

# DARE

## DIGITAL LIFELONG PREVENTION

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Spoke 3 Deliverable

### S3.D5.1 Concept and relevant design of the models

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## S3.D5.1 Concept and relevant design of the models

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## Publishable Summary

Within the Spoke 3 of the DARE project, entitled 'Digitally-enabled secondary and tertiary prevention', WP5 deals with the continuity of care interventions through innovative ICT infrastructures. The main obstacle to harnessing the enormous potential of ICT tools is the lack of integration of these tools in systemic interventions at the clinical level, precisely what the Spoke 3 pilot studies aim to overcome. In particular, WP5 activities will be carried out pursuing the specific objectives of six pilot studies. The common denominator among these pilots is the need of integration of ICT tools into protocols capable of exploiting their characteristics to achieve the goals of secondary and tertiary prevention. The six pilots integrate various tools, spanning from wearable devices to algorithms supporting clinical decisions, with different methodologies, ranging from observational to randomized study designs, involving diverse groups of patients such as infants, older adults, diabetics, Inflammatory bowel disease (IBD) patients, and chronic kidney disease patients. As documented in detail below in this document, the six pilots address various transversal issues, such as the risk of higher use of hospital services or the calculation of caloric intake. The proposed solutions will build upon previous experiences of the responsible research groups.

All the six pilots are intended to open new clinical and prevention pathways to improve both the quality of life of the patients and the effectiveness of health services. During the first 12 months of the project, the pilot concepts have been defined in detail in collaboration with the Spoke 1 staff, along with the list of indicators to measure the impact of the proposal. The robustness of the methodologies will be a crucial factor for the success of the pilot studies.

## 1. Introduction

### 1.1. WP5 overview and aims

Within Spoke 3 “Digitally-enabled secondary and tertiary prevention” of the DARE project, WP5 deals with the continuity of care interventions. More specifically, the WP5 objectives include to qualify and improve patient care pathway, and to support secondary and tertiary prevention, in a variety of physio-pathological conditions and ages (from preterm infants to adults/older adults), leveraging digital platforms which integrate data registries, wearable sensor and IoT technologies, decision support systems, home/mobile apps and AI methodologies. These objectives are pursued using six pilot studies, focused on secondary and tertiary prevention intervention supported by ICT- infrastructures, as a model.

As it will be better documented in the following, WP5 focuses on developing and implementing ICT tools to enhance clinical and prevention outcomes for specific populations. The planned use of ICT tools/systems within different pilots will enable physicians to establish models for prediction and monitoring across various use cases, aiming to harness the potential of ICT in prevention and care. The wide range of applications demonstrates that ICT is a flexible tool suitable for various situations. Investigating the adaptability of new ICT developments to different clinical and public health fields is expected to be one of the main tasks of the WP5 pilots, which are set to be deployed.

WP5 includes studies on diverse populations with the objective of identifying procedures that can improve the quality of life for patients and simultaneously provide clinicians with more numerous, accurate, and easily manageable information – an achievement impossible without ICT. These studies could serve as the foundation for further development of ICT applications for prevention and treatment procedures, contingent upon demonstrating their effectiveness through accurate indicators.

Specifically, the adoption of digital eHealth/mHealth platforms for home/remote monitoring, IoT and wearable devices, decision support systems, and data integration is expected to:

- Improve the capability to evaluate treatment practices and promote good clinical practices.
- Enhance the ability to encourage a healthy lifestyle (e.g., through newly developed tools for measuring caloric intake).
- Reduce the time spent by specialists reassessing previous medical history.
- Assist specialists and non-specialists in managing pathologies in challenging clinical situations (e.g., diabetes management, IBD, Chronic Kidney Disease).
- Improve patient therapy, compliance, and the ability to self-monitor individual habits.
- Decrease the occurrence of adverse events (such as hypoglycemic events, intra-hospital infections, etc.).
- Enhance prevention strategies (e.g., drug dosage optimization, proper nutrition).
- Reduce the number of improper admissions, readmissions, and median length of stay.
- Improve the quality of life for the elderly frail population.
- Positively impact budget/resource allocation at the institutional level.

## 1.2. Project status at month 12

A multidisciplinary approach is fundamental to the success of a project aiming to integrate technology with clinical and prevention approaches. The objective is not only for technology to deliver performance but also to open unforeseen scenarios for clinical and prevention activities. DARE researchers must meticulously assess these scenarios to address concerns about the use of personal data that have arisen during the preparation phase of the pilot studies. As it will be shown in Section 2 of the present document, at Month 12 all pilots have reached the stage of 'concept and relevant design of the model' after thorough deliberation at different levels of the DARE program dedicated to proposal revision. Ethical approval is still pending for all pilots, and their field commencement is anticipated in 2024, aligning with the overall program timeline. In two instances, discussions on the ICT architecture are already underway, and additional collaborations have been established in the field to foster synergies that will fortify the experimental designs. Additionally, where feasible, academic

positions have been filled to enhance the multidisciplinary composition of the research groups.

### 1.3. Deliverable outline

Section 2 reports, at the single task level, an overview of the aims and challenges of the WP, as well as reporting details about the study design, expected results, and the progresses made at month 12. The design of the study performed in the first 12 months of the project is then documented. Expected results are finally described. Section 3 reports some general conclusions and a list of the major steps and challenges to deal within the forthcoming period.

## 2. Research concept and design

### 2.1. Task 5.1 - IBD care through hub&spoke infrastructure (responsible: IRCCS-AOUBO)

#### 2.1.1. Overview

Task 5.1. revolves around the further development of the Emilia-Romagna Inflammatory Bowel Disease (IBD) hub&spoke infrastructure to enable continuous assessment of the quality of care, facilitate research, provide timely alerts on clinical pathway management, support benchmarking, and engage patients.

Particularly, the objective of Task 5.1 is to create a data collection tool for managing patients with IBD. This tool will be self-implemented, drawing data from routine healthcare activities or entered directly by patients through a self-reporting system. Integrated into a hub-and-spoke network, this system will not only facilitate the collection of real-life data from a large cohort of patients but also support internal and external evaluation/validation of clinical performance and correction of critical issues.

The collection of data from routine healthcare activities, with a focus on the time factor as a primary determinant, will enable the identification of predictive factors for the unfavorable evolution of the disease or the ineffectiveness of treatment. Identifying predictive factors for treatment ineffectiveness or the development of disability will facilitate the modification of

current therapeutic schemes recommended by existing guidelines and allow for the evaluation of their effectiveness.

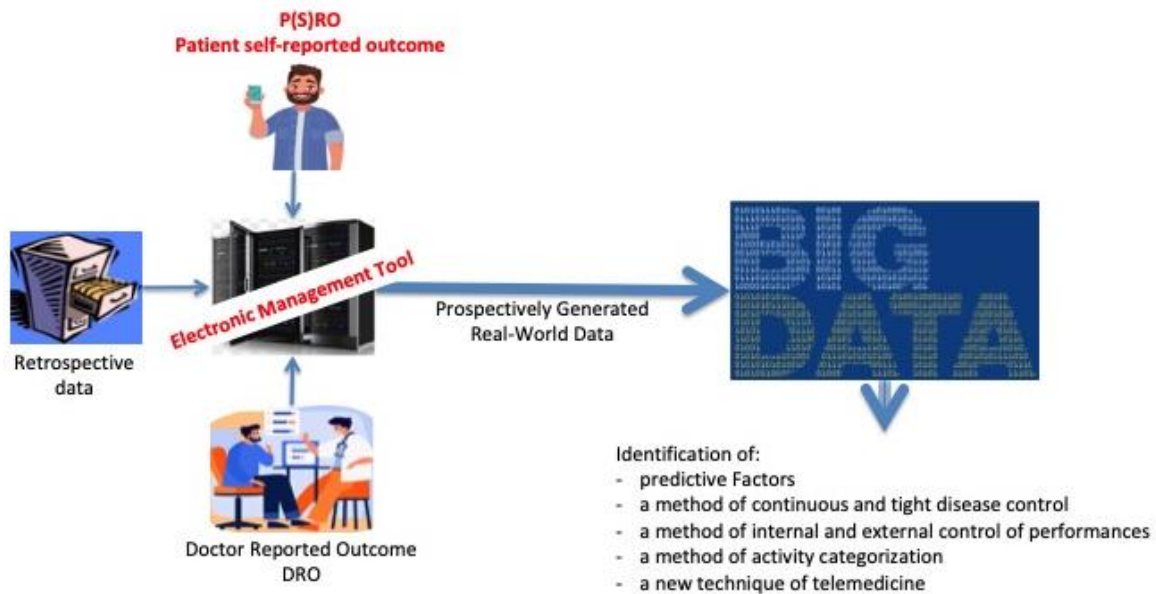


Figure 1. Graphical overview of Task 5.1

### 2.1.2. Objectives

#### General objective

The project's overarching goal is to address unmet needs in managing Inflammatory Bowel Disease (IBD). These needs include identifying prognostic factors for disease aggressiveness, predicting treatment efficacy, determining optimal care timing, and reducing variability in patient management within a hub&spoke system. The project, conducted at the IRCCS University Hospital of Bologna Policlinico di Sant'Orsola, involves developing architectural needs, methodologies, and technologies for a research support platform. The project aims to create a dedicated data entry tool for routine and outpatient care, enabling patient self-monitoring. The sequential data collection will predict disease outcomes, treatment responses, and efficacy, facilitating the evaluation of subsequent clinical decisions. Applying this methodology to the Emilia Romagna IBD network will assess center performance, minimize variability, and implement corrective actions as needed.

#### Specific Objectives

In the initial phase, the project will focus on developing an electronic medical record tool with specific functionalities. This includes the ability to upload comprehensive medical histories and examination results. Moreover, there will be a standardized, prospective collection of clinical information during routine patient visits. The system will automatically incorporate laboratory exams and diagnostic tests conducted within the center. Notably, patients will have the option to self-report outcomes and relevant data through a user-friendly web-based or mobile app-based platform.

The primary objectives during this first step are twofold. Firstly, it aims to identify prognostic factors associated with treatment response, failure, adverse events, and complications. Secondly, the project seeks to evaluate and address any inter-center variability in the criteria for patient selection regarding biologic treatment or surgical indications.

Moving to the second step, the project will involve the identification of patients requiring hospital referrals versus those who could effectively be managed through videocalls or telemedicine. Additionally, a comparative study will be conducted to assess patients' preferences and acceptance of telemonitoring in comparison to traditional management, employing a cross-over study design.

In the third and final step, the project will establish an electronic routine for evaluating center clinical performances. This involves internal assessments and the potential for external audits to ensure high clinical standards. The system will facilitate consultation activities between hub and spoke centers, providing direct access to the electronic medical record system. Multidisciplinary evaluations will be emphasized, particularly for complex patients. Furthermore, the data entered into the Emilia-Romagna network (megadata) will be harnessed for clinical studies.

The ultimate objective of this step is to conduct both internal and external clinical audits, ensuring the ongoing improvement of clinical practices and fostering collaboration among healthcare centers.

### 2.1.3. Study design

**Study characteristics:** The study will be ambispective and will involve all patients with IBD treated in the IRCSS-AOUBO center who provide written informed consent (up to 10,000 patients).

**Ethical Committee authorization status:** The Ethical Committee has already evaluated and authorized the part of the project protocol regarding data collection, and the section regarding the creation of the digital tool will be submitted by January 2024.

### 2.1.4. Expected results

Task 5.1 expected outcomes include:

- **Clinical Outcomes and Timeframes:** Define measurable clinical outcomes for IBD with realistic achievement timeframes.
- **Evidence-Based Standards of Care:** Develop and implement evidence-based IBD care standards to minimize variations and enhance outcomes.
- **Telemedicine-Managed Patients:** Identify IBD patient groups suitable for telemedicine management.
- **Center Clinical Performances Evaluation:** Evaluate center clinical performances against external benchmarks for continuous improvement.
- **Standardized Patient Management:** Standardize patient management across hub and spoke centers for consistent, optimized care.

### 2.1.5. Project progress

A pilot study proposal was submitted to the DARE coordinators in July 2023. During the third trimester of DARE, the proposal underwent the scrutiny of referees from Spoke 1 and Spoke 3. At the time of writing, the comments from Spoke 3 have been addressed and resolved, and the final version of the pilot has been submitted to Spoke 1.

At the same time, the proponents are actively collaborating with the software engineers to develop the digital tools for data collection and evaluation, and weekly meetings are being held to discuss the progress.

## 2.2. Task 5.2 – Digital therapy and telemedicine approaches for nutritional intervention in chronic diseases (responsible: UNIBA)

### 2.2.1. Overview

The application of Internet of Things (IoT) technology holds significant promise in advancing the prevention and prediction of end-stage renal disease (ESRD) in individuals with Autosomal Dominant Polycystic Kidney Disease (ADPKD). By leveraging IoT, a sophisticated system of remote monitoring can be established, offering the capability to continuously track key health parameters. This includes early detection of declines in kidney function, which is crucial in the context of ADPKD where the progression to end-stage renal disease is a major concern.

Furthermore, IoT technology enables not only the monitoring of physiological metrics but also facilitates the seamless integration of medication and lifestyle management into the healthcare ecosystem. This integration ensures a holistic approach to patient care, allowing for timely interventions based on real-time data.

Moreover, the wealth of data generated by IoT devices can be subjected to advanced data analytics. This analytical approach can uncover patterns, correlations, and predictive insights, thereby enhancing the understanding of disease progression and response to interventions. By harnessing the power of data analytics, healthcare professionals can make more informed decisions, tailor treatment plans, and potentially intervene at earlier stages, thereby improving outcomes for individuals with ADPKD at risk of developing ESRD.

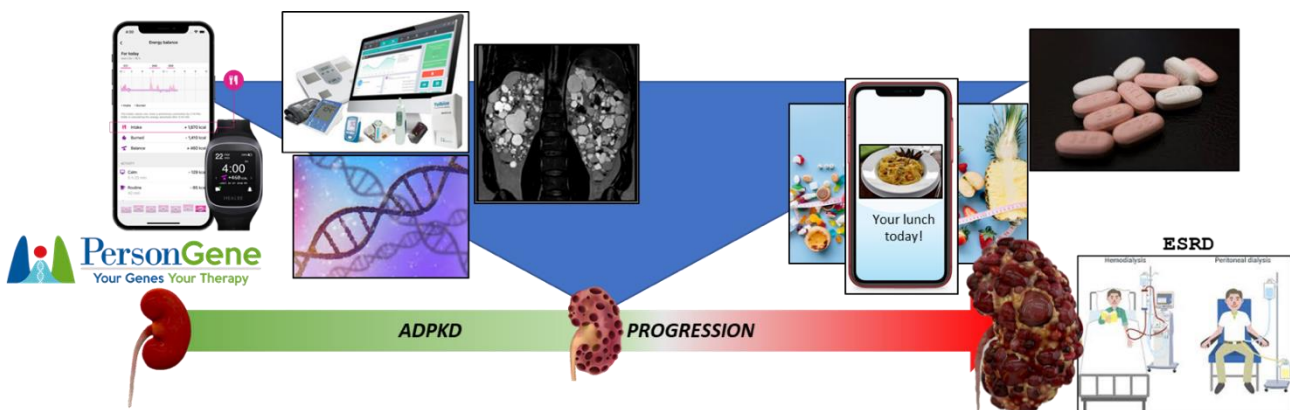


Figure 2. Graphical overview of Task 5.2

### 2.2.2. Objectives

#### General objective

Develop novel systems for therapeutic management, based on integrated information derived from genetic and clinical data with tailored nutritional and pharmacological approaches.

### Specific Objectives

The integration of multiple data sources is a crucial aspect of this initiative. The algorithm seamlessly combines information from various channels, encompassing wearable devices, mobile applications, clinical records (inclusive of laboratory estimations), and genetic data. The specific goal is to tailor protocols based on a ketogenic diet for patients diagnosed with Autosomal Dominant Polycystic Kidney Disease (ADPKD).

The project also entails a comprehensive evaluation of the ketogenic diet's impact on both renal function decline and changes in microbiota. This assessment aims to provide insights into the potential benefits or effects of the diet on these critical aspects of health.

To facilitate a cohesive and effective approach, the project aims to establish an integrated operational system that fosters seamless communication between hospitals and patients. This system ensures efficient coordination in the implementation of the ketogenic diet protocols, monitoring processes, and overall patient management.

#### 2.2.3. Study design

**Study characteristics:** The study will be observational and will involve patients (around 150 subjects) with Autosomal Dominant Polycystic Kidney Disease aged 18-60 years with a defined genetic cause of the disease, with baseline eGFR > 30 ml/min/1.73m<sup>2</sup>, randomized to receive a ketogenic diet (high-fat, moderate protein and low-carbohydrate intake based on a ratio of 10:4:1 (in grams) and calorie requirements based on specific patients' condition (at least 20-25 kcal/kg body weight) or a control group with a normal dietary approach.

**Ethical Committee authorization status:** The proposal will be submitted to the Ethical Committee within December 2023.

#### 2.2.4. Expected results

Task 5.2 expected outcomes include the:

- Demonstration of the impact of a ketogenic dietary approach on the disease progression in terms of increase of total kidney volume, cyst number and growth and the consequent decline of renal function over time.
- Improvement of remote monitoring of ADPKD patients and clinical outcomes by the introduction of specific wearable devices able to accurately detect and track patients' parameters and habits, including adherence to the prescribed diet and treatments.

### 2.2.5. Project progress

A pilot study proposal was submitted to the DARE coordinators in July, 2023. During the third trimester of DARE, the proposal underwent the scrutiny of referees from Spoke 3 and spoke 1. At the time of writing, the process has completed revision by Spoke 1.

## 2.3. Task 5.3 - NICU at home: a pilot study to promote family-centered care via telemedicine and e-health to prevent health issues in preterm and term infants (responsible: IRCSS-AOUBO)

### 2.3.1. Overview

Task 5.3 involves two clinical trials utilizing commercially available wearable devices for the continuous monitoring of preterm and term infants at risk for early adverse events and later neurodevelopmental impairment.

In Italy, approximately 1 in 14 newborns is born preterm, significantly impacting mortality and morbidity rates. Family-Centered Care (FCC) has been recognized for its role in fostering bonding, family involvement in infant care, reducing Neonatal Intensive Care Unit (NICU) stays, and improving clinical outcomes.

Sudden Unexpected Perinatal Collapse (SUPC) is a rare event, occurring in approximately 1 in 10,000 live newborns, with the highest incidence in the first hours of life. Despite its rarity, the consequences of SUPC can be substantial. Currently, the pathogenesis is not fully understood, and there is no established preventive tool for SUPC. Therefore, the project aims to leverage e-health tools and telemedicine to implement FCC in the NICU, enabling early discharge for preterm newborns. Additionally, it seeks to enhance early monitoring in healthy newborns in the delivery room and during rooming-in, allowing for the prompt recognition and management of adverse events such as SUPC.

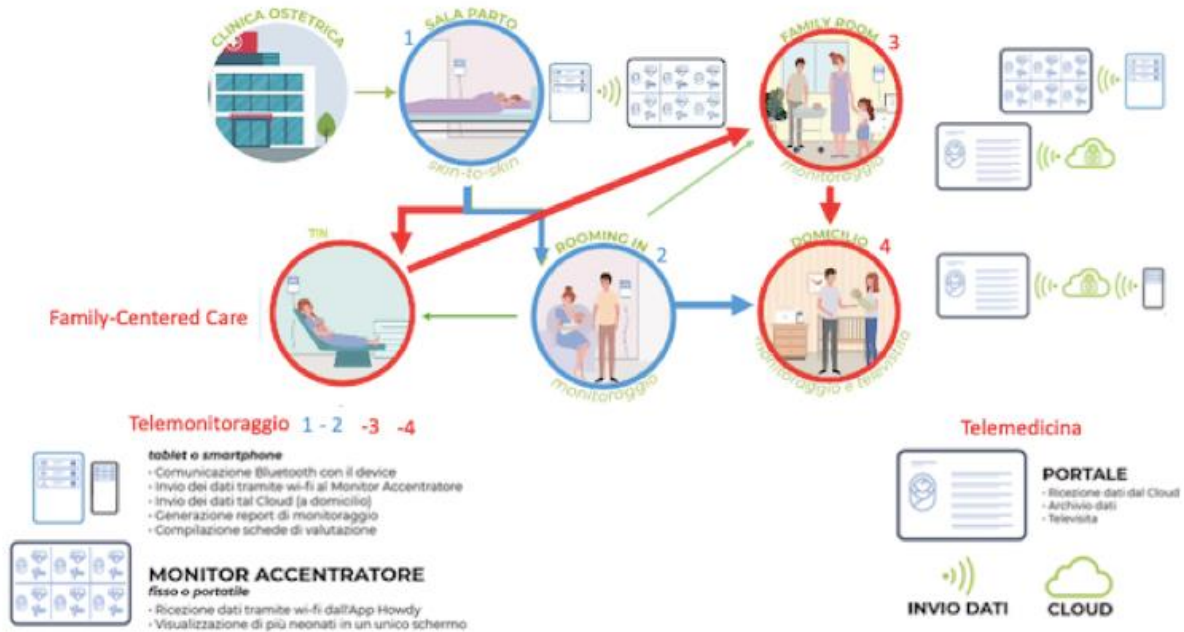


Figure 3. Graphical overview of Task 5.3

### 2.3.2. Objectives

#### General objective

Task 5.3 aims to assess how combining FCC with e-health tools and telemedicine prevents health issues and neurodevelopmental impairment in both term and preterm infants. The evaluation focuses on the integrated impact of these approaches, examining their collective effectiveness in promoting infant well-being and developmental outcomes.

#### Specific objectives

The initiative involves the implementation of FCC within the NICU setting, aiming to facilitate early discharge for preterm newborns. This implementation is augmented by the utilization of wearable devices, e-health tools, and telemedicine technologies, collectively contributing to a comprehensive approach in caring for preterm infants. These innovative tools enable continuous monitoring, enhancing the capacity for remote healthcare management and ensuring the well-being of preterm newborns.

Furthermore, the project seeks to enhance early monitoring practices in healthy newborns within the delivery room and during rooming-in. This strategic improvement aims to enable early detection and diagnosis of potential adverse events, such as SUPC. By leveraging advanced monitoring tools and a proactive approach to clinical management, the project aims to promptly address any unforeseen complications, ensuring the early and effective intervention in the event of adverse occurrences during this critical period of newborn care.

### 2.3.3. Study design

**Study characteristics:** The study will be an ambispective observational study with medical device involving preterm infants admitted to the NICU (40 subjects per year to be recruited) and healthy term neonates during the first hours/days of life (2000 subjects per year to be recruited).

**Ethical Committee authorization status:** The feasibility of the two pilot projects belonging to task 5.3 has been discussed with the Institutional Ethical Committee advisor. The draft of one of the projects has been shared with the Institutional Ethical Committee advisor, who required some changes and technical clarifications. The submission of the final draft to the Ethical Committee is planned in the next two months.

### 2.3.4. Expected results

Task 5.3 expected outcomes include:

- Potential Impact for Preterm Infants' Management: Enhancement of FCC is expected to contribute to an improved quality of life for both infants and their families. The implementation of FCC is anticipated to lead to a reduction in the length of hospital stays, subsequently lowering the risk of nosocomial infections, resulting in an overall enhancement of clinical outcomes.
- Potential Impact for Term Infants' Management: Improved diagnosis of SUPC events is anticipated to enable prompt clinical management of potentially life-threatening situations. The promotion of mother-infant bonding, facilitated by enhanced rates of breastfeeding, is expected to contribute to an overall improvement in clinical outcomes for term infants.

### 2.3.5. Project progress

The feasibility of the two pilot projects under Task 5.3 has undergone discussion with the Institutional Ethical Committee advisor. The projects' framework, encompassing methods, study design, and legal considerations, has been reviewed and approved by Spoke 1. Methodological evaluation from WP1 Spoke 3 has been obtained. Assessment of available spaces for Family rooms and various e-monitoring tools has been conducted in collaboration with IRCCS AOU BO and potential sellers.

Presentation sessions introducing the neonatal monitoring devices have been held for obstetricians and midwives in multiple meetings. Subsequent steps include organizing the tender procedure for e-monitoring tools and recruiting personnel through a dedicated procedure under the auspices of IRCCS AOU BO.

## 2.4. Task 5.4 - A digital, integrated and scalable mobile platform based on wearable sensors to prevent/reduce the risk of complications in type 1 diabetes (responsible: UNIROMA2; co-responsible: UNIPD)

### 2.4.1. Overview

Type 1 Diabetes (T1D) is a chronic disease consisting of a lack of insulin secretion by the pancreas. As a result, intensive insulin therapy, normally administered through smart pens or pumps, is mandatory. Despite the recent advances of wearable technologies and advanced decision support algorithms for T1D management, identifying the optimal strategy for T1D treatment remains a challenge, especially in pediatrics. In this population, T1D management presents unique challenges due to the evolving physiology and the need for close monitoring and intervention, and effective tools to help clinicians formulating optimal therapy recommendations are currently limited. In response to these challenges, this pilot project aims to develop and assess a new mobile platform integrating a clinical decision support system (DSS) designed to provide useful suggestions to tune and optimize key T1D therapy parameters in pediatrics. The DSS will incorporate advanced technologies such as continuous glucose monitoring (CGM) devices, smart insulin pens, and wearable physical activity trackers to collect large amounts of user-generated data. At its core, the system will leverage an open-source digital twinning methodology called ReplayBG to create virtual clones of patients, representing their unique physiological characteristics.

These virtual clones will then be utilized in multiple simulation iterations to personalize and optimize therapy parameters. Finally, to promote the transparency of the generated results, the DSS will employ a large-scale linguistic model to formulate clear explanations and contextual information regarding the recommended therapy parameters. The DSS will integrate these algorithms within a state-of-the-art digital platform to offer a user-friendly interface for patients and healthcare providers. The safety and feasibility of the DSS adoption in the current clinical practice, will be evaluated through a 6-months prospective study.

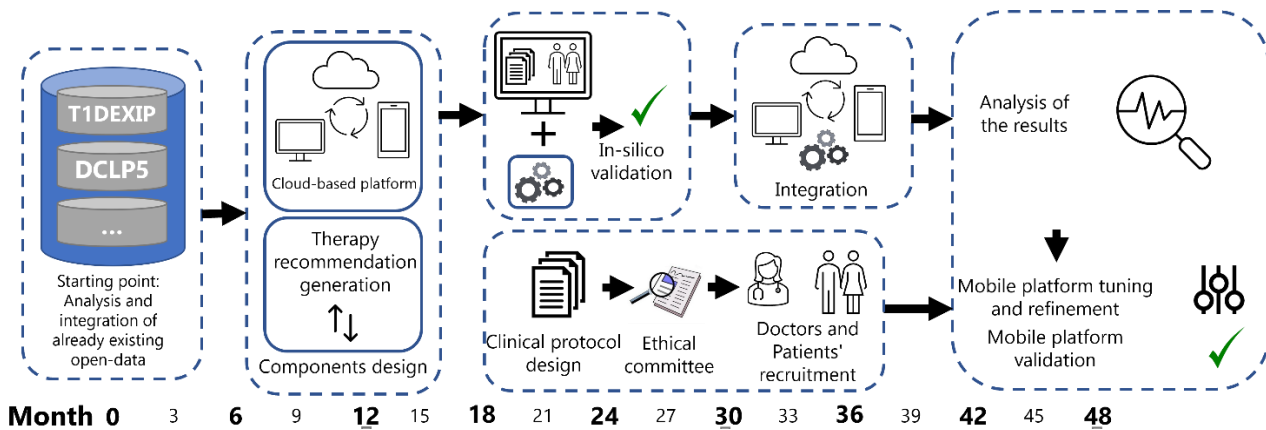


Figure 4. Graphical overview of Task 5.4

### 2.4.2. Objective

#### General objective

Develop and evaluate a digital platform for clinicians to automatically analyze wearable-derived data of pediatric population with T1D and generate useful insights and targeted therapy suggestions to support clinicians' decisions.

#### Specific Objectives

The project has several objectives:

- Developing an Innovative DSS: The primary aim is to create a novel DSS tailored for clinicians, enhancing the efficacy of treatment for the pediatric population with T1D.
- Integration of CGM, Wearable Devices, and Algorithms: Incorporating CGM, wearable devices, and advanced algorithms into a unified, modular, and mobile platform for comprehensive data analysis.

- **Introducing Digital Twinning Concept:** Introducing a groundbreaking approach to the DSS using the concept of digital twinning, capable of capturing both intra- and inter-patient physiological variability for a more nuanced understanding.
- **Utilizing Large Language Model for Explainability:** Deploying a technique based on a large language model to provide explainability for therapy optimization suggestions, ensuring clinicians comprehend and trust the recommendations.
- **Reducing Complications and Adverse Events:** Aiming to minimize the occurrence of complications and adverse events associated with T1D treatment through optimized therapy recommendations.
- **Feasibility and Safety Evaluation:** Conducting a dedicated clinical trial to assess the feasibility and safety of the platform, along with evaluating the effectiveness of the DSS in delivering personalized therapy recommendations for the pediatric T1D population.
- **Generating a Unique Pediatric T1D Dataset:** Generating a comprehensive dataset specific to the pediatric T1D population, with the goal of fostering future research endeavors in this critical healthcare domain.

### 2.4.3. Study design

**Study characteristics:** The study will be a randomized prospective two-arms study with medical devices involving pediatric patients with T1D with a disease duration of at least one year. Particularly, 80 T1D patients divided in 4 main groups according to age range and pubertal stage:

- 1-7 years of age (n=20, 10 people for each arm)
- 8-11 years of age + Tanner stage 1 (n=20, 10 people for each arm)
- 8-11 years of age + Tanner stage  $\geq 2$  (n=20, 10 people for each arm)
- 12-17 years of age + Tanner stage  $> 2$  (n=20, 10 people for each arm)

Data from CGM sensors, smart insulin pens, meals diary will be collected to optimize T1D therapy parameters which will be suggested to the clinician at each visit of the patient.

**Ethical Committee authorization status:** The proposal will be submitted to the Ethical Committee within January 2024, expecting an approval by October 2024. The clinical trial is expected to start in March 2025.

#### 2.4.4. Expected results

Task 5.4 expected outcomes include:

- Reduction of the burden on clinicians and clinical facilities to manage pediatrics with type 1 diabetes, measuring quality of life, fear of hypoglycemia, diabetes distress and glucose monitoring/insulin administration satisfaction through ad hoc questionnaires.
- Non-inferiority for percentage of time that the glucose level, as measured by the continuous glucose monitor, in the target range of 70–180 mg dl<sup>-1</sup> (3.9–10.0 mmol l<sup>-1</sup>) over the active treatment period between the two arms.
- More than 70% of accepted therapy optimization suggestions.
- Usability of the platform scored as excellent (i.e., score > 84) by both patients and clinicians according to the System Usability Score scale.

#### 2.4.5. Project progress

The pilot study proposal was submitted to the DARE coordinators on the second trimester of DARE initiative (April 15, 2023). During the next trimester, the proposal underwent the scrutiny of referees from spoke 3 and spoke 1. Currently, the pilot has been approved both from spoke 3 and spoke 1. Regarding the main activities, in the second trimester, Task 5.4 activities were formally initiated through a collaborative meeting between participating research units (UNIPD and UNIROMA2). During this meeting, the high-level design of the system architecture has been discussed and drafted. This allowed to identify project requirements in terms of data and enabling technologies and prioritize project activities. On August 1, 2023, the activities of Task 5.4 were disseminated by means of a conference paper describing the overall DSS design and architecture.

At the same time, open datasets crucial for the development and evaluation of the decision support system's methodological core have also been acquired. Dexcom and Novo Nordisk have been reached out to explore the possibility of acquiring their Software Development Kit (SDK) for integrating their smart insulin pen technology into our app. Additionally, the

protocol for submission to the ethical committee has been prepared, ensuring that the study adheres to all ethical standards.

Below, a graphical overview of the project progresses, and key milestones achieved in the first year of activities.

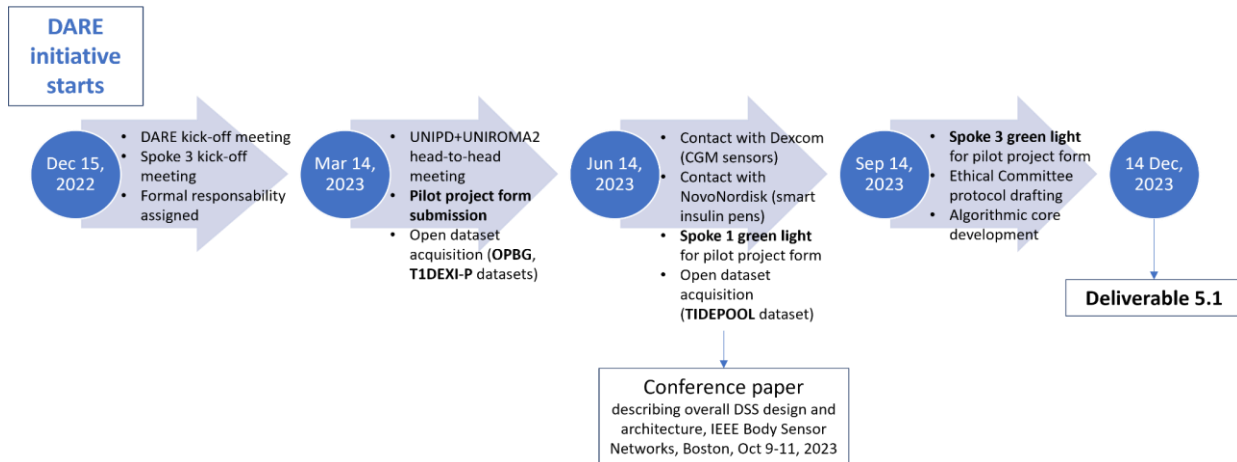


Figure 5. Graphical overview of the progresses and key milestones achieved in Task 5.4

## 2.5. Task 5.5 - FITMATE: Food Intake Tracker and Metabolic Evaluation for Health Enhancement (responsible: UNIPD)

### 2.5.1. Overview

Monitoring lifestyle, particularly caloric intake, and energy expenditure, poses a significant challenge for both individual and public health maintenance. Traditional methods, such as questionnaires, fall short in achieving an acceptable level of accuracy, with an estimated error of approximately 25% in daily caloric intake estimation.

This study seeks to address this challenge by developing a precise and stable algorithm for estimating caloric intake through the application of machine learning methodology. Initially, the study will focus on capturing categorized individual eating activities within specific populations, particularly those with special diet requirements, to inform algorithm development. Subsequently, the study will extend its scope to include healthy individuals within the Italian population.

Utilizing raw data collected from wearable devices, the study will employ an up-to-date machine learning approach to accurately predict the caloric contribution of individual

eating activities. The goal is to enhance the accuracy of caloric intake estimation, thereby contributing to more effective lifestyle monitoring and improved public health outcomes.

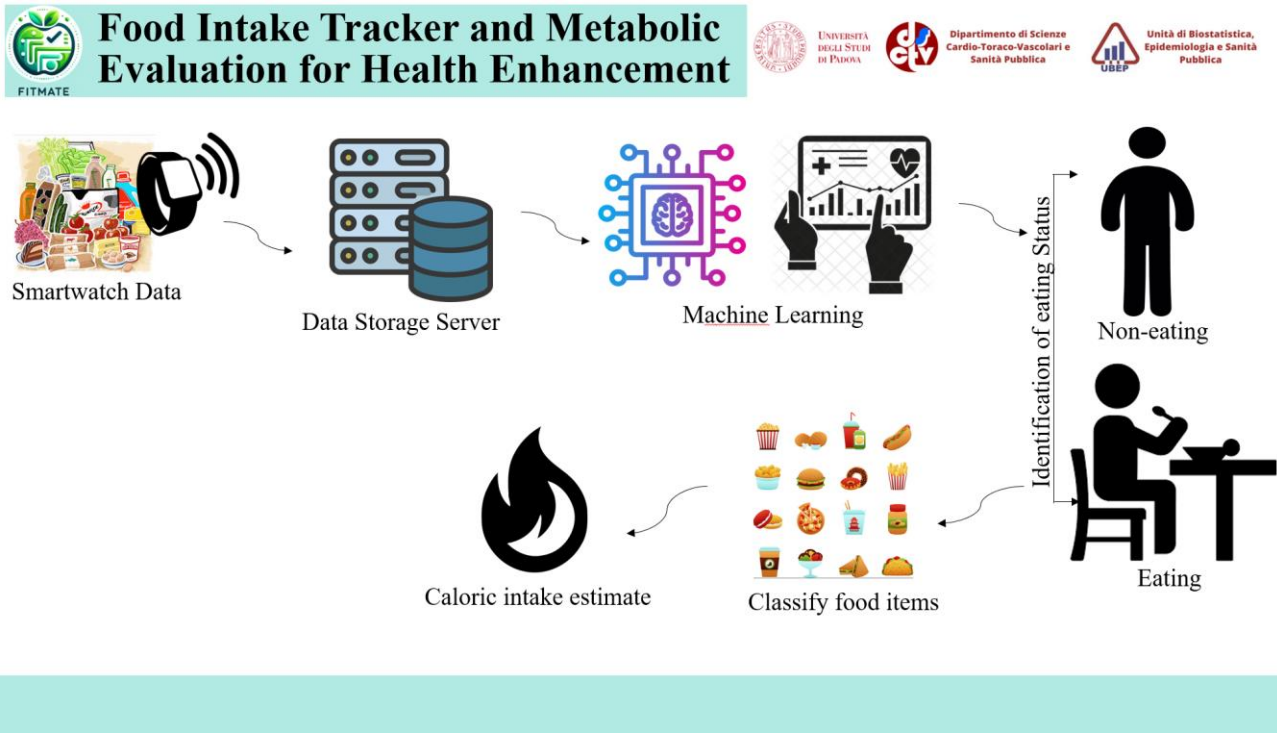


Figure 6. Graphical overview of Task 5.5

### 2.5.2. Objective

#### General objective

This study aims to estimate caloric intake using smartwatches and machine learning models. Focusing initially on individuals with special diets, the research then extends to the general population. By analyzing signals from wearable devices, the study seeks to enhance accuracy in estimating caloric intake, providing practical insights for improved fitness and lifestyle management.

#### Specific Objectives

Specific objectives of this task are twofold:

- **Objective Evaluation of Caloric Intake:** The study aims to assess caloric intake without requiring active participation from subjects. By adopting an objective evaluation approach, the research seeks to minimize the impact of subjective reporting and potential biases in measuring caloric intake.

- **Monitoring Food Types Ingestion in Fragile Populations:** The study places a specific focus on monitoring the ingestion of different food types, particularly in populations with specific health considerations such as polycystic kidneys, phenylketonuria, or diabetes. These populations are often fragile, and monitoring their food intake is critical for managing their health effectively.

### 2.5.3. Study design

**Study characteristics:** The study will be ambispective observational with medical device. Both data from a former project (NOTION) (adapted for this pilot) and new data from newly enrolled subjects will be used.

The prospective part of the study will consist of two phases: in the first phase (pilot development), 200 patients with diseases that requires a particularly strict diet (i.e., with phenylketonuria - PKU, diabetes or on ketogenic diet for polycystic kidneys) will be followed by a nutritionist that compile a precise food diary. In the second phase, the general population (from 800 to 1000 subjects) will be involved.

**Ethical Committee authorization status:** The proposal will be submitted to the Ethical Committee within December 2023.

### 2.5.4. Expected results

Task 5.5 expected outcomes include:

- **Improved accuracy in estimating caloric intake:** The development of a precise and stable algorithm for estimating caloric intake using machine learning methodology is expected to significantly improve the accuracy of estimating caloric intake, with a targeted error rate of less than 10%.
- **Improved monitoring of food types ingestion:** The proposed algorithm is expected to accurately predict the caloric contribution of individual eating activities, which will enable better monitoring of food types ingestion in particularly fragile populations, such as those with phenylketonuria or diabetes.

### 2.5.5. Project progress

A pilot study proposal was submitted to the DARE coordinators in March 2023. During the second trimester of DARE, the proposal underwent the scrutiny of referees from Spoke 3, WP1 (statistics) and Spoke 1 (methodology and terminology). The final version of the pilot

was sent to the Spoke 3 coordinators on October 18<sup>th</sup> 2023. The project was named as “FITMATE: Food Intake Tracker and Metabolic Evaluation for Health Enhancement”. An assistant professor (RTDa) position was opened, and the selection was won by Dr. Luca Vedovelli that took service in August (4/08). Moreover, a PhD position was opened, and Dr. Mohammad Junayed Bhuyan won the selection and officially enrolled the PhD program that started on October 1st. We conducted a literature survey on available and state-of-the-art methodologies for the analysis of wearable devices data, including grey literature. We developed multiple pipelines to get data from the devices of different vendors (Garmin and FitBit) exploring the possibility of a direct interface with RedCap database through an open-source R package that is being developed. Data from a former project involving wearable devices (NOTION) were accessed and tidied for the first tests on machine learning algorithms with simple tasks (i.e., to detect if the subject is eating or not).

## **2.6. Task 5.6 - Developing of a social and health care integrated model to reduce the overcrowding of Emergency Room and inappropriate hospital admissions (responsible: UNIROMA2)**

### **2.6.1. Overview**

Overcrowded Emergency Rooms (ER) pose a significant public health emergency, characterized by inappropriate accesses and challenges in accessing in-hospital services. This situation is further exacerbated by difficulties in inpatient discharge. The hindrances to discharge are, in part, attributed to the lack of effective out-of-hospital care, where health and social professionals operate in isolated silos due to the absence of integration in funds, procedures, tools, and measurable outcomes.

The pilot initiative seeks to test a health and care integration model, commencing with the identification of Frequent Users (FU) of the ER – patients accessing the ER more than four times in a year. This integration is reinforced by the incorporation of telemedicine and Artificial Intelligence (AI) support. Additionally, the pilot aims to develop an algorithm capable of predicting the risk of extended Length Of Stay (LoS) for inpatients aged over 65. The objective is to implement appropriate interventions to prevent prolonged hospital stays, involving community care services.

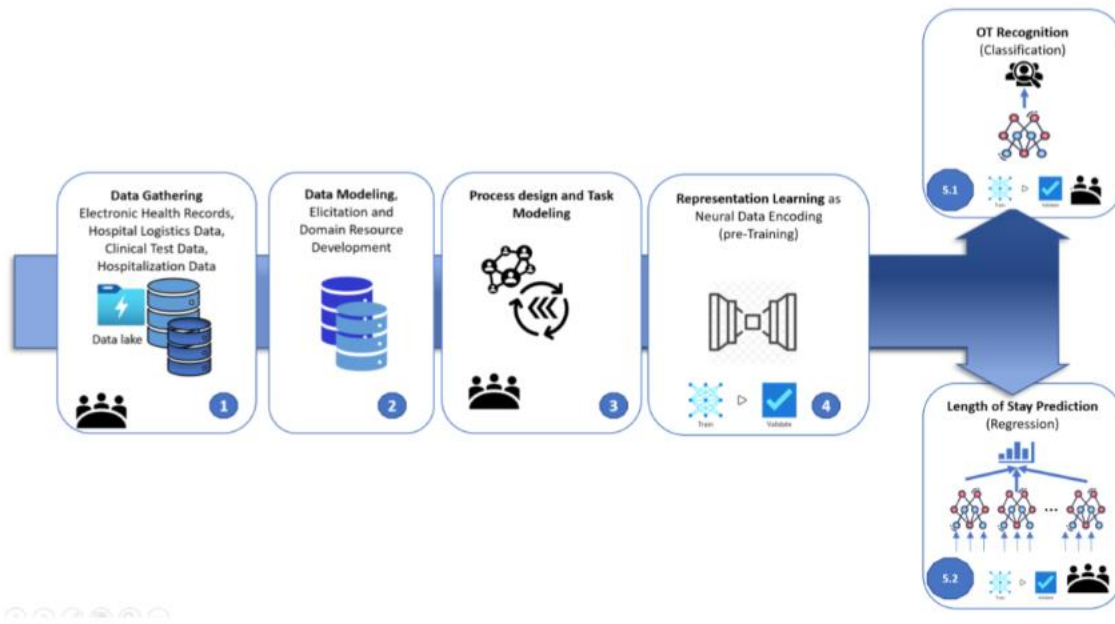


Figure 7. Graphical overview of Task 5.6.

### 2.6.2. Objective

#### General objective

The project aims to utilize AI for predicting in-hospital length of stay, preventing admissions beyond DRGs' threshold, and reducing Emergency Room visits by Frequent Users. Through AI-driven insights, it seeks to optimize hospital resource use, enhance patient care, and address the specific needs of frequent ER visitors efficiently.

#### Specific Objectives

The project involves the establishment of a sophisticated algorithm designed to profile the risk of various negative events, including but not limited to deaths, multiple hospitalizations, and extended Lengths of Stay (LoS) surpassing the average defined by Diagnosis-Related Groups (DRGs).

Simultaneously, the initiative seeks to implement an integrated operational system that seamlessly connects hospital activities with telemedicine. This integration is pivotal in fostering a cohesive approach to healthcare, where data, communications, and interventions between hospital-based services and telemedicine activities are harmonized.

### 2.6.3. Study design

**Study characteristics:** The study will be ambispective and will consist of collecting retrospective information from the hospital database and continue to include ongoing information from in-patients admissions and ER accesses. Study target populations will make up by individuals accessing the University Hospital ER more than 4 times in a year, and individuals older than 65 years, who experienced an admission longer than the average for the DRG reported in the Hospital Discharge Form. Both populations should be made by 400 individuals each.

**Ethical Committee authorization status:** The proposal will be submitted to the Ethical Committee within December 2023.

### 2.6.4. Expected results

Task 5.6 expected outcomes include:

- Early (at the time of the ER access or in the first 3 days of in-patient's admission) identification of subjects both repeatedly accessing ER and/or candidate to longer LoS;
- More than 20% identified as at risk of Multiple Accesses/admissions longer than the threshold followed up by telemedicine/telemonitoring systems.

### 2.6.5. Project progress

A pilot study proposal was submitted to the DARE coordinators in June 2023. During the third trimester of DARE, the proposal underwent the scrutiny of referees from spoke 3 and spoke 1. At the time of writing, the process is still ongoing with spoke 1, on the issue of privacy when using AI to analyze data stemming from the hospital database. This activity is the core of the project and focus of discussion is about use of data of previous access to the ER and hospital wards already collected, or to start knowing collecting data under a new consent form. Probably, the final solution will be a mixed approach (retrospective for wards admissions covered by a detailed consent form and prospective for the ER accesses). At the same time the project staff worked in close collaboration with the spoke 1 staff for designing the model of AI to be implemented: the different sources of data have been identified and the machine learning model have been drafted and it is under evaluation. The protocol to implement the data collection has been drafted to provide ongoing data to the evaluation model to increase its validity over time.

### 3. Conclusion and next steps

The key features of model design are summarized in the following synoptic table, which shows that the devised architecture of the six pilot studies meets the general aim of testing new procedures to integrate ICT technologies into clinical and prevention pathways.

Task	Task responsabile	Task leader	Title	Tools	N patients	Expected outcome
5.1	IRCCS-AOUBO	M Salice	<b>IBD care through hub &amp; spoke infrastructure</b>	Data collection tool filled by clinicians and patients	Up to 10000 patients with IBD	standardize patient management between hub and spoke centres
5.2	UNIBA	L Gesualdo	<b>Digital therapy and telemedicine approaches for nutritional intervention in chronic diseases</b>	Wearable devices integrated in an IoT infrastructure	150 patients with CKD	Improving Monitoring of patients with Chronic Kidney Disease
5.3	IRCCS-AOUBO	MG Capretti	<b>Prevention of adverse events in preterm and term infants by remote monitoring</b>	Wearable devices for continuous monitoring	About 2000 pediatric patients	Improving quality of life and clinical outcomes of pre-term/ term infants
5.4	UNIROM A2 (co-responsible UNIPD)	S Cianfarani (co-leader A Facchinetti)	<b>A digital, integrated and scalable mobile platform based on wearable sensors to prevent/reduce the risk of complications in type 1 diabetes</b>	Virtual clones of patients supported by advanced tech devices	80 T1D patients younger than 18 years	Set up a Decision Support Systems able to improving quality of life of patients and optimize clinical performances
5.5	UNIPD	D Gregori	<b>Monitoring Caloric Intake and Lifestyle at Population Level via Non-Medical Wearable Devices</b>	Machine Learning methodology to develop an algorithm for estimating caloric intake	About 1200	Accurate prediction of individual caloric intake to improve the management of diet for patients affected by metabolic diseases
5.6	UNIROM A2	G Liotta	<b>Developing of a social and health care integrated model to reduce the overcrowding of Emergency Room and inappropriate hospital admissions</b>	Development an algorithm to predict the risk of longer hospital length of stay or multiple accesses to ER	About 10.000	Early (at the time of the ER access or in the first 3 days of in-patients admission) Identification of subjects both repeatedly accessing ER and/or candidate to longer LoS



At the time of writing, the development of the pilot studies is in line with the timing of the DARE project. The objectives of the pilot studies are clearly defined and appropriate to the scope of the program. The collaboration with Spoke 1 and with WP1 of Spoke supported pilots design in legal, technological and statistical aspects. All the pilots have presented the ethical committee authorization request, which is of crucial importance considering that the pilots deal with delicate issues related to the use of personal data by implementing new approaches based on emerging technologies.