimental design and key performance indicators at the very beginning of the process.

Dr. Frans Folkvord, researcher at Open Evidence, explains "**Gatekeeper** provides us with a great opportunity to establish all necessary elements of a large pilot site deployment of highly promising technological solutions to improve healthcare across Europe. Conducting these important methodological activities *a priori* is essential to reap the benefits of this large European project efficiently". Whereas most interventions do not have the opportunity to use a multidisciplinary team like in **Gatekeeper**, this creates the possibility to conduct this important work from a large number of perspectives. This has not gone unnoticed to **Dr. Jordi de Battle**, researcher at Lleida Biomedical Research Institute's Dr. Pifarré Foundation (IRBLleida) and work package leader in **Gatekeeper**, "Open Evidence and the individual pilot sites are doing great work on establishing the evaluation framework for the Gatekeeper project. This is much needed, considering the usefulness and relevance of valid and reliable outcomes that are the result of methodological sound designs to test advanced ICTs to improve quality of life of citizens across Europe".

Designing a methodological sound evaluation framework with valid and reliable key performance indicators is necessary to **effectively test the outcomes of digital solutions in the healthcare sector**. Subsequently, it provides the opportunity to conduct cost-effectiveness analyses to support evidence-based decision-making processes for stakeholders, such as health or social care providers, policy makers, companies or researchers, and also users in the health and care sector. **Prof. Francisco Lupiáñez-Villanueva**, Director at Open Evidence and professor at Universitat Oberta de Catalunya, emphasises the flexibility of the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing – **MAFEIP tool** to support evidence-based decision-making processes for all institutions and users in the health and care sector.