

**DARE**

**DIGITAL LIFELONG PREVENTION**

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Spoke 3 Deliverable

**S3.D1.3 Communication and  
Dissemination plan for Spoke 3**

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## S3.D1.3 Communication and Dissemination plan for Spoke 3

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## Publishable Summary

In Spoke 3 of the DARE project, titled 'Digitally-enabled secondary and tertiary prevention', WP1 is dedicated to devising and implementing an effective communication and dissemination plan. A critical challenge is integrating digital communication tools into clinical settings to maximize their impact. This is precisely what Spoke 3's initiatives strive to achieve. WP1's encourages and help developing tailored communication protocols that leverage digital tools to enhance secondary and tertiary prevention efforts. The presented initiatives, coming from the strategies of 38 pilots, encompass a diverse array of digital platforms, from social media channels to more specialized communication tools, catering to various demographic groups like infants, older adults, and patients with chronic conditions such as diabetes, inflammatory bowel disease (IBD), and kidney disease. These efforts are aimed at not just improving patient outcomes but also enhancing the efficiency of healthcare services. The first year has seen significant progress in defining these communication strategies and identifying key performance indicators to assess their effectiveness. Ensuring these communication methods are robust and well-integrated into clinical practice remains a priority for the success of the project.

## 1. Introduction

### 1.1. WP1 overview and aims

Within Spoke 3 “Digitally-enabled secondary and tertiary prevention” of the DARE project, one of the WP1 aims is coordination, harmonization, and implementation of a comprehensive Communication and Dissemination Plan. The primary aim of WP1 is to enhance the effectiveness of communication strategies in various healthcare settings, targeting a wide range of populations from infants to older adults. Utilizing digital platforms and tools, WP1's objectives include the integration of innovative communication methods like social media, mobile apps, and digital information systems to support secondary and tertiary prevention. The emphasis is on creating communication models that are adaptable and effective in disseminating crucial healthcare information and in engaging diverse patient groups. WP1's initiatives are designed to not only improve patient awareness and engagement but also to facilitate better healthcare practices through efficient information dissemination. The use of digital communication tools is expected to lead to improved healthcare outcomes, increased patient compliance, and more effective prevention strategies. These initiatives will also aim to reduce misinformation and enhance the overall quality of healthcare communication, thereby positively impacting healthcare efficiency and resource allocation. Furthermore, it is essential to underscore that the emerging results from the DARE pilot projects are poised to influence not only clinical and therapeutic aspects but also to foster significant economic savings in the National Healthcare System (NHS). This is achieved by introducing innovative methods for the prevention and monitoring of diseases, which could reduce the incidence and severity of complications, thereby decreasing the associated long-term treatment costs. The effective dissemination of these findings to health policy makers is crucial, as it can inspire a revision and updating of current monitoring and prevention procedures. This process will not only improve the quality of care but also optimize resource allocation, leading to more efficient management of NHS funds.

## 1.2.Task status at month 12

A relative heterogenic situation was delineated along the pilots where, the most advanced in terms of development are already planning to present their methodologies and early findings at international meetings specific of their fields.

Along with the traditional ways of knowledge dissemination (i.e., peer-review publishing and meetings) we asked the pilots to also monitor and specifically evaluate the impact of their work for example monitoring the number of citations, peers' feedback at meetings, online engagement analytics, stakeholder feedback, and pre and post intervention surveys.

## 1.3.Deliverable outline

Section 2 reports, at the single pilot level, a description of communication and dissemination activities, specifying specific activities, target audience, objective and expected impact, how the researchers plan to gather feedback, and finally how they plan to evaluate their impact.

## 2. Research concept and design

### 2.1.Task 2.1 - A Digital Twin technology to monitor the risk of fragility bone fractures in osteoporotic patients (responsible: Fabio Baruffaldi - IOR)

#### 2.1.1. Title

A Digital Twin technology to monitor the risk of fragility bone fractures in osteoporotic patients.

#### 2.1.2. Abstract

The pilot consists in the adoption of the BBCT-hip digital twin technology within a clinical study carried out in Rizzoli Orthopedic Institute. BBCT-hip is able to predict the subject-specific risk of fracture at the proximal femur starting from the femur Computed Tomography (CT) images of the subjects, their weight and height. The clinical study aims to enrol about 150 fractured subjects and 150 control subjects and to implement BBCT-hip

on them. Comparing BBCT-hip outcome between the fracture and control group a cross-sectional study will be performed, allowing to assess BBCT-hip classification accuracy. Moreover, the control group will be follow-up for 5 years to identify any femur fracture events, allowing to assess BBCT-hip predictive accuracy as well.

### 2.1.3. Description of Communication and Dissemination Activities

The outcomes of the pilot will be mainly disseminated through scientific publications in peer-reviewed journals and international/national conferences.

Both clinical and more engineering-related peer-reviewed journals will be targeted: Bone (Elsevier), Osteoporosis International (Springer), Clinical Biomechanics (Elsevier).

The pilot outcomes will be presented both in biomechanics and clinical conferences, such as Congress of the European Society of Biomechanics, International Symposium on Computer Methods in Biomechanics and Biomedical Engineering, Conference of the European Calcified Tissue Society, Annual Meeting of the American Society for Bone and Mineral research, Virtual Physiological Human conference.

### 2.1.4. Target Audience

The target audience is wide and diversified. On one hand dissemination activities will be targeting researchers in bioengineering working on analogous in silico methodologies. On the other hand also clinicians will represent a crucial target to enhance the performances of similar clinical studies. Eventually also regulators could play an important role in granting support to eventually bring BBCT-hip or similar technology within the clinical practice.

### 2.1.5. Objectives and Expected Impact

- Engagement of further clinical partners
- Engagement of regulators

### 2.1.6. Feedback and Evaluation

The effectiveness of dissemination and communication activities will be mainly evaluated through number of citations, peers' feedbacks during conferences/meeting and above all engagement and feedbacks of new stakeholders.

## 2.2.Task 2.2 - Predicting risks of Osteoarthritis and Joint Replacement failure (responsible: Matteo Berni - IOR)

### 2.2.1. Title

Predicting the risk of Osteoarthritis and Joint Replacement failure.

### 2.2.2. Abstract

The pilot aims to develop preliminarily digital health technologies quantifying the risk of a knee adverse event, i.e., progression of osteoarthritis, and failure of the joint replacement. More in detail, and concerning the management of osteoarthritis, a clinical study will be conducted on subjects more prone to the development and progression of the pathology. The physiopathological condition of the knee will be investigated prospectively through clinical, i.e., magnetic resonance imaging, and functional assessments, i.e., gait analysis. By combining functional and clinical assessment, patient-specific multibody dynamic models will be implemented, with the purpose of getting insights into the loading pattern distribution within the joint. Aiming to improve the diagnostic capability of clinical imaging, an ex-vivo study evaluating the relation between joint status and tissues' structural and mechanical features will be performed. The outcomes retrieved by the developed in-silico framework will be compared to the standard clinical scoring system, i.e., Kellgren-Lawence, of osteoarthritis (OA), aiming to provide a sensitive approach quantifying the risk of progression of the pathology.

Regarding the estimation of the joint replacement failure risk, the study will focus on the prediction of the contact mechanics peculiar of total knee replacement. In this regard, clinical imaging and functional assessments retrieved by a retrospective study will serve as input for a Finite Element (FE) model. More in detail, the relative pose of the tibial and femoral components, extracted during daily living activities in the post-operative phase will be employed to predict key parameters defining the functionality of the joint, e.g., defined by the sliding distance and contact pressure on the tibial insert component. The predicted results will be analyzed and compared to clinical outcomes obtained from questionnaires administered to patients.

### 2.2.3. Description of Communication and Dissemination Activities

The peculiarities of the health technologies developed within this pilot study, together with the relative outcomes will be disseminated through international/national conferences and scientific publications in peer-reviewed journals.

The developed methodologies and the outcomes retrieved by the pilot will address mainly engineering- and clinical peer-reviewed journals, e.g., Journal of the Mechanical Behavior of Biomedical Materials, Osteoarthritis and Cartilage, Journal of Biomechanics (Elsevier), IEEE Journal of Biomedical and Health Informatics (IEEE), Annals of Biomedical Engineering, International Orthopaedics, Biomechanics and Modeling in Mechanobiology (Springer).

Concerning meetings, the pilot outcomes will be presented mainly in biomechanics conferences, organized e.g., by the International/European Society of Biomechanics (ISB/ESB), the Orthopaedic Research Society (ORS), the European Society of Movement in Adults and Children (ESMAC).

### 2.2.4. Target Audience

Communication and Disseminations activities will be targeting researchers working on the methodologies peculiar of the pilot. Clinicians will be an additional target audience, whose suggestions will be crucial to enhance the effectiveness of the developed methodologies aiming to endorse their employment in the clinical practice.

### 2.2.5. Objectives and Expected Impact

- Engagement of further research partners
- Engagement of further clinical partners

### 2.2.6. Feedback and Evaluation

The effectiveness of dissemination and communication activities will be mainly evaluated through i) peers' feedbacks during conferences/meeting, ii) number of citations of scientific publications, and iii) feedbacks of clinicians.

## 2.3.Task 2.3 - Personalized functional models for pre-operative planning of High Tibial Osteotomy (responsible: Claudio Belvedere - IOR)

### 2.3.1. Title

Personalized functional models for pre-operative planning of High Tibial Osteotomy.

### 2.3.2. Abstract

The degree of interaction between surgeons, bioengineers and industry in high tibial osteotomy (HTO), and in knee osteotomy in general, is low. Just a general design of the procedure is offered by one hand (i.e., industry), and little modifications plus the approval are provided on the other hand (i.e., surgeon). To this end, a few tools are on-site applications, proprietary of the industry. Furthermore, the remote access to imaging, modelling and design software tools are still very much necessary for those surgeons working in small centres, also to support strict interactions with designers. This access also is about large clinical datasets, and implies data to be anonymized. The major objective of this pilot is to arrange an accessible platform for 'smart' planning of personalized knee osteotomies, whose operability is tested in a selected group of distributed specialized surgeons. The platform will be created and standard HTO cases planned and operated accordingly. This "smart" approach for personalized knee osteotomy is expected to have positive effects on the workflow of surgical planning, possibly also reducing surgery and hospitalization times. In addition, this allows access to modern tools and high-level expertise even remotely, thus providing excellent services to all citizens, as well as socioeconomic equity in health care.

### 2.3.3. Description of Communication and Dissemination Activities

The pilot addresses a complex and multidisciplinary clinical issue, which involves a number of different disciplines, such as orthopedics, medical imaging, biomechanics, CAD modeling, information technology, etc. Therefore, communication and dissemination related to this pilot should be directed to all the relevant communities. The professionals involved in the present pilot, particularly those surgeons working in the area of HTO and in knee osteotomy in general, and those biomechanical and technological experts, are among the world's leading experts; thus, the technical and clinical solutions which are going to be identified in the pilot, as well as the related results of the study, will likely be

well received at national and international conferences, as well as in peer-reviewed journals. The establishment of the proposed new web-based interactive smart platform that can be accessed by a large number of authorized persons, even from different hospitals, should have a likely return on the organization of health care related to this surgical procedure, very frequently performed in Italy.

Abstracts will be sent to the conference organizers for possible oral or poster presentations. Manuscripts including text, figures and tables will be sent to major international journals. Communities and scientific societies for surgeons, their journals and international channels will all be considered; the language will be English, to give the project and the results greater visibility and to reach as many stakeholders as possible.

#### 2.3.4. Target Audience

We intend to reach out first to researchers and scientists, those in the disciplines mentioned above, to share concepts and preliminary results and to receive support and possibly suggestions. Surgeons will be involved then, as here above. Eventually, with the established tool in our hands, policymakers as well as relevant stakeholders in Orthopedics will be informed, through appropriate channels.

#### 2.3.5. Objectives and Expected Impact

With the definition of this interactive web-based smart planning platform made accessible to a large number of professionals, it is hoped to arouse greater and deeper interest in surgeons toward surgical planning in the field of knee osteotomies, as well as larger knowledge (also in patients) of what digitization in Orthopedics and in Personalized medicine can achieve nowadays. It is also expected that with the dissemination of the culture of planned, rapid, accurate and effective knee osteotomy, many more patients affected by gonarthrosis request medical examination earlier, before the final stage of joint arthritis, possibly at the time when osteotomy can still be performed and total knee replacement can be delayed or avoided. This may have a great impact in the national health care system, where nearly one hundred thousand knee replacements are performed every year. Knee osteotomy definitely is less expensive and less invasive, and also faster, and with reduced hospitalization and rehabilitation time, for final benefit for patients and NHS.

### 2.3.6. Feedback and Evaluation

For the scientific part of communication, participants in presentations, acceptance of journal editors, and citations of articles are expected and easily counted. Proposals, outcomes and general findings related to this pilot will be discussed also with policymakers in Orthopedics, mainly in meetings and direct contacts, where relevant feedbacks will be experienced immediately.

## 2.4.Task 2.4 - Predicting the risk of bone fracture in patients with metastatic carcinoma (Laura Campanacci - IOR)

### 2.4.1. Title

Predicting the risk of bone fracture in patients with metastatic carcinoma.

### 2.4.2. Abstract

Bone metastatic cancer management is a growing problem due to the improved prognosis offered by cancer therapies. The risk of under or overtreatment is common, thus raising healthcare system expenses and discomfort to patients. The main aim of this pilot project is to define and evaluate prognosis and fracture risk more efficiently and accurately, aiming to provide personalized treatment in a multidisciplinary care setting for patients with metastatic cancer. Due to the complex nature of the task, we will begin by considering patients affected by proximal femoral metastasis and a mechanistic biophysical model. The biophysical model is a digital twin methodology that uses a subject-specific FE model to predict femoral bone strength. Quantitative Computed Tomography (QCT) scans of the hip region and patient data (e.g., weight, height) inform a patient-specific computer model capable of predicting the risk of femoral fracture at the time the CT is performed. Different loading scenarios will be considered, such as walking, side-falling, stair climbing, in order to have a comprehensive overview of metastatic femur fracture risk.

By using digital methodologies, we expect to better predict the prognosis of bone metastatic patients as well as the risk of fractures. The system should enable a transition from a subjective clinic's single experience to a big-data-based result of a machine learning approach; hence, decisions will be more objectively supported by a Decision Support System (DSS).

We also aim to obtain a dataset from a retrospective study to train an AI-based algorithm supporting healthcare providers in defining the optimal personalized bone metastatic treatment.

#### 2.4.3. Description of Communication and Dissemination Activities

Dissemination and communication activities performed using various methods and channels are essential for the amplification of impacts, and are targeted to: Oncology patients, Caregivers, Hospital managers, Health/eHealth technology developers, Healthcare providers, Healthcare personnel, Oncology Health Professionals (Surgical oncologists), Scientific/Medical Community, Quality and Patient safety professionals, University students.

Dissemination and communication will be performed through:

- Publication of results in Open Access journals (e.g., Quality and Safety in Healthcare, Journals on management of tumors and metastases);
- International conferences, which provide a valuable platform for the immediate presentation of results and will be seen as a major means of dissemination.

Scientific journals focused on cancer treatment, both clinical and surgical. National (i.e. Italian Sarcoma Group annual meeting) and International (i.e. annual meeting of the European Musculo-Skeletal Oncology Society and International Society of Limb Salvage) meetings focused on oncological patients, metastatic patients, local and systemic treatment of bone metastases.

We also plan to implement specific communication through institutional social network.

#### 2.4.4. Target Audience

Oncology patients, Caregivers, Hospital managers, Health/eHealth technology developers, Healthcare providers, Healthcare personnel, Oncology Health Professionals (Surgical oncologists), Scientific/Medical Community, European Commission, Quality and Patient safety professionals, University students, Local health authorities.

#### 2.4.5. Objectives and Expected Impact

The aim is the production of a context-specific dissemination and communication strategy designed to ensure effective communication of the project's objectives, ongoing work, research findings, final outcomes and product to predefined stakeholder groups.

The overall aim is to ensure communication consistency across the project work packages and communication platforms.

The expected impact is to develop interpretable predictive models based on fuzzy reasoning that support doctors' decisions on possible treatments.

#### 2.4.6. Feedback and Evaluation

A feedback and evaluation of the effectiveness of dissemination and communication of the project will be obtained by number of citations, peer's feedback at meetings.

### 2.5.Task 2.5 - Cardiovascular radiomics to stratify risks of post-operative adverse events (responsible: Francesco Garaci - UNIROMA2)

#### 2.5.1. Title

Cardiovascular radiomics to stratify risks of post-operative adverse events.

#### 2.5.2. Abstract

Coronary artery disease (CAD) and stroke are the leading causes of death and disability in the world. There is a close link between the two diseases; in fact, the prevalence of CAD is consistent in patients with stroke, even in those asymptomatic for coronary artery disease, this is because the two diseases share common risk factors and similar pathophysiological bases, often related to the atherosclerotic process. Over the past two decades, the mdc angio-CT study has assumed an increasingly prominent role in the early diagnosis of stroke and the evaluation of CAD. There is great interest in the literature in the search for blood biomarkers that can guide clinical decision making in stroke patients. The literature has also drawn attention to several blood biomarkers that appear to be associated with features of coronary plaque instability and vulnerability. It has been shown that cardiac computed tomography angiography (CCTA) is an optimal on which to perform Texture Analysis (TA). Radiomics has already been shown to improve the performance of CCTA.

#### 2.5.3. Description of Communication and Dissemination Activities

The Pilot addresses a complex and multidisciplinary clinical issue, which involves different disciplines, such as radiology, neurology, and cardiovascular diseases.

Therefore, communication and dissemination to these disciplines' world shall address the relevant communities. We are certain that communication and dissemination to the world of these disciplines should target interested communities through national and international conferences, as well as in peer-review journals. Regional and national health policy references will also be kept up-to-date, for the likely return to health care organization.

Because the communities and the topics are very relevant, international communities, journals and channels will be used, and the language shall be English.

We will use abstract for inclusion in international conferences and original papers for publication in international journals.

#### 2.5.4. Target Audience

Our target audience will mainly be researchers in the disciplines mentioned above, to communicate and deepen preliminary findings, including through an exchange of views with other experts.

We also think that the results, disseminated through known channels, may be of corporate interest for the purpose of economic and health management of the Patient under our study.

#### 2.5.5. Objectives and Expected Impact

The goal of the project is to provide a stroke risk score based on specific CT features of coronary atheromasic disease.

We want to be able to identify CT features of coronary plaque related to high stroke risk. And in this way improve secondary prevention in cerebrovascular disease using noninvasive imaging.

#### 2.5.6. Feedback and Evaluation

For the scientific part of the communication, participants to the presentations, acceptance of the journal editors, citations of papers are expected and easily countable. The recommended overall procedures will be discussed mostly in meetings and direct contacts, and the honest feedback will be experienced straightaway.

## 2.6.Task 2.6 - Risks of Sleep Disorders in Older Sarcopenic and Physical Frail Patients (responsible: Marcello Maggio - UNIPR)

### 2.6.1. Title

The role of sleep disorders in the motoric and cognitive trajectories of older physical frail sarcopenic and healthy active subjects (SOMNUS-DARE).

### 2.6.2. Abstract

Sleep physiology, skeletal muscle and bone health, body composition, cardiovascular system, cognitive and motoric functions are strictly interconnected. However, how sleep disorders, sarcopenia, impaired bone and systemic metabolism, physical frailty and cognitive decline mutually interact is still far from being clarified. Sleep disorders should not be considered as normal age-related changes. During aging, brain, cardiovascular physiology, as well as several components of body mass and function (skeletal muscle, adipose tissue and bone) are affected by sleep health. In current clinical practice, sleep disorders are not routinely screened and monitored. They usually require second level techniques (with higher healthcare systems and patient costs) often not integrated in the comprehensive assessment of older patient. Sarcopenia is one of the most important determinants of physical frailty and is influenced by sleep duration through different mechanisms. According to restorative theory, protein synthesis, muscle repair, the release of anabolic hormones (growth hormone, IGF-1, testosterone and insulin) involved in restoration of muscle structure, strength and function occur during sleep. All these factors have a circadian rhythm, and chronic insomnia may induce the dysregulation of the hypothalamus-pituitary-peripheral glands axes<sup>1</sup>.

The restoration of favorable sleep patterns could be a promising preventive and therapeutic strategy for attenuating the age-related dysregulation of somatotropic and hypothalamus-pituitary-adrenal axes, stimulating muscle recovery and delaying sarcopenia onset and progression. Epidemiological studies performed in community-dwelling elders have found a U-shape relationship between the risk of sarcopenia and either short or long sleep duration, compared to normal sleep duration. Similarly, usual short ( $\leq 5$  hours per day) and long ( $\geq 8$  hours per day) sleep duration were both associated with lower lean mass and higher fat mass, compared with normal sleep duration. These



data suggest that sleep disorders could affect body composition phenotypes in humans; in particular, body adiposity, sarcopenia and physical frailty are fundamental patterns of sarcopenic obesity. The association between sleep disorders and changes in body composition, namely sarcopenic-obesity, and sarcopenia, has proven to be bidirectional. Findings from both the EPISONO and ELSA-Brasil studies have shown that obstructive sleep apnea and nocturnal hypoxia are related to sarcopenic obesity. The risk of obstructive sleep apnea is greater in older obese adults with low muscle mass and low muscle strength. The coexistence of sleep disorders and unfavorable changes in body composition, including sarcopenia, may further worsen the consequences of the individual components. Thus, understanding the intertwined pathophysiological mechanisms (Figure 1) shared by these conditions could be crucial to highlight potential targets for future interventions aimed at preventing and mitigating multimorbidity, physical and cognitive frailty. The overall world prevalence of sleep disorders in the elderly population is around 50%, while comparable estimates in the Italian population range are about 45%. However, the knowledge on frailty-related sleep disorders and related preventive models for dementia and mobility-disability is still poor. Even less, the importance of sleep health perception in healthy middle-aged and older citizens is very well-known. Thus, it is necessary to build-up a prospective observational database of middle-aged and elderly individuals unknown to health services but not disabled, not demented, and not institutionalized. This construct is necessary to change the current healthcare system approach from reactive into proactive. The analysis of relevant outcomes for older population needs the comparison between abilities of current and innovative, digital measurements in predicting trajectories of low physical and cognitive function and quality of life. A step forward is required in terms of methodological approach for strategic plans aimed at intercepting physical and cognitive frailty, and to investigate the contribution of the related sleep disorders. These studies are necessary to preventing or slowing their progression into mobility-disability and dementia.

There is need of building the rationale for innovative and multi-professional preventive responses, sharing common digital methodologies for sleep characteristics assessment. Future studies are expected to support significant changes in local and national clinical practice and decision-making, highlighting the importance of sleep as a determinant of muscle, brain, and metabolism health. Furthermore, they will support the effectiveness of

sleep disorders as early markers of physical and cognitive frailty, speeding up the implementation of clinical and psychosocial interventions aimed to slow down these phenomena, preventing mobility-disability, dementia and improving quality of life.

### Objectives

Detect, in a comprehensive and translational way, changes in brain, muscle, bone, cardiovascular system, hormonal milieu and body composition to gain a deeper understanding of the impact of sleep disorders on Mild Cognitive Impairment (MCI) and cognitive frailty, sarcopenia and physical frailty, dementia and mobility-disability.

Primary objectives are to evaluate the effect of sleep disorders on the incidence of both sarcopenia and physical frailty in healthy active elderly individuals and mobility-disability in physical frail sarcopenic elderly individuals.

Secondary objectives are to evaluate, in healthy active and physical frail sarcopenic elderly individuals with and without sleep disorders, prevalence and incidence of MCI, cognitive frailty, recognized pre-frailty conditions (i.e., motoric cognitive risk syndrome), malnutrition, polypharmacy and multimorbidity; changes in bone, skeletal muscle, and body composition through X-ray, ultrasonography, and bioimpedance; brain volume and function through magnetic resonance and nuclear medicine; cardiovascular system function through cardiac ultrasound; anthropometric parameters and nutritional markers; differences in sun exposure, melatonin and cortisol salivary levels; quality of life, social well-being, and reward level; use of healthcare services and mortality; incidence of dementia in cognitive frail elderly individuals; criterion validity between Mini Mental State Examination/neuropsychological assessment and brain MRI/FDG/Amyloid PET; characteristics of future clinical trials targeting older persons in order to address the role of recognized pre-frailty conditions in affecting the adherence to a multi-component treatment.

### Study design

We will evaluate a well-characterized sex balanced sample of community dwelling physical frail sarcopenic and healthy active elderly people from 70 years of age, not demented and independent in the Basic Activities of Daily Living. Considering the primary objectives to evaluate the effect of sleep disorders on the incidence of sarcopenia and physical frailty as well as mobility-disability in community dwelling healthy active and physical frail sarcopenic elderly individuals respectively, a statistical power

calculation will be performed using the relative risk of developing sarcopenia and physical frailty as well as mobility-disability in the two groups above mentioned. Assuming an effect size of 0.3 and  $\alpha$  of 0.05, a power of 0.95, the obtained a priori calculation suggests a sample size of 145 subjects per group (healthy active and physical frail sarcopenic). The resulting sample size will be rounded to 150 per group to account for possible drop-outs. The role of sleep disorders on physical, cognitive and cardiovascular function, bone and muscle metabolism and body composition will be evaluated through observational and prospective fashion (Figure 2), at baseline, 12 and 24 months by performing: comprehensive geriatric assessment; sleep analysis and environmental monitoring through wearable sleep profilers and sensors; brain MRI/FDG/Amyloid PET (baseline and 24 months); dual-energy x-ray absorptiometry; radiofrequency echographic multi spectrometry; bioimpedance analysis; cardiac ultrasonography; muscle ultrasonography; serum neurofilament light chain analysis; salivary cortisol and melatonin.

#### Expected results

Employing some of the most advanced diagnostic and digital health techniques, the project will allow to analyze relevant outcomes for older population, to compare the ability of current and innovative, digital measurements in predicting trajectories of low physical and cognitive function and quality of life. The expected findings will highlight the importance of sleep as a significant determinant of muscle, brain and metabolism health, as well as sleep disorders as an extremely relevant public health problem for the elderly population. These acquired data will also contribute to the personalization of pharmacological treatment targeting these conditions, where environmental hygiene measures and routine therapeutic expedients have not provided substantial benefits.

#### 2.6.3. Description of Communication and Dissemination Activities

Raising scientific and public awareness of researchers and social/health policies stakeholders regarding sleep health and its impact on functional aspects of aging, through submission of our methodologies and results to peer reviewed journals, national or international seminars and meetings, we expect that both social and economic spill overs are possible, improving the knowledge on frailty-related sleep disorders and promoting innovative preventive models for dementia and mobility-disability.

We plan to expose methodologies and results of our study, through oral and/or poster presentations, at congresses of the major scientific societies in the geriatric (Italian Society of Gerontology and Geriatrics National Congresses, European Geriatric Medicine Society Congresses) and sleep medicine fields (Italian Association of Sleep Medicine Congresses, European Sleep Research Society Congresses).

We plan to submit methodologies and results of our study, through original articles, to journals of the major scientific societies in the geriatric (Journal of Cachexia, Sarcopenia and Muscle; Journal of the American Geriatrics Society; European Geriatric Medicine Journal), internal medicine (Frontiers in Medicine; Annals of Internal Medicine; JAMA Internal Medicine) and sleep medicine fields (Journal of Sleep Research; Sleep).

#### 2.6.4. Target Audience

Researchers in the fields of geriatrics, internal medicine, sleep medicine, and neurology, as well as those figures involved in the social and health policies of elderly people.

#### 2.6.5. Objectives and Expected Impact

This study will significantly impact the knowledge on frailty-related sleep disorders and promote innovative preventive models for dementia and mobility-disability. It is both planned to build-up a prospective observational database of older subjects unknown to health services but not disabled, demented, and institutionalized and designed to change the current healthcare system approach from reactive into proactive. The findings are expected to support significant changes in local and national clinical practice and decision making, highlighting the importance of sleep as a determinant of muscle, brain, and metabolism health. Our group has the unique opportunity to take advantage of the experience and pitfalls faced during relevant European projects (i.e., SPRINTT and SUNFRIL) to translate the findings in extraordinary innovative pathways in healthcare. This is somewhat unusual in European projects because most of them complete their process with publication of the results without analyzing factors limiting the application and translation of the human and scientific experience in the daily practice. The project will allow to analyze relevant outcomes for older population, to compare the ability of current and innovative, digital measurements in predicting trajectories of low physical and cognitive function and quality of life. Results from the study are expected to bridge existing gaps in terms of knowledge on the impact of physical and cognitive frailty in the

real world, as well as to improve the methodology used at hospital and community in approaching these problems. Furthermore, they will support the effectiveness of sleep disorders as early markers of physical and cognitive frailty, speeding up the implementation of clinical and psychosocial interventions aimed to slow down these phenomena, preventing mobility disability, dementia and improving quality of life. In addition, particular relevance will be devoted to the importance of sleep health perception in healthy middle aged and older citizens, together with frail ones. We realized that harmonizing assessment of standardized criteria of physical frailty and sarcopenia, cognitive frailty and sleep quality, through the outstanding emerging digital technologies available today, we could help public health stakeholders to predict the trajectory of motoric-cognitive disability and the quality-of-life decline in older persons. By raising public and scientific awareness regarding sleep health and its impact on functional aspects of aging, both social and economic spill overs are possible. A better understanding of how to study sleep disorders, as well as how to anticipate and personalize its treatments would be able to slow down the trajectories of functional decline during aging in both healthy and frail individuals, with obvious social beneficial consequences for the individual, for his or her actual or potential caregivers, as well as for the community he or she serves. Inevitably, this will lead to the abatement not only of the direct costs of sleep disorders but, from a longer-range perspective, of the indirect costs resulting from their effects in promoting accelerated population aging and functional decline in elderly individuals.

#### 2.6.6. [Feedback and Evaluation](#)

We intend to collect feedback and assess the effectiveness of our communication and dissemination activities through the evaluation of bibliometric performances of our publications, peer's feedback at meetings, social welfare and healthcare stakeholder's engagement analytics, as well as submission of post surveys to the leading scientific societies in the field.

## 2.7.Task 2.7 - Physiological models to neurorehabilitation (responsible: Myrka Zago and Francesco Lacquaniti - UNIROMA2)

### 2.7.1. Title

Toward a digital twin of postural stability in the elderly.

### 2.7.2. Abstract

In a prospective clinical study, we aim to assess the individual posterior probability of the risk of falling in older persons, based on a prior and individual likelihood. The prior is taken from a reference population and the likelihood is estimated for each individual using multiple behavioral, anamnestic, anthropometric, and clinico-haematological, parameters. The results of the pilot will inform the generation of digital twins of postural stability in older people from multimodal individual data, population data, and real-time updates on individual and environmental variables. Our approach should be instrumental to design personalized preventive measures tailored on individual responses to simple postural tests.

### 2.7.3. Description of Communication and Dissemination Activities

We plan dissemination in terms of publications in peer reviewed journals, seminars, national and international meetings.

Journals: Frontiers in Bioengineering and Biotechnology, Journal of Biomechanics

Meetings: AHFE Emerging technologies in healthcare and medicine

### 2.7.4. Target Audience

Researchers, policymakers, general public.

### 2.7.5. Objectives and Expected Impact

We expect to disseminate our approaches to monitor postural stability and detect increased risk of falls earlier than with current methodologies.

### 2.7.6. Feedback and Evaluation

Impact of our work is typically measured using standard bibliometric parameters, such as citations, article downloads, altmetric plus post surveys.

## 2.8.Task 3.1a - Digital Tools in children and aged frail subjects (responsible: Palombi/Legramante - UNIROMA2) - 1

### 2.8.1. Title

Data mining and AI approaches to predict/prevent risk of Healthcare Associated Infections (HAIs).

### 2.8.2. Abstract

Healthcare-associated infections (HAIs) and antimicrobial resistance (AMR) are major public health threats in upper-and lower-middle-income countries. In Europe, HAIs are responsible each year for about 16 million additional hospital days, 37,000 deaths, and 110,000 deaths for which infection is a contributing cause. In Italy, the burden of HAIs is estimated to be 702.53 DALYs per 100,000 population, which has the same magnitude as the burden of ischemic heart disease. Electronic health records (EHRs) are an invaluable source of data for achieving different goals, including the early detection of HAIs and AMR clusters within healthcare settings; evaluation of attributable incidence, mortality, and disability-adjusted life years (DALYs); and implementation of governance policies. However, data in EHRs are usually not homogeneous, not properly linked and engineered, or not easily compared with other data. Moreover, without a proper epidemiological approach, the relevant information may not be detected. The use of Artificial Intelligence (AI), which through deep learning can establish a measure of infectious risk, may prove to be a relevant tool for combating HAIs.

### 2.8.3. Description of Communication and Dissemination Activities

The aim of communication and dissemination activities of Task 3.1a is to communicate about the progress and outcomes of the task. In particular, strategies for data collection, data analysis and the achieved results will be communicated and disseminated to all the relevant end-users, stakeholders and, when appropriate, to the general public.

Communications and dissemination activities will include:

- Publication of relevant intermediate and final results on peer-to-peer journals.
- Submission of abstracts to relevant scientific meetings such as 17th EUPHA public health conference (Lisbona 12-14 November 2024); 57° congresso nazionale SItI (Palermo 23-26 ottobre 2024) etc.

- Publication of news on the University official communication channels.
- Dissemination and communication during workshops and networking events.

#### 2.8.4. Target Audience

- Hospital personnel (MD, Registered Nurses, Health direction personnel, DPO, Ethical committee members).
- Social and health personnel involved in community care.
- Policy makers at district, Local, regional and national level.
- Public health researchers.

#### 2.8.5. Objectives and Expected Impact

The general objective of Pilot 3.1a is to achieve a decrease in care associated infections resulting in lower social, human and economic costs. This will be achieved by setting up a multidimensional infectious risk model and by the implementation of AIs techniques to create an algorithm able to predict risk and prevent healthcare-associated infections. The expected impact includes: decreased incidence of care related infections, decreased timelines for HAIs detection, decrease in patient outliers for LOS, improve of patients' Quality of Life.

#### 2.8.6. Feedback and Evaluation

The effectiveness of the communication and dissemination activities will be evaluated through the collection of feedbacks in the form of:

- peer-to-peer publication metrics (number of reads, downloads, citations, etc.),
- end-users and stakeholder feedback,
- ad hoc surveys when applicable.

### 2.9.Task 3.1a - Digital Tools in children and aged frail subjects (responsible: Umberto Tarantino - UNIROMA2) - 2

#### 2.9.1. Title

Data mining, artificial intelligence, and machine learning approaches predict risk of infections and acute adverse events in a) "elderly frail frequent users" of the Emergency Department (ED) : OSTEOPOROSIS.

### 2.9.2. [Abstract](#)

Age-related musculoskeletal diseases represent a major cause of disability and mortality in the geriatric population. The poor bone quality and strength that characterizes osteoporosis, frequently associated with a condition of generalized muscle atrophy known as sarcopenia, is responsible for fracture events that significantly reduce mobility in frail elderly individuals, burdening quality of life and the national health care system. Unfortunately, the diagnosis of osteoporosis is often reached following the fracture event, so pharmacological and nonpharmacological interventions are mostly aimed at slowing the disease progression. The identification of early biomarkers of osteoporosis could be the key to the development of early diagnosis and an appropriate preventive pathway. Machine learning, in combination with diagnostic techniques already in use and information obtained from opportunistic image retrieval screening and biomarker analysis, could be the key to early diagnosis of osteoporosis, helping to provide fracture risk stratification for mass prevention of fracture events.

### 2.9.3. [Description of Communication and Dissemination Activities](#)

The purpose of our pilot project is to identify clinical features or molecular markers that are closely associated with fracture risk, laying the foundation for the development of an algorithm for the early diagnosis of osteoporosis and the reduction of the incidence of fracture events associated with disability and mortality. This goal will also be achieved through careful communication and dissemination of our research activities, which will include participation in national and international conferences, online and in-person seminars, as well as the writing of books and scientific contributions in indexed, impacted, and specialized journals in the field.

The communication and dissemination activities of our pilot project will include participation in national and international conferences to disseminate our research activities. Specifically, these are specific congresses on the topic of our pilot project, such as the Italian Orthopaedic Research Society (I.O.R.S.) National Congress Biotechnology & Orthopaedics, the National Congress of the Italian Society of Orthopaedics and Traumatology (SIOT), as well as the World Congress on osteoporosis, osteoarthritis and musculoskeletal diseases (ESCEO). In addition, the results of our research activities will be submitted to international journals, such as Journal of Clinical Medicine, Therapeutic

Advances in Musculoskeletal Disease and Aging - Clinical and Experimental Research, all of which are specific to the subject matter.

#### 2.9.4. Target Audience

Communication and dissemination activities will be aimed at researchers, experts in the field, as well as the general public and the entire scientific community.

#### 2.9.5. Objectives and Expected Impact

Communication and dissemination of our research activity will have the main objective of highlighting the problem of osteoporosis and fracture risk, with significant impact on several levels, including public awareness, prevention, early diagnosis, and management of the problem. Specifically, we believe that effective communication can increase general awareness of osteoporosis and associated risk factors, promoting the adoption of preventive behaviors and encouraging people to adopt a healthier lifestyle. Effective communication can positively influence the clinical management of osteoporosis, ensuring appropriate treatment and regular monitoring of patients at risk. Therefore, an effective outreach and communication campaign on osteoporosis can lead to positive changes in individual behavior, clinical management, and social perception of the disease, with benefits at both the individual and public health levels.

#### 2.9.6. Feedback and Evaluation

The effectiveness of our communication and outreach activities will be evaluated through feedback with colleagues and other experts in the field while attending national and international meetings and conferences. Additional feedback will be provided during the peer review process, where our results will be evaluated by expert reviewers who will provide comments and advice on the topics covered. Undoubtedly, publications in international journals and the resulting impact on the scientific community, which will be assessed primarily through the number of citations, peer feedback during meetings, online engagement analysis, stakeholder feedback, and pre and post surveys.

## 2.10. Task 3.1b - Digital Tools in children and aged frail subjects (responsible: Paolo Palma - UNIROMA2)

### 2.10.1. Title

Data mining, artificial intelligence, and machine learning approaches to stratify response to vaccinations in children and vulnerable populations.

### 2.10.2. Abstract

Vaccines prevent 3 mln of deaths every year and are a key approach to combat antimicrobial resistance. An additional 1.5 mln deaths and substantial disability could be averted with those same vaccines if better used. Indeed, vulnerable populations (VPs), including pregnant women, newborns, preterm infants, elderly and patients affected by chronic diseases are frequently under-vaccinated and/or at risk of reduced vaccine efficacy, explaining a major health and economic burden to society. The overall goal of the present pilot is to establish an in-vitro and in-vivo platform defining new tools and biomarkers to predict vaccine immunity and safety and to tailor vaccine intervention in VPs. The present project will promote the development of new generations of high precision vaccines that take into account the host profile. Starting from a centralized data platform including demographic, clinical, immunological and "Omics" data belonging to VPs and healthy, we will develop an initial model to stratify host factors related to safe and protective responses towards several vaccines. In vitro and in vivo proof-of-concept studies assessing safety, immunity and acceptability of pertussis, flu, HBV, MenB and SARS-CoV2 vaccination in newly enrolled VPs will be conducted. These studies will be used to refine the bioinformatic model which will inform an online tool aiming to assist healthcare providers with immunization and follow-up of VPs.

### 2.10.3. Description of Communication and Dissemination Activities

- Development of international conferences;
- Creation of special issue about the topic of vaccine safety and immunogenicity in Vulnerable populations;
- Joining International workshops;
- Submission of abstracts to International Conferences;

- Development of an international conference gathering all the major experts in the field of Vaccinology [www.precisionvaccines2023.com](http://www.precisionvaccines2023.com);
- Creation of a special issue about with the journal Vaccine for a special themed issue entitled “Precision Vaccines: Biomarkers of vaccine safety & efficacy in vulnerable populations”: [www.sciencedirect.com](http://www.sciencedirect.com) . The submission portal will be open until April 15, 2024;
- Joining International the VACCELERATE’s workshop to address all the aspects of an APT as contribution to pandemic preparedness. Break-out sessions and plenary discussions will cover methodological and practical features of a large-scale vaccine APT;
- Submission of abstracts to the International Precise Vaccine Conference [www.precisionvaccines2023.com](http://www.precisionvaccines2023.com).

#### 2.10.4. Target Audience

Dissemination plan is directed at a variety of experts, including vaccinologists, infectious disease clinicians, decision makers from EU institutions, patient advocates and statisticians. Good Participatory Practice in Emerging Pathogens (GPP-EP as per WHO definition) is of particular importance for this endeavor.

#### 2.10.5. Objectives and Expected Impact

Results from these studies will be used to refine the bioinformatic model which will inform an online tool aiming to assist healthcare providers with immunization and follow-up of VPs. Overall, the proposed efforts will inform the design of a clinical trial to assess efficacy of a personalized vaccine intervention.

#### 2.10.6. Feedback and Evaluation

- Post survey;
- Citation Index.

### 2.11. Task 3.2a - Digital Tools in Cancer - COLON (responsible: Luigi Ricciardiello and Sergio Cinocca - AOU BO)

#### 2.11.1. Title

Generating AI-risk stratification strategies for improved colorectal cancer screening.

### 2.11.2. Abstract

For highly prevalent cancers, such as Colorectal cancer (CRC), screening programs for prevention and early detection have been implemented in several European countries. Most countries are adopting an approach which relies on an age-targeted population with the promotion of Fecal Immunochemical Test (FIT), a cheap, repetitive test which would then trigger a total colonoscopy (TC). Such a strategy relies on a well-coordinated effort involving citizens, public health and endoscopic units, with significant economic and human resources that need to be allocated. Depending on the positivity cut-off adopted, the proportion of FIT positive subjects with a negative result at the subsequent TC is substantial, resulting in a large number of colonoscopies performed in pure loss. The pandemic emergency highlighted the need to implement approaches, which could redistribute screening resources from low-risk to high-risk individuals.

Recently, cumulative fecal hemoglobin (f-Hb) concentration has been found to be associated with subsequent advanced colonic neoplasia thus providing a new strategy to optimize the utilization of endoscopy resources. Indeed, there is a need for scaling up new strategies through a risk-based approach integrating information on the individual sex, genetics, comorbidities, and exposome, in large, prospective cohorts. Artificial Intelligence Colonoscopy (AI-TC) has been found to improve Adenoma Detection Rate (ADR). However, uncertainty remains regarding their real effectiveness.

In our study every patient positive to FIT will participate in an interview to recollect specific data and will randomly be assigned to TC or AI-TC.

The aim is to integrate all the data (acquired through specific questionnaires and sanitary data) with the FIT and TC to define specific predictive models to personalize screening programme (which patient - and when - need to undergo first level screening - FIT - and second level screening - TC -).

Thus, we hope our strategy will lead to improving the prescription adequacy and surveillance procedures, tests, reducing costs for healthcare providers, unlocking healthcare system resources, minimizing the number of unnecessary invasive procedures on patients, while targeting those who would benefit the most.

### 2.11.3. Description of Communication and Dissemination Activities

We plan to submit the result of the study in peer reviewed journals and to present it in seminars and national/international meetings.

Meetings:

- FISMAD – National Meeting of the Italian Society for Digestive Diseases
- GISCOR – National screening meeting
- UEG Week – Annual Meeting of the United European Gastroenterology
- DDW – Digestive Disease Week Annual Meeting

Journals:

- Digestive and Liver Disease – Italia Journal of GE
- Gut – International Journal
- Gastroenterology – International Journal
- Clinical Gastroenterology and Hepatology – International Journal

### 2.11.4. Target Audience

Researchers, health professionals and policymakers.

### 2.11.5. Objectives and Expected Impact

Expanding knowledge about tailored colorectal cancer screening and future implementation of personalized management of patients with higher risk for CCR.

### 2.11.6. Feedback and Evaluation

We plan to evaluate feedbacks by:

- Number of citations;
- Peer's feedback at meetings;
- Stakeholder feedback;
- Survey administration during meetings.

## 2.12. Task 3.2b - Digital Tools in Cancer - LUNG (responsible: Nicola Sverzellati - UNIPR)

### 2.12.1. Title

Data mining, artificial intelligence, and machine learning approaches to identify subnetworks of cancer associated with early prediction, survival, metastasis or phenotypes in cancer subtypes focusing on lung.

### 2.12.2. Abstract

Lung cancer (LC) is the leading cause of oncologic death worldwide.

This new prospective pilot will develop a multi-dimensional/-omic organizational model exploiting the highly digitalized nature of radiology for the informatization of secondary prevention and integrated management of LC. AI systems will be implemented into the radiology workflow with comprehensive approaches for LC management, from digital environment for secondary prevention to personalized medicine for oncologic patients.

### 2.12.3. Description of Communication and Dissemination Activities

Communication and dissemination activities of our pilot aim to promote participation in a lung cancer screening (LCS) program with the AI-Optimization of LC workflow. With this aim, public awareness campaigns will be organized using social media, brochures, digital platforms/websites, testimonials, community workshops and media Interviews.

The final results of our study will be the subject of presentations at national and international conferences, seminars and publications on peer reviewed journals.

To promote our study and participation in the lung cancer screening program, we aim to:

- organize public awareness campaigns through media advertisements (print and online media) and social media campaigns (like Facebook, Twitter, and Instagram);
- prepare educational / informative material, including brochures / pamphlets / posters;
- organize community workshops, seminars, interviews with healthcare professionals and ambassadors;
- develop digital platforms and/or websites allowing interaction for potentially enrolled subjects.

The results of our study could be discussed at the national and international congresses, including the Italian National Congress of Radiology, as well as international meetings (e.g., European Congress of Radiology, Meeting of the European Society of Thoracic Imaging). Results will be submitted to peer-reviewed journals.

### 2.12.4. Target Audience

General public, possible volunteers to LCS (i.e. smokers or former smokers), researchers interested in contributing to the pilot with their experience.

### 2.12.5. Objectives and Expected Impact

- Increase screening participation;

- Increase awareness about the existence of lung cancer screening programs, emphasizing the importance of early detection of lung cancer and of smoking cessation;
- Promote accessibility of information about LCS to diverse populations, including “hard-to-reach” individuals;
- Reduce stigma associated with LC and debunk misconceptions about screening procedures.

#### 2.12.6. Feedback and Evaluation

- Proportion of high-risk subjects enrolled in the study population;
- Number of enrollments through the website ;
- Number of appointments and rate of “no-show”: comparison between hospital-based and mobile CT unit sessions;
- Surveys could be prepared and administered to volunteers to evaluate the effectiveness of communication of the LCS program;
- Stakeholder feedbacks.

### 2.13. Task 3.2c - Digital Tools in Cancer - MYELOMA (responsible: Angelo Vacca - UNIBA)

#### 2.13.1. Title

Data mining, artificial intelligence, and machine learning approaches to identify subnetworks of cancer associated with early prediction, survival, metastasis, or phenotypes in cancer subtypes focusing on myeloma.

#### 2.13.2. Abstract

Multiple myeloma (MM) is a malignancy of plasma cells which shows a rising incidence in the developed world. Despite several progression risk stratifications have been employed and validated, new reliable, interpretable, and trustworthy Machine Learning (ML) tools for considering the disease complexity and improving personalized medicine of MM are largely needed. The project aims to face these challenges and unmet needs based on the consortium solid and established experience in the field.

### 2.13.3. Description of Communication and Dissemination Activities

The communication and dissemination of the results occurs through publication in international journals and the organization of national and international seminars and conferences.

International journals of hematology, immunology, internal medicine, oncology, statistics, computer science, health economics. The published papers will be disseminated by mean web pages and on the social channels: LinkedIn, Facebook, and Instagram.

In late 2023 two works reporting the first results obtained were submitted for publication. On November 25, 2023, meeting: *“Lo sviluppo tecnologico a supporto della sanità: la medicina 4.0”* was organized in Bari during which the DARE Project and the Research Doctorate: "DIeH - Digital Innovation and e-Health" activated at the University of Bari in scope of the project were presented.

In the years to come, further publications will be produced, and other meetings will be organized. Already scheduled for November 2024, the international meeting Multiple Myeloma and related malignancies, 7th edition, will see a session regarding telemedicine, and particularly its development in the diagnosis of multiple myeloma.

### 2.13.4. Target Audience

The target audience is represented by doctors specializing in hematology, internal medicine, oncology, general practitioners, biologists, biotechnologists, and other interested healthcare professionals. Doctors in specialist training and students at the school of medicine and surgery, biology and biotechnology are also targets of the project results. Finally, healthcare administrators will also be interested.

### 2.13.5. Objectives and Expected Impact

Increase the number of clinicians involved in MM are starting to use AI-based technologies in their healthcare activities. Thus, can have an impact on cost reductions because of reducing patient hospitalizations and improve of quality of care. Significant improvement in patients' quality of life.

### 2.13.6. Feedback and Evaluation

The evaluation of the effectiveness of communication and dissemination will be evaluated based on the citations of published works, dissemination in social networks and the extent of participation in meetings.

## 2.14. Task 3.2d - Digital Tools in Cancer - AI PREDICTIONS (responsible: Raffaella Massafra - UNIBA) - 1

### 2.14.1. Title

Radiogenomic approaches predicting response to neoadjuvant therapy in breast cancer patients.

### 2.14.2. Abstract

The adoption of NAC is growingly performed especially against some molecular subtypes, such as TN and HER2+ tumors, as there is concrete evidence of a greater clinical improvement in terms of survival and QoL. Due to the high heterogeneity of breast cancers, less than 30% of patients receiving NAC achieves pCR. In this context, AI-based reliable models are requested to aid clinicians in decision-making processes.

The study aimed to develop an early prediction model of neoadjuvant chemotherapy (NAC) efficacy in breast cancer patients evaluated in terms of pathological Complete Response (pCR) through multimodal artificial intelligence (AI) models. Pre-treatment MR and digital pathology images will be analyzed through AI to extract quantitative imaging features to be evaluated as early indicators of pCR. Moreover, a stratification by BC molecular subtypes will be performed using a panel of IHC surrogates (St Gallen Consensus Statement for early breast cancer).

Our proposal could be a great impact on the overall improvement on both patients' quality of life and clinical governance could be reached.

### 2.14.3. Description of Communication and Dissemination Activities

Communication and dissemination activities of preliminary, intermediate, and final results will be implemented to reach the target audience of doctors and researchers.

A conference will also be organized on the topics covered by the pilot and related topics within the DARE project to strengthen the collaboration network. Moreover, the channels used for the dissemination of scientific results will be publications in indexed international journals, as well as participation in national and international conferences focused on the treatment of oncological pathologies. The main findings of the research project will also be shared via major social networking platforms, such as Facebook, LinkedIn and Twitter.

The dissemination activities that we intend to implement concern participation in national and international conferences with oral communications and posters. The scientific results will be submitted to international journals with a high impact factor such as journals from the Springer, Wiley, Science, Elsevier Editorials groups. Furthermore, the main scientific results will also be disseminated on the main social networks with visual abstracts, abstracts and links to the published papers.

#### 2.14.4. Target Audience

The target audience for the scientific results of the proposed pilot are doctors and researchers involved in cancer research, specifically for breast pathology, as well as patient associations and the main national and international.

#### 2.14.5. Objectives and Expected Impact

The implementation of the pilot proposal will have an important impact on clinical patient governance: patients could be spared from potential toxic or ineffective treatments. Starting from the technology concept formulation of the study (TRL 2), the pilot could bring the proposal to the technology validation in a relevant environment (TRL 5).

#### 2.14.6. Feedback and Evaluation

The direct comparison during the conferences with the main players of the scientific community and the interest found following the publications in high impact journals and social networks will allow the research group to constantly evaluate the progress of the research activity and detect any critical issues to improve and better plan the progress of the studies.

## 2.15. Task 3.2d - Digital Tools in Cancer - AI PREDICTIONS (responsible: Fabio Vandin - UNIPD) - 2

### 2.15.1. Title

Network-based AI predictions of survival and clinical phenotypes of cancer subtypes.

### 2.15.2. Abstract

Cancer is one of the leading causes of death. While several studies have characterized genomic alterations in several cancer subtypes, there is still a need for robust tools for the identification of genomic alterations providing reliable predictions of clinical phenotypes and survival. We will develop computational methods for the identification of such alterations and provide network-based AI tools for the prediction of such survival and relevant clinical phenotypes.

### 2.15.3. Description of Communication and Dissemination Activities

We plan to communicate and disseminate the results of this pilot through several activities, including: publication in peer reviewed journals in the area of computational biology, bioinformatics, and health informatics; seminars at international research institutions; presentations at international meeting on computational biology, bioinformatics, and health informatics.

As peer reviewed journals, we will target journals such as PLOS Computational Biology, Bioinformatics, Frontiers in Genetics, and IEEE Journal of Biomedical and Health Informatics. As international meetings, we will target major conferences such as the annual conference on Intelligent Systems for Molecular Biology (ISMB), the annual conference on Research in Computational Molecular Biology (RECOMB), and the annual European Conference on Computational Biology (ECCB). Additional meetings for seminars include the NCI Spring School on Algorithmic Cancer Biology.

### 2.15.4. Target Audience

The main audience for the dissemination and communication activities are researchers in computational biology, bioinformatics, and cancer biology.

### 2.15.5. Objectives and Expected Impact

With our dissemination and communication activities we expect to reach two main objectives. First, to start building a community of researchers interested in developing advanced artificial intelligence methods for prediction of cancer phenotypes. Second, to show the potential of using advanced tools for predictions in cancer research to researchers in cancer biology and in computational biology.

### 2.15.6. Feedback and Evaluation

The feedback will be collected mostly by peer's feedback.

## 2.16. Task 3.3a - Digital Tools in Cardiometabolic Diseases - DM COMPLICATIONS (responsible: Barbara Di Camillo - UNIPD)

### 2.16.1. Title

Digitally-Empowered Management of Type 2 Diabetes: From the Diagnosis to the Prediction of Complications.

### 2.16.2. Abstract

This pilot project will develop a predictive model of kidney outcomes related to a worsening in estimated glomerular filtration rate (eGFR), e.g., acute kidney injury (AKI) or chronic kidney disease (CKD), based on the application of AI to routinely acquired data. Specifically, the model will be trained to make an effective use of the information that is typically acquired whenever a patient affected by type 2 diabetes (T2D) visits a diabetes outpatient clinic, with the objective of anticipating possible deteriorations in eGFR, whose timely recognition might drive therapeutic decisions (e.g., early switch to a SGLT2-inhibitor-based therapy).

The model will be evaluated according to the best practices in the field of machine learning for healthcare data; then, it will be implemented as a prototype and tested by the clinicians of a single diabetes outpatient clinic, in order to obtain a qualitative assessment of its perceived utility; finally, based on these results, the design of a clinical trial to assess the effectiveness of using the model in terms of renal outcomes will be provided.

### 2.16.3. Description of Communication and Dissemination Activities

The communication and dissemination strategy for our pilot project encompasses a multifaceted approach aimed at reaching diverse audiences. Our primary objective is to share findings through peer-reviewed journals and academic publications, ensuring the scientific rigor of our work. Complementing these efforts, we aim to conduct seminars and presentations at both national and international levels, fostering engagement with experts and stakeholders. Participation in key conferences and meetings within relevant fields will further facilitate the dissemination of our insights. By tailoring our communication strategies to these different platforms, we seek to maximize the impact of our pilot project on a broad audience, from academia to industry and beyond.

Target journals are methodological journals such as Artificial Intelligence in Medicine, Journal of Biomedical Informatics, IEEE Journal of Biomedical Health Informatics but also clinical journals in the field of Diabetes and its complications.

Target conferences are the IEEE Engineering in Medicine and Biology Society and the International Conference of Artificial Intelligence in Medicine

### 2.16.4. Target Audience

The target audience for our activities are researchers and clinicians. In a second stage, it might be interesting to contact industry representatives possibly interested in developing our solutions as software as medical devices.

### 2.16.5. Objectives and Expected Impact

The specific objectives of our communication and dissemination activities are centered on fostering widespread awareness, understanding, and utilization of the insights generated by our pilot project. Firstly, we aim to establish a strong presence in peer-reviewed journals, ensuring the academic community is well-informed about our research. Secondly, through seminars and presentations, we intend to facilitate direct interaction and knowledge exchange.

### 2.16.6. Feedback and Evaluation

We will track the number of citations our work receives in peer-reviewed journals, providing a quantitative measure of its impact within the academic community. Additionally, feedback from peers during meetings, conferences, and seminars will be

solicited to gather qualitative insights on the perceived value and relevance of our research.

## 2.17. Task 3.3b - Digital Tools in Cardiometabolic Diseases - NAFLD (responsible: Massimo Federici - UNIROMA2) - 1

### 2.17.1. Title

Digital Tools in Cardiometabolic Diseases: Digital Predictors of NAFLD complications.

### 2.17.2. Abstract

Non-alcoholic fatty liver disease (NAFLD) is a potentially serious liver disease that affects approximately one-quarter of the global adult population, causing a substantial burden of ill health with wide-ranging social and economic implications. It is a multisystem disease, considered the hepatic component of metabolic syndrome and encompasses NAFL (Non-alcoholic Fatty Liver) and Non-alcoholic steatohepatitis (NASH). NASH is a chronic disease that can progress to end-stage liver disease (ESLD). The global prevalence of non-alcoholic steatohepatitis (NASH) is increasing, such that NASH is predicted to become the leading cause of liver transplantation (LT) in Europe. A large proportion of early-stage NASH patients remain undiagnosed compared to those with advanced fibrosis, who are more likely to receive disease management interventions. However, diagnosis of fibrosis is problematic because of technical (i.e. need of Magnetic Resonance imaging-derived proton density fat fraction or MR elastography) or procedural (liver biopsy) limitations, which are especially serious in people living with obesity.

Since the majority of economic and wellbeing costs of NASH are experienced in late disease stages, earlier diagnosis and care of NASH patients could reduce future healthcare costs.

### 2.17.3. Description of Communication and Dissemination Activities

This task addresses the risk of complications of metabolic associated liver steatosis which is a disease that is without specific treatments but of interests for hepatologists, diabetologists as well as cardiologists and internists at national and international meetings. The communication/ dissemination activities will be therefore focused more on

the science environment rather than lay press. The final results will be communicated also using specialized platforms such as ResearchGate, LinkedIn, TopDoctors.

Abstracts with preliminary results will be sent to meetings of the international and national scientific societies such as American Diabetes Association (ADA), European Association for The Study of Diabetes (EASD), European Society of Cardiology (ESC), International Diabetes Federation (IDF) and Società Italiana di Diabetologia (SID) meetings.

The final results will be communicated also using specialized platforms such as ResearchGate, LinkedIn, TopDoctors.

Results will be also communicated through international and national organizations such Euroepan Diabetes Forum (EUDF) and International Barometer for Diabetes and Obesity (IBDO).

#### 2.17.4. Target Audience

We intend to reach out first to researchers and scientists, those in the disciplines mentioned above, to share concepts and preliminary results and to receive support and possibly suggestions. Eventually, policymakers as well as relevant stakeholders preventive medicine will be informed, through direct communication (i.e. Italian Ministry of Health, Istituto Superiore di Sanità) .

#### 2.17.5. Objectives and Expected Impact

The Pilot aims to define a signature to identify patients with NAFLD at high risk for metabolic and cardiovascular outcomes and to translate the findings into the clinical practice. The dissemination of the results may lead the policymakers to fund the clinical translation which will require funding to generate diagnostic tools that may be applied to the general medicine level (i.e. general practitioners, emergency room).

#### 2.17.6. Feedback and Evaluation

For the scientific part of communication, participants in presentations, acceptance of journal editors, and citations of articles are expected and easily counted. Proposals, outcomes and general findings related to this pilot will be discussed also with policymakers in Hepatology/Diabetology/Cardiology, mainly in meetings and direct contacts, where relevant feedback will be experienced immediately.

## 2.18. Task 3.3b - Digital Tools in Cardiometabolic Diseases - NAFLD (responsible: Luca Miele - UNIROMA2) - 2

### 2.18.1. Title

CALIBRE - seCOnDary and tertiAry digitaL preventiOn of non-alcoholic and dysmetaBolic liveR disease.

### 2.18.2. Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) and its severe form, Metabolic dysfunction-associated steatohepatitis (MASH), are major causes of liver diseases like cirrhosis, hepatocellular carcinoma (HCC), and liver transplantation needs. By 2030, MASLD prevalence is expected to reach 33.5%, with MASH cases rising from 20% in 2015 to 27%. Decompensated cirrhosis cases are projected to surge by 168% to 105,430, and HCC incidence by 137%, leading to a 178% increase in liver-related deaths.

Early detection of MASLD is challenging due to its asymptomatic nature, resulting in late diagnoses. This is evident as 73% of first-time cirrhosis or liver failure patients had not been previously referred to liver clinics. Liver-related complications, mortality, healthcare costs, and quality of life decline mainly occur in cirrhotic patients.

MASLD is closely linked to metabolic syndrome, obesity, insulin resistance, and hyperlipidemia, which contribute to chronic inflammation, altered lipid metabolism, fibrosis, cirrhosis, and a pro-carcinogenic state.

Currently, MASLD treatment is limited to lifestyle changes, like diet and exercise. No specific drugs are available, although some are in development for inflammation and fibrosis. Weight loss significantly impacts fibrosis regression in MASLD, but adherence to lifestyle programs is low.

Poor adherence is due to time constraints in clinical settings and the difficulty of integrating lifestyle changes into daily life. Secondary prevention and digital technology implementation in MASLD care are unmet needs.

A potential solution is a new care model integrating standard clinical procedures with a digital approach, including a mobile app for patients, a clinical dashboard for healthcare professionals, wearable sensors, and AI analysis. This model aims to improve patient

lifestyle education, remote monitoring, decision-making, and patient engagement. However, sustainable patient volumes and long-term engagement are challenges.

CALIBRE study aims to test digital secondary and tertiary prevention in MASLD, increase self-protective behaviors, educate patients on lifestyle and diet, integrate clinical and behavioral data for risk stratification, and identify microbiome signatures linked to behavior paths.

### 2.18.3. Description of Communication and Dissemination Activities

MASLD management require a multidisciplinary approach.

The study's primary objective is to test the feasibility of a digital intervention for better patient engagement and early identification of advanced MASLD. Secondary objectives include screening for steatosis and fibrosis, early identification of high-risk MASLD patients, and linking them to digital interventions for self-management.

General objectives of dissemination activities will be: i) to raise awareness about MASLD; ii) engage stakeholders; iii) disseminate results.

- Presentation of results in scientific meetings of national and international scientific societies. Abstract will be sent to the main scientific society in the field of hepatology; public health; gastroenterology; internal medicine; nutrition; diabetology;
- Results will be shared in conferences and public events;
- Article will be submitted for publication in scientific Journals indexed in PubMed, Scopus;
- Press release and social media will be used for public engagement;
- Educational activities (seminars, webinars, courses) will be assured for scholars and students;
- Networking activities will assure dissemination with several stakeholders (policy makers, industry).

### 2.18.4. Target Audience

- Academia community: researchers and scholars by publishing in peer-reviewed journals, presenting abstracts and talks at conferences, seminars, and symposia (national and international).
- Industry and companies (including start-ups) by workshops, webinars, industry-focused conferences.
- Policy makers by briefing and meetings in dedicated forums.
- General population: media and social media articles.

### 2.18.5. Objectives and Expected Impact

The innovative care pathway integrates standard clinical practice with digital technologies for seamless secondary prevention integration into patients' daily lives, aiming to delay liver disease progression and reduce cirrhosis effects. This includes multimodal patient characterization, a digital platform for advanced self-care, remote disease management, and an AI-based predictive model for prevention and early severe event management.

### 2.18.6. Feedback and Evaluation

Feedback will be guaranteed by meetings with small groups from our target audience by using questionnaires and survey forms. A qualitative analysis will be provided on the basis of feedback with peers and stakeholders.

Publications from the project will be tracked for number of citation and by social media analysis of shares and likes. Number of attendees for dissemination events will be a measure of interest.

The impact analysis (evaluation) will assess whether the target audience has implemented changes based on the dissemination by using follow-up interviews or surveys. Moreover, we will also monitor if our communications have led to changes in policy or practice within scientific societies.

## 2.19. Task 3.4a - Digital Tools and psychiatric and cognitive disorders - FROM PRECLINICAL TO PSYCHOSIS (responsible: Alessandro Bertolino and Linda A. Antonucci - UNIBA)

### 2.19.1. Title

Digital Tools for psychiatric and cognitive disorders: identify subjects at risk for conversion from preclinical conditions to psychosis.

### 2.19.2. Abstract

In this longitudinal study, individuals at several stages of risk for psychosis, as well as patients with psychosis and healthy controls, will be recruited and followed up over one year to estimate their clinical outcomes in terms of symptoms and functioning. Data from relevant psychosis risk domains will be collected, including brain, clinical and cognitive-behavioral measures. Artificial Intelligence will be employed to build risk calculators and

normative models as cutting-edge digital tools combining multi-domain information to predict worse outcomes.

### 2.19.3. Description of Communication and Dissemination Activities

- Peer reviewed journals
- National or international meetings
- Seminars for both scientific and non-scientific audiences

Two abstracts and one symposium have been submitted and accepted to the 2024 Congress of the Italian Society of Psychopathology (Rome, February 2024). One of the abstracts has been mentioned as one of the top 14 of the conference. Other two abstracts have been submitted to the 2024 Schizophrenia International Research Society Conference (Florence, April 2024). Seminars in high-school institutes are already taking place in the Bari area, aimed at raising sensitivity of students and teachers about the importance of early identification and intervention within psychosis risk pathways. We plan to keep these two activities (dissemination in conferences and through seminars) for the entire duration of DARE. We aim at submitting in international peer-reviewed journals in the field of psychiatry and clinical psychology (e.g., Psychological Medicine, Impact Factor 9) the results of our DARE pilots.

### 2.19.4. Target Audience

- Researchers
- High-school Students
- University and PhD students
- High-school teachers

### 2.19.5. Objectives and Expected Impact

Scientific dissemination is aimed at proving the feasibility of machine learning-based methodology in the psychiatry and clinical psychology field to bridge research and clinical practice.

Non-scientific dissemination is aimed at increasing awareness regarding the importance of recognizing and identifying early environmental and social risk factor for psychosis in order to early intervene on such factors and facilitate contacts between help seekers and clinical services.

### 2.19.6. Feedback and Evaluation

- Number of abstracts submitted at conferences
- Awards achieved at conferences
- Peer's participation and feedback at meetings
- Feedback from teachers
- Feedback and questions from the scientific audience of the conferences where abstracts have and will be submitted.

## 2.20. Task 3.4b - Digital Tools and psychiatric and cognitive disorders - DOWN SYNDROME (responsible: Chiara Locatelli - AOU BO)

### 2.20.1. Title

Artificial Intelligence approaches for predicting factors affecting progression to intellectual disability in genetic conditions using Down Syndrome as a model.

### 2.20.2. Abstract

Down syndrome (DS) or Trisomy 21 is the most common genetic cause of intellectual disability. The purpose of this study is to use a dataset comprising personal, diagnostic, clinical, auxological and molecular data of children with DS to build a model useful to better understand the pathogenesis of DS. In particular, models built using Artificial Intelligence approaches may assist researchers in identifying key features likely associated with intellectual disability in DS, and ultimately, may improve Diagnostic-Therapeutic Care Pathways for children with DS.

### 2.20.3. Description of Communication and Dissemination Activities

- Peer reviewed journals, seminars, national or international meetings.
- Peer reviewed journals: BioFactors, Open Biology, Frontiers in Immunology, Helyon.
- Seminars for students (from high school to university), citizen-oriented seminars.
- National and international meetings: Associazione Italiana Biologia e Generica (A.I.B.G.) Congress, Trisomy 2 Research Society (T21RS) International Conference

### 2.20.4. Target Audience

Researchers, students, families, general public.

### 2.20.5. Objectives and Expected Impact

Sharing of new data with the scientific community, new collaborations with national and international research centers, communication of the progress of the research to families and general public.

### 2.20.6. Feedback and Evaluation

Impact factors and number of citations of the scientific publications, peer's feedback at meetings.

## 2.21. Task 4.1 - Accessible measurements of mobility and deformity as biomarkers for orthopedic treatments (responsible: Paolo Caravaggi - IOR)

### 2.21.1. Title

Accessible measurements of mobility and deformity as biomarkers for orthopedic treatments.

### 2.21.2. Abstract

Osteogenesis Imperfecta (prevalence 6-7:100.000; ORPHA:666) and Multiple Osteochondromas (prevalence 1-2:100.000; ORPHA:321) are rare genetic bone disorders (RBDs) which significantly decrease the quality of life from an early age by altering joints mobility and posture due to deformities, increased bone fragility and alterations in plate cartilage growth. RBDs are characterized by a wide clinical variability and by progressive degeneration of the overall health conditions. Only few highly specialized centers treat RBDs and there is need for wider monitoring and evaluation of the disease progression across the territory.

In order to improve the quality of life of patients suffering from RBDs, this pilot aims at monitoring the status and progression of the effects of the pathology on the musculoskeletal system via novel, accessible and easy-to-use instruments and relevant tools. These include Inertial Measurement Units (IMUs), plantar pressure measurement systems and 3D body scanners. These tools should be made available in small clinics,

community hospitals and at patients' homes for the continuous monitoring of the disease to support the clinicians in the diagnosis and in the prescription of corrective strategies.

### 2.21.3. Description of Communication and Dissemination Activities

The main scientific outcomes on the development of specific protocols and tools for the instrumental assessment and monitoring of the pathology will be published on relevant peer reviewed journals. The outcome on the biomechanical characterization of the pathology will be disseminated at national and international conferences on clinical biomechanics. The main breakthroughs of the pilot will be shared to the general community via the social media pages - such as LinkedIn and Facebook - of the researchers involved in the pilot and of Istituto Ortopedico Rizzoli.

Abstracts will be submitted to the meetings of the Società Italiana di Analisi del Movimento in Clinica (SIAMOC), of the European Society for Movement Analysis in Adults and Children (ESMAC) and of the International Society of Biomechanics (ISB). Results may be disseminated also to events with larger and multi-disciplinary audience, such as Exposanità, in Bologna every two years. The main scientific outcomes will be submitted as original research papers to the Journal of Biomechanics and to Gait and Posture and/or to other open access peer-reviewed journals.

### 2.21.4. Target Audience

The main target audience of the dissemination activities are the families of the RBDs patients and the relevant national and European Patient Advocacy Organizations. The pilot will also help strengthening the scientific collaboration with industrial partners developing and manufacturing novel technological solutions for these rare pathologies of the skeletal system. Networking with other clinical spokes on RBDs across the national territory will be enhanced and promoted.

### 2.21.5. Objectives and Expected Impact

With the dissemination activities we are expecting to bring more media and institutional attention to these rare bone diseases and to steer policymakers on allocating more funding and resources to support the research on these pathologies. In addition, we are aiming at increasing the awareness of physicians and families on the biomechanical and clinical

aspects of the progression of the pathology and on the preventive strategies to limit its effects.

#### 2.21.6. Feedback and Evaluation

The direct feedback, involvement, and participation of the scientific community at national and international meetings in the dedicated sessions will provide an indication of the strength of the communication activities. Surveys filled by the RBDs patients and/or their caregivers may also be used to score the effectiveness of the dissemination campaign.

### 2.22. Task 4.2 - Biomechanical features for early detection of diabetic foot complications (responsible: Alberto Leardini - IOR)

#### 2.22.1. Title

#### 2.22.2. Abstract

Diabetes is a global epidemic affecting about 530 million people worldwide, and it is definitely a heavy burden on all health-care systems. In particular, foot functions and locomotion are severely affected, and the costs for associated treatments are huge. Clinical assessments are performed routinely in these patients, but additional biomarkers shall be searched to prevent as much as possible complications at the foot. Techniques for the identification of circulating biomarkers and for multi-instrumental biomechanical measurements (plantar pressure, kinematics, kinetics, medical imaging, etc.) are thus exploited in this Pilot as modern combined biomarkers to better predict ulcerations and other foot ailments.

The general objective is therefore to enhance prevention, to limit or to delay critical foot and function conditions as effects of the diabetes, and thus to reduce the present huge health-care costs. We expect in fact that those instrumental tests can be added to the traditional clinical assessments and can result in a better identification of those patients at higher risk of foot ailments, long before more severe conditions and even amputation.

#### 2.22.3. Description of Communication and Dissemination Activities

The Pilot addresses a complex and multidisciplinary clinical issue, which involves a number of different disciplines, such as diabetology, podology, cardiovascular diseases,

medical imaging, biomechanics, physiatry, etc. Therefore, communication and dissemination to these disciplines' world shall address the relevant communities. The professionals involved in this Pilot however are among the major experts worldwide, and their reports and results, together with the novel techniques and the conclusions of the study are expected to be very well received into national and international conferences, as well as into peer-review journals. In addition to this more scientific area of the dissemination, also the health policy shall be informed and possibly affected: connections and information will be maintained to regional and national references, for the likely translational return of these findings to the health-care organization. For this scope, aims, activities, and results can be disseminated also to events with larger and multi-disciplinary audience, such as Exposanità, in Bologna every two years (2024 and 2026).

Abstracts from about 300 to 600 words will be sent to conference organizers, for a possible, likely, oral or poster presentation. Manuscripts from about 2500 to 6000 words plus figures and tables will be sent to major international scientific journals. Because the communities and the topics are very relevant, international communities, journals and channels will be used, and the language shall be English. In addition, for those possible messages to be distributed to patients, relevant communications will be arranged in general or specific magazine and newspapers.

#### 2.22.4. Target Audience

We plan to address researchers and scientists first, those in the disciplines mentioned here above, to share concepts and preliminary results, and to receive support and possibly suggestions about the techniques adopted and the interpretation of the results. Then, toward the end of the project, with established techniques and tools in our hands, policymakers as well as Patient Advocacy Organizations (PAOs) will be informed, through traditional channels.

#### 2.22.5. Objectives and Expected Impact

We expect to improve considerably prevention in foot ailments in patients with Diabetes Mellitus: thus, we shall be able to provide a) techniques and procedures to health-care providers, b) good practices to these patient populations and stakeholders, and c) overall indications and pathways to policymakers. The expected impact is amelioration of foot

care in these patients, both in term of self-attention, and for the promotion of prevention in possible specific campaigns.

#### 2.22.6. Feedback and Evaluation

For the scientific part of the communication, participants to the presentations, acceptance of the journal editors, citations of papers are established and easily countable. The recommended overall procedures will be discussed mostly in meetings and direct contacts, and the honest feedback will be experienced straightaway.

### 2.23. Task 4.3 - Single oncological marker detection for early diagnosis (responsible: Luisa Torsi - UNIBA) - 1

#### 2.23.1. Title

Single oncological marker detection for early diagnosis.

#### 2.23.2. Abstract

The Single-Molecule with a large Transistor (SiMoT) smart handheld system embedding a bio-electronic disposable cartridge will be deployed for early detection of the HPV infection. The sensing measurements will be processed using machine learning approaches to reach a reliable fully digital output. The identification of the markers for the HPV infection with a limit-of-detection (LOD) of one single molecule in a patient sample (saliva, brushing specimens, etc.) will be validated, and the performance levels will be compared to the gold-standard technique.

#### 2.23.3. Description of Communication and Dissemination Activities

Along with assessing the platform, the pilot will include communication and dissemination activities which will serve to reach the target audience of clinicians, to promote HPV screening using a fast and cost-effective device such as the SiMoT technology. Also, the objective of these activities will serve to share knowledge about single-molecule detection in peripheral body fluids, moving research towards liquid biopsy. The results of the laboratory activities will be published in international peer-reviewed journals as scientific papers or review works, as well as presented at national and international conferences, to share the progress with other researchers and industries.

The strategies that will be used for the communication and dissemination activities will include well-known channels like both oral and poster presentations at national and international conferences, as well as photo and video sharing on social media (LinkedIn, X, Facebook etc.). Some relevant meetings will be attended by the personnel included in the pilot activities, the planned one include the Boston 2024 MRS Fall Meeting, the 2024 edition in Milan “XXVIII National Congress of Società Chimica Italiana”, the eMRS, SPIE Optics and Photonics. The work will be possibly submitted to some international journals at high impact factor such as journals of Springer, Wiley, Science, Elsevier Editorials' groups.

#### 2.23.4. Target Audience

The pilot communication and dissemination activities will be mostly addressed to clinicians and researchers who are interested in new forefront technologies for early diagnosis of clinically relevant biomarkers. Also, the involvement of industrial stakeholders interested in the development of the technology is foreseen as well as dissemination activities addressed to the general public who should be aware of the technological progress reached by the public health.

#### 2.23.5. Objectives and Expected Impact

The main objective of the communication and dissemination plan is the spread of information regarding single-molecule detection and the importance of the development of new technology that can conjugate high sensitivity with fast, reliable and non-invasive assays. Also, the relevance of HPV early detection to prevent cancer appearance will be addressed, to raise awareness on screening campaigns.

#### 2.23.6. Feedback and Evaluation

The comments and questions raised during conferences will be collected and used to improve the research plan. Also, the evaluation of on-line survey through social media could be implemented.

## 2.24. Task 4.3 - Single oncological marker detection for early diagnosis (responsible: Amalia Azzariti - GPII BA) - 2

### 2.24.1. Title

Potential Liquid-Biopsy and Liquid-based Cytology Biomarkers for early diagnosis and monitoring of HPV positive and negative Gynaecological Cancers.

### 2.24.2. Abstract

Even today, gynecological cancers as other oncological diseases are detected at an advanced stage, with limited treatment options and often poor prognosis. Being able to detect them early can substantially improve survival because cancers early are more treatable. Additionally, predicting cancer recurrence allows doctors to make effective treatment decisions improving patient survival.

In the pilot-study we plan to identify two panels of biomarkers for the early diagnosis of gynecological cancers, such as ovarian, cervical, endometrial and vulvar cancers and for the recurrence risk assessment. Post-translational modified proteins (PTM proteins), differentially expressed in tumors compared to healthy ones, and metabolites, again differentially expressed in the two populations, patients and controls, will be evaluated. Furthermore the Single-Molecule with a large Transistor (SiMoT) platform will be the innovative device to early detect PTM proteins.

### 2.24.3. Description of Communication and Dissemination Activities

The communication and dissemination activities, undertaken by the GPII BA, of the results of the pilot study on the identification of two panels of biomarkers for the early diagnosis of gynecological tumors and for assessing the risk of recurrence will focus on the dissemination of the results through presentations, such as oral reports or posters, at national conferences and internationally in order to reach a broad audience of global experts in translational oncology. Furthermore, the results will be published in international peer-reviewed journals to allow all interested researchers to have access to them. A wider audience, including patients and patient associations, will be reached through specific meetings that will be organized and through social media, such as LinkedIn and Facebook.

The relevant conferences in which the staff involved in the pilot study will participate will include the AACR Annual meeting, the EORTC-PAMM meeting, the meeting of the Italian Society of Oncology (SIC), Translational MITO meeting during which the results obtained will be presented as oral and poster presentations at in order to promote its diffusion among Translational Oncology experts.

#### 2.24.4. Target Audience

The communication and dissemination activities of the results of the pilot study will involve both doctors and researchers interested in the identification of biomarkers for the early diagnosis of gynecological tumors and for assessing the risk of recurrence as well as patient associations.

#### 2.24.5. Objectives and Expected Impact

The pilot project may lead to the development of scientific collaboration with industrial partners for the development of tools for the rapid and accurate identification of panels of biomarkers identified for the early diagnosis of gynecological tumors and for assessing the risk of recurrence. This could allow for a more rapid and accurate early diagnosis or risk of recurrence of these oncological pathologies, significantly reducing healthcare costs.

#### 2.24.6. Feedback and Evaluation

The feedback obtained from both the scientific community and patient associations will help improve the research plan and will provide an indication of the strength of the communication and dissemination activities implemented by GPII BA.

## 2.25. Task 4.4 - Bringing Medicine Digitalization into the Italian Solid Organ Transplant Network (responsible: Patrizia Burra - UNIPD) - 1

### 2.25.1. Title

Bringing Medicine Digitalization into the Italian Solid Organ Transplant Network.

### 2.25.2. Abstract

Liver and kidney transplantation represents an effective therapeutic option for patients with end-stage disease. Predicting post-transplant graft function, as well as forecasting the

development of post-operative complications (both graft-related and unrelated) still represents a significant goal in such setting. A proper matching of donor and recipient features, in combination with intraoperative factors and graft quality, currently represents the best method to predict post-operative outcomes.

As in other fields of Medicine, Artificial Intelligence has been proposed as a valuable tool to increase the predictive accuracy of post-transplant patient and graft survival.

Therefore, the present study aims at evaluating whether the implementation of an artificial intelligence model in donor-recipient matching can improve the outcome prediction of liver and kidney transplant recipients.

This will be a single-center, retrospective, observational study, including n.240 transplant recipients (n. 120 liver and n. 120 kidney), with available pre-transplant graft histology, who underwent liver or kidney transplant between 2018 and 2021 at Padua University Hospital. Patients aged < 18 years at time of transplant, with acute liver failure or acute-on-chronic liver failure, undergoing dual kidney transplantation or receiving a graft from donation after cardiac death will be excluded.

After digitization of pre-transplant graft biopsies, donor morphological features will be combined with clinical donor and recipient features in a novel artificial intelligence model, able to predict post-transplant patient and graft outcome.

This artificial intelligence model, improving donor-recipient matching, will ultimately lead to a more individualized management of complex clinical situations.

### 2.25.3. Description of Communication and Dissemination Activities

Data provided by this pilot will be presented at National and International Meetings, in the field of Solid Organ Transplantation, Hepatology, Nephrology and Artificial Intelligence. Data will be submitted for publication in extenso, as original papers, into peer-reviewed, high-impact Journals.

We will plan to submit data provided by this study in abstract form, to be presented at National and International Meetings on Solid Organ Transplantation (e.g., International Liver Transplant Society Annual Meeting; European Society for the Organ Transplantation Annual Meeting), Hepatology (e.g., American Association for the Study of the Liver Annual Meeting; European Association for the Study of the Liver International Liver Congress; Italian Association for the Study of the Liver Annual Congress; European Liver

and Intestine Transplant Association Annual Congress), Nephrology (European Kidney Transplant Association Annual Congress; European Renal Association Annual Congress). We will plan to present data at Local, Regional and National levels through Hospital meetings, as well.

Data provided by this pilot will be submitted for publication as original papers into high-impact, peer reviewed, international Journals, as Journal of Hepatology (ISSN 0168-8278, IF 25.7), Lancet Gastroenterology and Hepatology (ISSN 2468-1253; IF 45.042), Gastroenterology (ISSN 0016-5085, IF 29.4) Transplantation (ISSN 0041-1337, IF 6.2)

#### 2.25.4. Target Audience

The target audience will be Researchers actively involved into Local, National and International Liver and Kidney Transplant Programs, including Hepatologists, Nephrologists, Surgeons, Pathologists. Moreover, our plan is to present data to National and International Policymakers, in order to update the current policies on kidney and liver allocation.

#### 2.25.5. Objectives and Expected Impact

We expect that our model, which incorporates also pre-transplant histological features, will perform better than commonly used, non-AI based predictive models. Therefore, we expect a refinement of donor-recipient matching at the time of organ allocation, to ensure a better post-operative outcome. This could expand the role of organ transplantation as an effective therapeutic option for patients with end-stage liver/kidney disease, improving attitudes, knowledge, and social perceptions toward organ donation.

#### 2.25.6. Feedback and Evaluation

We will be committed to promoting results of this study, providing visibility through data presentation at International Congresses and subsequent submission at high-impact, peer reviewed Journals.

We expect that, once published, the papers reporting data from this study will reach a consistent number of citations.

External validation of our model from other Centers will be viewed as further, valuable positive feedback. Furthermore, we expect that these studies will offer tools for updating current National and International allocation policies.

## 2.26. Task 4.4 - Bringing Medicine Digitalization into the Italian Solid Organ Transplant Network (responsible: Luciano Potena – AOU BO) - 2

### 2.26.1. Title

Use of machine-learning algorithms, biomarkers and measures of quality of life to personalize medical management of liver and heart transplant recipients (DARE BIO-QU).

### 2.26.2. Abstract

Advancements in heart and liver transplant management have improved short-term outcomes, yet long-term challenges persist due to complications and clinical complexity of patients.

The evidence-based approaches necessitate a shift towards digitalization, artificial intelligence (AI), and biomarkers for a better personalized care, and in this context the Machine learning (ML) and the Deep Learning (DL) models, analyzing extensive datasets, offer potential in predicting long-term complications and management strategies. Current efforts often focus on specific outcomes, but in solid organ transplantation area, a comprehensive model which includes infections, cardiovascular issues, malignancies, and graft dysfunction is essential. Moreover, integrating biomarkers like cell-free DNA and T-lymphocyte subpopulations, the analysis of quality of life (QoL) and frailty, a dynamic state affecting both recipients and pre-transplant patients, is crucial.

Based on this background, we designed DARE BIO-QU study that is structured in two phases:

- 1) a retrospective phase that will use the data acquired during clinical practice and aiming at developing ML-based scores that can allow to predict at patient level the risk of infections, cardiovascular diseases, new onset malignancies and chronic graft dysfunction, and describing the trajectory of this risk over time,
- 2) a prospective phase in which we will test the association of biomarkers, QoL and frailty assessments with the ML-scores applied prospectively in heart and liver transplant recipients.

DARE BIO-QU is an observational, low risk tissue-based, non-pharmacological, retrospective-prospective study that will include adult patients undergone or that will undergo heart and liver transplant followed or that will follow at Heart Failure and Transplant Unit and Internal Medicine Unit for the Treatment of Severe Organ Failure at IRCCS Azienda Ospedaliero-Universitaria di Bologna (IRCCS AOUBO).

We estimate to include in the analysis about 1000 patients.

The primary aim of this study is to predict the risk of infections, cardiovascular events, new onset malignancies and chronic graft dysfunction at 3, 5 and 10 years after transplantation by applying AI methods.

The secondary aim of the study is to test the hypothesis that relevant biomarkers and scores of frailty, quality of life and cognitive ability may correlate with the AI-developed algorithms and therefore these may represent early markers of subsequent clinical events.

We believe that the outcomes of this project will support clinical progress over three sequential steps:

The results of DARE BIO-QU will provide the clinical framework to improve post-transplant care in the outpatients setting, therefore improving clinical outcomes and patients' quality of life, while reducing the need for hospitalizations and costly therapeutic interventions, the technological background to develop AI-based approaches to customize therapeutic management in patients with complex disease mechanisms and given the peculiar characteristics of transplant recipients representing a multimorbid frail population at high risk of cardiovascular, neoplastic and infectious events, the information gained from this project, in the context of global risk assessment, may serve as a hypothesis-generating for future studies aiming to assess profiles for cardiovascular and neoplastic risk in the general population.

### 2.26.3. Description of Communication and Dissemination Activities

Use of machine-learning algorithms, biomarkers and measures of quality of life to personalize medical management of liver and heart transplant recipients" (DARE BIO-QU) is a clinical study that will involve solid organ transplant patients at IRCCS Azienda Ospedaliero-Universitaria di Bologna (IRCCS AOUBO). The communication and dissemination plan for DARE BIO-QU include a multifaceted approach aimed at reaching

diverse audiences. The primary objective is to share research findings, advancements, and insights and results derived from the study by peer-review, papers and abstracts.

In order to promote knowledge exchange and collaboration, the study plans to organize and participate in seminars and meetings, both at the national and international levels. These events will offer a platform for direct interaction with healthcare professionals, encouraging the exchange of ideas and the incorporation of study findings into clinical practice.

Target audiences include transplant surgeons, physicians, nurses, and researchers specializing in solid organ transplantation.

Additional ways of dissemination include social networks, by the sharing of specific posts, directed to medical personnel and the general population.

The communication and dissemination strategy for the DARE BIO-QU includes targeted activities to maximize impact.

- publishing its findings in reputable peer-reviewed journals
- contributing to national and international conferences, such as the International Society for Heart and Lung Transplantation (ISHLT), American Transplant Congress (ATC), European Society for Organ Transplantation (ESOT). These platforms will facilitate direct engagement with key stakeholders, allowing for the exchange of insights and the integration of study outcomes into clinical practice;
- social media platforms;
- liaise with IRCCS AOUBO press office to plan activities directed to general public.

#### 2.26.4. Target Audience

The target audience for DARE BIO-QU will include a diverse range of stakeholders within the healthcare and research communities. Specifically:

- Researchers and Clinicians;
- Transplant Surgeons and Physicians;
- Nurses and Healthcare Providers;
- International and National Medical Conferences;
- Patients;
- General population.

#### 2.26.5. Objectives and Expected Impact

The DARE BIO-QU aims to contribute new knowledge to the scientific community, in order to improve the understanding and management of solid organ transplantation patients. By publishing in transplant journals and presenting at conferences, the goal is to

establish the study's findings and the artificial intelligence application as a valuable resource for researchers and clinicians, influencing future studies and medical practices. Secondly, the activities target healthcare professionals directly involved in transplantation procedures, aiming to improve patient outcomes by disseminating evidence-based insights. The study seeks to bridge the gap between research and clinical application, fostering a more immediate and tangible impact on medical decision-making.

Furthermore, the dissemination efforts aspire to contribute to improve the knowledge of medical professionals, ensuring that the study's findings become integrated into training programs and medical curricula. By engaging with the general public through health website, the study aims to raise awareness about the significance of organ transplantation advancements, garnering support for ongoing research and fostering a broader understanding of the field.

#### 2.26.6. Feedback and Evaluation

- Citations in peer-reviewed journals will be monitored over time, providing a quantitative measure of the study's impact within the academic community (i.e. Web of science, Scopus).
- Online feedback including showing posts and social media interactions.

### 2.27. Task 4.4 - Bringing Medicine Digitalization into the Italian Solid Organ Transplant Network (responsible: Giuseppe Tisone UNIROMA2) - 3

#### 2.27.1. Title

Non-invasive biomarkers for early diagnosis of delayed graft function and acute rejection after solid organ transplantation

#### 2.27.2. Abstract

Solid organ transplant recipients represent a very frail population with high risk of morbidity and mortality at short term after transplantation. The current project aims to assess a new non-invasive biomarker, the Mid-regional pro-adrenomedullin (MR-proADM), for the diagnosis of delayed graft function (DGF) and acute rejection (AR) after kidney and liver transplantation, which represents the major complications after solid

organ transplantation. Mid-regional pro-adrenomedullin (MR-proADM) is a peptide with a variety of physiological functions such as immunomodulatory, direct bactericidal, and has a function in maintaining renal homeostasis and vasodilator activity. The hypothesis of the study is that MR-proADM may increase in the early stages of post-transplant organ dysfunction (delayed graft function/early graft dysfunction) and acute rejection, both after kidney and liver transplantation, as a response to endothelial damage and immune activation.

The research activity consists in a prospective pilot study based on the dosage of MR-proADM from peripheral blood sampling in kidney and liver transplant recipients. Peripheral blood analysis will allow the serum assay of MR-proADM via the time-resolved amplified cryptate emission assay. The sampling will be performed together with the routine samplings in ordinary hospitalization and outpatient settings according to the common clinical follow-up practice of post-operative transplant patients. The examination will be performed on the day of the transplant, on the 1st and 5th post-operative day, 1-3-6-12 months after the transplant, and in case of suspicion of acute rejection and post-operative complications. The study will use advanced technology for MR-Pro-ADM dosage and digital pathology for graft biopsy and will develop an online platform to collect and correlate data on post-transplant biopsy and MR-Pro-ADM levels.

### 2.27.3. Description of Communication and Dissemination Activities

The current study has the objective to assess the role of a new biomarker, the Mid-regional pro-adrenomedullin (MR-proADM), in predicting the risk of post-transplant complications such as early allograft dysfunction and acute rejection after kidney and liver transplantation, which might guide physicians to personalize therapies and prevention. The specific objectives include a) to define the sensibility and the specificity of increased levels of MR-proADM for early, non-invasive, diagnosis of AR and DGF after kidney and liver transplantation; and b) to create a predictive model of complications after kidney and liver transplantation based on the pre-operative and post-operative levels of MR-proADM by machine learning process.

Our target audience include clinicians involved in solid organ transplantation (transplant surgeons, nephrologist, hepatologist, infectiology) and researchers involved in immunology. The results of our study will be disseminated in national meetings (Società

Italiana dei Trapianti d'Organo, Società Italiana di Nefrologia, Associazione Italiana Studio del Fegato) and international meetings (International Liver Transplant Society, European Society of Organ Transplantation) and published as original research in international peer review journal with high rank (Q3).

The study's result will provide useful tools for the clinical management of kidney and liver transplant recipients developing complications such as acute rejection and delayed graft function after transplantation. The results will be disseminated by 1) oral/abstract presentation at national (Società Italiana dei Trapianti d'Organo, Società Italiana di Nefrologia, Associazione Italiana Studio del Fegato) and international (International Liver Transplant Society, European Society of Organ Transplantation) meetings concerning solid organ transplantation; 2) the institutional channel of the University of Rome Tor Vergata (social media) and authors' networks; 3) we plan to submit an original article reporting the project to an high rank journal (Q3) -Transplantation or American Journal of Transplantation; 4) by the Immunology Special Interest Group of the International Liver Transplant Society to the transplant community social network.

#### 2.27.4. Target Audience

The target audience are researchers working on solid organ transplantation, immunology, biochemistry, and infection diseases as well as transplant surgeons, nephrologist, hepatologist and infectiology. As the study aims to identify tools useful for the early detection of post-transplant, also the associations of solid organ transplant patients (national and international) of kidney and liver will be targeting audience.

#### 2.27.5. Objectives and Expected Impact

The communication of the study and its results has the specific objectives of:

- Development of a software algorithm predicting the risk of post-transplant complications;
- Development of digital pathology for graft biopsy;
- Development of an online platform to collect and correlate data on post-transplant biopsy and MR-Pro-ADM levels.

We also expect that the project will permit to improve the post-operative management of kidney and liver transplant recipients, by early detection of complications and personalized therapies.

### 2.27.6. Feedback and Evaluation

We will evaluate the effectiveness of our communication and dissemination activities by the number of citations of the article reporting the study as well as the type of peer review journal accepting the article and eventual commentary from experts in the field. We will evaluate feedback during the project's presentation at meetings and on social media. Finally, we will assess the effectiveness of the project dissemination by evaluating the number of transplant center adopting the studied bio-marker Pro-ADM, participating to the digital pathology and using the developed software algorithm predicting the risk of post-transplant complications.

## 2.28. Task 4.5 - Digital biomarkers for Parkinson and Alzheimer diseases in subjects with psychiatric and cognitive disorders or with Down Syndrome (responsible: Raffaele Lodi - ISNB)

### 2.28.1. Title

Digital biomarkers in Parkinson and Alzheimer diseases and with Down Syndrome. Implementation of biomarkers to identify subjects at risk for conversion from preclinical or pauci-symptomatic conditions to Parkinson and Alzheimer diseases.

### 2.28.2. Abstract

Neurodegenerative diseases (ND; including Alzheimer's and Parkinson's disease, AD and PD) are preceded by a long prodromal phase, that represents the best therapeutic window but whose diagnosis is difficult. In the project we will focus on prodromal patients (RBD, SCD/MCI, DS) with a high conversion rate to overt ND. We will integrate clinical/neuropsychological, imaging, biochemical and omic data to identify markers for the early diagnosis of ND, potentially applicable to the general population.

### 2.28.3. Description of Communication and Dissemination Activities

The communication and dissemination activities will include:

- Presentation of project results in national and international meetings, in particular in conferences related to neurology;
- Publication of project results in peer reviewed journals, preferring open access journals;

- Dissemination of project results to the general public through the website and the Facebook page of the IRCCS Istituto delle Scienze Neurologiche di Bologna;
- Tentative names of the meetings: meeting of the Società Italiana di Neurologia (SIN), meeting of the Associazione autonoma aderente alla SIN per le demenze (SINDEM), national congress "Sindrome di Down: dalla diagnosi alla terapia", IV annual RIN Meeting, International meeting of the T21 Research Society, congress of the European Academy of Neurology;
- Tentative names of the journals: NPJ Parkinson's disease, Movement disorders, Alzheimer's Research & Therapy, Brain, Neurobiology of disease, European Journal of Neurology, Journal of Neurology, Frontiers in Neuroscience, Frontiers in Aging Neuroscience, Frontiers in Genetics.

#### 2.28.4. Target Audience

- Researchers
- General public

#### 2.28.5. Objectives and Expected Impact

- Promote scientific knowledge transfer and collaborations among researchers
- Promote evidence-based decision-making
- Increase general public awareness on prodromal conditions of neurodegenerative diseases

#### 2.28.6. Feedback and Evaluation

- Number of citations
- Researchers' feedback at meetings
- Number of visits and sharing of website and Facebook page

### 2.29. Task 4.6 - Human microbiome Eubiosis/dysbiosis state prediction based on DNA-metabarcoding data collection and analysis (responsible: Bruno Fosso - UNIBA)

#### 2.29.1. Title

A ML-based approach to establish an effective and accurate indicator of the eubiosis/dysbiosis status through DNA metabarcoding microbiome assessment.

#### 2.29.2. Abstract

The human body is a complex ecosystem that houses trillions of microorganisms, collectively known as the human microbiome, which plays a critical role in maintaining our overall health and wellbeing. In particular, the physiologic balance among the gut

microbiome and the host (eubiosis) is characterized by high taxonomic diversity, whose perturbation (dysbiosis) is often coupled to reduced diversity and pro-inflammatory microenvironment. The advent of metagenomics allowed to fully access the complexity of microbial communities. Among the others, DNA-metabarcoding represented the most applied approach. Indeed, it is fast and cheap both in terms of experimental procedure and bioinformatic analysis. It relies in the selective amplification and sequencing of a barcode and its taxonomic classification to profile the microbiota composition. The main features of a barcode are ubiquitousness in the target taxonomic range of interest, suitable variability needed for the classification specificity, and the possibility to use “universal” primers for its amplification thanks to the conserved regions on both sides. Finally, the overall length of the barcode should be compatible with technical limitation of sequencing platforms. A remarkable example of barcode is the prokaryotic 16S rRNA gene. It is characterized by 9 hyper-variable regions suitable for taxonomic classification flanked by constant ones, useful for primer design. These features allowed researchers to target one or more 16S rRNA hyper-variable regions and ensure an amplicon length compatible with NGS technical limitations. In the current state of the art, an operational and objective definition of a healthy microbiome is lacking, likely because of many confounding factors particularly gender and age. In 2020 Gupta et al., introduced the Gut Microbiome Health Index (GMHI), a statistical approach to predict the likelihood of eubiosis/dysbiosis by using shotgun metagenomics data available in public repositories. Within this framework, machine learning (ML) approaches emerge as potentially powerful tools for forecasting the state of eubiosis or dysbiosis, circumventing the limitations inherent in traditional statistical methodologies. The overall goal of this proposal is to define a precise and accurate model able to predict eubiosis/dysbiosis.

### 2.29.3. Description of Communication and Dissemination Activities

Dissemination activities will take advantage of publications on peer reviewed journals, seminars, national or international meetings.

The proposed pilot project aims to develop both a bioinformatic framework for DNA-metabarcoding data analysis and a ML-based model to predict eubiosis/dysbiosis. From a scientific point of view our aim is to publish the achieved results in peer reviewed journals (e.g. Bioinformatics, BMC Bioinformatics, Genes, Scientific Reports, Microbiome). In order,

to improve papers diffusion we planned to take advantage of social media platforms, such as X and LinkedIn.

Regarding dissemination activities we planned to participate to both national (BITS and SIBBM annual meeting) and international (Human Microbiome Congress) conferences. Considering the conferences target, we planned to employ conventional tools for data showing, such as Power Point Presentations and Posters, by also augmented reality tools, such as QR code, to facilitate the access to data and resources.

Power Point presentations and YouTube videos will be employed to disseminate project results and applications to high school alumni.

#### 2.29.4. Target Audience

Researchers, and general public audience.

#### 2.29.5. Objectives and Expected Impact

At least 2 peer reviewed papers describing pilot project methodologies and results.

Through the participation at national and international activities we aim to disseminate methods and data generated within the pilot project and show the obtained results.

Finally, we aim to raise awareness about a healthy lifestyle through the participation to outreach initiatives addressing high school alumni.

#### 2.29.6. Feedback and Evaluation

According to the dissemination strategy we aim to collect:

- Number of citations and Altmetric scores for peer reviewed publications;
- Number of participants to national and international conferences;
- Number of participants to outreach activities.

### 2.30. Task 4.7 - Neurotransmission enriched connectivity as a biomarker of healthy and accelerated ageing in human brain (responsible: Mattia Veronese - UNIPD)

#### 2.30.1. Title

Neurotransmission enriched connectivity as a biomarker of healthy and accelerated ageing in human brain.

### 2.30.2. Abstract

Age-related diseases are becoming increasingly important in developed countries due to their association with increasing life expectancy. This project will impact a significant portion of the global population. The World Health Organization predicts that by 2040, neurodegenerative conditions such as Alzheimer's Disease and Parkinson's Disease will become major leading causes of death in western countries (World Health Organisation, World Health Statistics 2022, <https://www.who.int>). Currently, more than 55 million people worldwide live with dementia, and there are nearly 10 million new cases every year. Therefore, this project will significantly influence the quality of life for millions of people.

The aim of this research project is to develop a neuroimaging method capable of modelling healthy aging at an individual level and providing biologically informed early predictions of neurodegeneration and cognitive decline. This idea is based on the fact that individuals on fast-aging trajectories have been associated with cognitive impairment and other brain disorders. The project will span four years, beginning with the definition of the model on healthy controls and concluding with the implementation of the method on patients' data. It will leverage the use of functional Magnetic Resonance Imaging to measure both normal and abnormal brain connectivity.

### 2.30.3. Description of Communication and Dissemination Activities

- Publication of 3+ scientific papers in peer reviewed journals;
- Presentation of findings at international and/or national scientific meetings, with a focus on the neuroscience and neurobiology of aging, including at least one presentation per year – either oral or poster presentations;
- Participation to public engagement activities (like “pintofscience” or similar) to present the project aims and explain its findings to general public.

### 2.30.4. Target Audience

- Scientific community;
- General public.

### 2.30.5. Objectives and Expected Impact

#### SCIENTIFIC COMMUNICATION

- To collect feedback from scientific community on the project methodology and outcomes;
- To gain scientific recognition of project activities and its findings;

## PUBLIC ENGAGEMENT

- To raise awareness on problems of ageing and mental health
- To promote healthy lifestyle and behavior that could benefit people mental health throughout the lifespan

### 2.30.6. Feedback and Evaluation

## SCIENTIFIC COMMUNICATION

- Researchers' feedback (e.g. reviews' comments from paper submissions, questions during conferences)

## PUBLIC ENGAGEMENT

- Attendance of participants during the public engagement events
- Satisfaction questionnaire at the end of the activities

## 2.31. Task 5.1 - IBD care through hub&spoke infrastructure (responsible: Marco Salice - AOU BO)

### 2.31.1. Title

IBD care through hub&spoke infrastructure.

### 2.31.2. Abstract

The Emilia-Romagna Inflammatory Bowel Disease (IBD) hub&spoke infrastructure will be developed further to allow for continuous quality of care assessment, research facilitation, timely alerting on clinical pathway management, benchmarking, and patient engagement.

The goal of our project is to create a data collection tool on the management of patients with inflammatory bowel disease that is self-implemented by data coming from routine healthcare activity or from data entered directly by patients through a self-reporting system. This system, inserted in a hub-spoke network, will allow not only the collection of real-life data on a large cohort of patients, but also to carry out internal and external evaluation/validation of clinical performance and correction of critical issues.

The collection of data from routine healthcare activity, including the time factor as a principal determinant, will allow for the identification of predictive factors of unfavorable evolution of disease or of ineffectiveness of treatment. The identification of predictive factors of ineffectiveness of treatment or development of disability will enable the

modification of current therapeutic schemes proposed by current guidelines and to evaluate their effectiveness.

### 2.31.3. Description of Communication and Dissemination Activities

The pilot project will be presented in medical meetings in order to stimulate discussion on the topic and identify a network of IBD centers which, subsequently, can be part of the territorial extension program of the project itself.

The project will be presented during the IBD-extra meeting which will be held in Reggio Emilia on 15 January 2024 and during the IBD-Border meeting which will be held on 8 and 9 June 2024 in Bologna. The events will be posted on the linked-in pages of the pilot managers.

### 2.31.4. Target Audience

The target audience are medical specialists who deal with IBD and the medical directors of the hospital involved.

### 2.31.5. Objectives and Expected Impact

The objective is to raise awareness among doctors and stakeholders on the need to implement specialist network and telemedicine systems to improve the management of patients with IBD.

### 2.31.6. Feedback and Evaluation

Stakeholder feedback and reactions collected with the linked-in system will be collected.

## 2.32. Task 5.2 - Home monitoring - based approach to support diagnostic, therapeutic and assistance pathway of patients with chronic kidney disease (responsible: Loreto Gesualdo - UNIBA)

### 2.32.1. Title

Digital therapy and telemedicine approaches for nutritional intervention in chronic diseases.

### 2.32.2. Abstract

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited renal disease occurring in 1:400 - 1:1000 live births. It affects 4 to 6 million persons worldwide and about 205.000 people in Europe. Although several different treatments have been proposed in the last years, a discrete amount of ADPKD patients presented kidney function decline during disease course and develop End Stage Renal Disease (ESRD) requiring dialysis. Nutritional approaches represent a crucial aspect in the treatment of ADPKD with the aim to limit CKD progression.

The aim of the study is to integrate an IoT infrastructure with clinical, imaging data and genetic background to guide a tailored nutritional (e.g., ketogenic diet) and pharmacological intervention (e.g., metformin vs tolvaptan) for improving patient care in relation to the risk of disease progression. IoT technology has the potential to improve the prevention and prediction of ESRD in patients with ADPKD by providing remote monitoring, early detection of kidney function decline, medication and lifestyle management, also enabling data analytics.

Using a wearable device, it will be possible to monitor patients' eating habits, provide an accurate estimate of the quality of diet and caloric/protein intake and analyse the impact of these interventions on kidney function decline and clinical outcomes in patients with ADPKD.

### 2.32.3. Description of Communication and Dissemination Activities

The pilot will include communication and dissemination activities which will serve to reach the target audience of clinicians and researchers as well as patients and patient's associations. The main scientific outcomes on the development of specific protocols and tools to improve the prevention and prediction of ESRD in patients with ADPKD will be published on relevant peer reviewed journals. The specific results will be disseminated at national and international conferences on nephrology and genetic diseases. The main breakthroughs of the pilot will be shared to the general community via the social media pages - such as LinkedIn and Facebook - of the researchers involved in the pilot or by specific meetings with patients or patient's associations.

Lectures, oral and poster presentations at national and international conferences, will promote communication and dissemination activities as well as description of results in

photo and video shared on social media (LinkedIn, X, Facebook etc.). Some relevant meetings will be attended by the personnel included in the pilot activities, such as the American Society of Nephrology, the European Renal Association, the Italian Society of Nephrology. Results will be submitted to international journals at high impact factor such as journals of Springer, Wiley, Science, Elsevier Editorials' groups.

#### 2.32.4. Target Audience

The pilot communication and dissemination activities will be mostly addressed to clinicians and researchers who are interested in ADPKD and clinical management of patients. Also, the involvement of patient's associations such as AIRP (Associazione Italiana Rene Policistico) or ANED (Associazione Nazionale Emodializzati Dialisi e Trapianto) is foreseen as well as dissemination activities addressed to the ERKnet Community (European Rare Kidney Disease reference network) of which the pilot leader is part.

#### 2.32.5. Objectives and Expected Impact

The pilot will help strengthening the scientific collaboration with industrial partners developing and manufacturing novel IoT solutions to Improve diet adherence and assess disease progression; this will help to reduce the significant burden on the healthcare system due to ADPKD patients, as individuals with ESRD require ongoing dialysis significantly increase healthcare costs.

#### 2.32.6. Feedback and Evaluation

Direct feedback after dissemination activities in meeting and conferences by the scientific community will provide an indication of the strength of the communication activities and will help to improve the research plan. Surveys filled by patients may also be used to score the effectiveness of the dissemination campaign.

## 2.33. Task 5.3 - Prevention of adverse events in preterm and term infants by remote monitoring (responsible: Maria Grazia Capretti - AOU BO)

### 2.33.1. Title

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.

### 2.33.2. Abstract

The project consists of two clinical trials using commercially available wearable devices for continuous monitoring of preterm and term infants at risk for early adverse events and later neurodevelopmental impairment. Approximately 1 in 14 newborns in Italy is born preterm. Prematurity strongly impacts on mortality and morbidity. Family centered care (FCC) is known to facilitate bonding and family involvement in infant care, to reduce length of stay in the Neonatal Intensive Care Unit (NICU) and to improve clinical outcomes. Sudden unexpected perinatal collapse (SUPC) is a rare event (approximately 1 in 10.000 live newborns), with its highest incidence in the first hours of life. Although rare, the consequences of SUPC can be substantial. At present, the pathogenesis is not yet fully elucidated and there is no established preventive tool for SUPC. Thus the project aim to apply e-health tools and telemedicine to implement FCC in the NICU and allow early discharge in preterm newborn and to improve early monitoring in healthy newborns in the delivery room and rooming-in, to promptly recognize and manage adverse events such as SUPC.

### 2.33.3. Description of Communication and Dissemination Activities

The use of the e-health tools and telemedicine in Neonatology is a new and intriguing opportunity to improve the quality of care. This topic has gained progressive importance in both clinical and research settings, so it is expected to successfully disseminate the results of the study in both fields, through presentation of the results at both local and national meetings in Neonatology and Pediatrics and through publication of the results in peer reviewed journals. The target audiences are both clinical practitioners and researchers in the field of non-invasive monitoring and bioengineering. The general public as well,

namely the families of preterm and term neonates, are expected to be target of the dissemination of the results.

The plan is to present the results of both parts of the study separately: one part regarding e-health tools and telemedicine to improve FCC in the preterm population and the other one regarding e-health tools to prevent SUPC in term neonates. The preliminary results will be sent as abstract presentations at the regional and national meetings of the Italian Society of Neonatology. The final data will be sent as original paper to a peer reviewed journal in the field of Pediatrics and Neonatology.

#### 2.33.4. Target Audience

The target audience is represented by clinical practitioners in Pediatrics and Neonatology, clinical researchers and researchers in the field of e-medicine and bioengineering, and the general public, particularly the families of preterm and term neonates. If these strategies will result in better outcomes for neonates, it would be advisable to share the results also with healthcare policymakers, to implement e-health tools and telemedicine as standard of care.

#### 2.33.5. Objectives and Expected Impact

In case of successful results of the projects, we expect our results to be disseminated for a routinely application of e-health tools and telemedicine in clinical practice to improve the care of preterm and term neonates.

Specifically, for preterm infants it is expected to reduce the hospital stay in the NICU, which can lead to a better management of neonates, with reduced stress and anxiety for families, reduced risk of conditions associated with a prolonged hospitalization for the neonates (e.g. hospital acquired infections) and money savings for the health-care system.

For term infants, in case of the successful use of tools for non-invasive monitoring in the delivery room and during rooming-in for the prevention of SUPC, it would be of outstanding importance to disseminate this practice.

#### 2.33.6. Feedback and Evaluation

The effectiveness of the communication and dissemination activities in the meetings will be evaluated through the received feedback by colleagues and experts in the field. The

effectiveness of the publications in journals will be evaluated through the number of citations of the papers.

## 2.34. Task 5.4 - Therapy optimization and prevention of adverse events in diabetes management (responsible: Stefano Cianfarani and Andrea Facchinetti- UNIROMA2 and UNIPD)

### 2.34.1. Title

A digital, integrated and scalable mobile platform based on wearable sensors to prevent/reduce the risk of complications in type 1 diabetes.

### 2.34.2. Abstract

This pilot project will develop and test a new mobile platform integrating a decision support system (DSS) for clinicians able to generate personalized indications for the optimization of the therapy of pediatric population with type 1 diabetes (T1D). To achieve this, a dedicated mobile app will automatically collect patient data from wearable devices such as continuous glucose monitoring, insulin delivery systems, and activity trackers. The system will then create a digital twin of the patient to ultimately generate therapy recommendations thanks to AI-based techniques. We will test the platform on retrospective data and then we will validate it through a prospective study.

### 2.34.3. Description of Communication and Dissemination Activities

The communication and dissemination activities of the pilot plan centers around:

- Peer-reviewed journals: publish 1-2 paper per year in high-impact international journals.
- National and International conferences: engage in major technological and clinical conferences focused on metabolic diseases.
- Social media updates: provide continuous project updates and share major achievements on popular social media platforms.

The communication and dissemination strategy aims to leverage peer-reviewed journals for in-depth research dissemination, active participation in relevant international conferences, and real-time updates through prominent social media platforms.

We plan to publish at least 1 paper on the DSS infrastructure design, 1 paper on the algorithmic core of the DSS, 1 paper on the system usability and overall engagement, 1

paper on the results of the clinical prospective study. Possible target journals include the IEEE Transactions on Biomedical Engineering, Journal of Diabetes Science and Technology, Diabetes Technology and Therapeutics, Diabetes Obesity and Metabolism, Diabetologia, and Diabetes Care.

Participation to important international conferences will represent a major activity in the second half of the project. This will include conferences focused on metabolic diseases, such as the International Conference on Advanced Technologies and Treatments for Diabetes, Annual Meeting of the European Association for the Study of Diabetes, American Diabetes Association Scientific Sessions, National meeting of Italian pediatric Endocrinology and diabetes Society, European Society for Pediatric Endocrinology, International Society for Pediatric and Adolescent Diabetes, as well as major conferences of engineering and data science, including the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, the IEEE Conference on Biomedical and Health Informatics, and the International Conference of Artificial Intelligence in Medicine.

Finally, a continuous report on project advancements will be provided to the scientific and technological community through the most important social media (Facebook, Twitter, Instagram and LinkedIn).

#### 2.34.4. Target Audience

The target audience of this communication and dissemination strategy includes a diverse group of stakeholders involved in the management and treatment of type 1 diabetes in children and adolescents (pediatric endocrinologists and diabetologists), ranging from academic researchers and healthcare practitioners to professionals in engineering, data science, and the broader scientific and technological community.

#### 2.34.5. Objectives and Expected Impact

The impact of this communication and dissemination strategy extends across academic, clinical, technological, community, and societal dimensions. It has the potential to improve current literature, influence healthcare practices by contributing to advancements in the management of children with T1D. Furthermore, it can attract attention from industry professionals, fostering potential collaborations and technology adoption.

### 2.34.6. Feedback and Evaluation

Feedback will be evaluated through:

- Citation analysis by tracking the number of citations for published papers.
- Online engagement analytics by monitoring social media engagement (likes, shares, comments) and website traffic.
- Gathering feedback from key stakeholders through surveys, interviews, or focus groups.
- User engagement with technology by monitoring user engagement metrics for any technology developed in the project (e.g., app downloads, usage patterns).

## 2.35. Task 5.5 - Non-medical wearable devices for monitoring caloric intake (responsible: Dario Gregori - UNIPD)

### 2.35.1. Title

FITMATE: Food Intake Tracker and Metabolic Evaluation for Health Enhancement.

### 2.35.2. Abstract

Monitoring lifestyle, and in particular caloric intake and energy expenditure, is currently a crucial challenge for maintaining individual and public health. Traditional methods (i.e., questionnaires) do not reach an acceptable level of accuracy, having an estimated error of 25% on the estimate of daily caloric intake.

This study aims to develop a precise and stable algorithm for estimating caloric intake using machine learning methodology. The study will capture categorized individual eating activities firstly in target populations (i.e., people with special diet requirements) for algorithm development, then in healthy Italian people. Raw data from wearable devices will be analyzed through an up-to-date machine learning approach to accurately predict the caloric contribution of individual eating activities.

### 2.35.3. Description of Communication and Dissemination Activities

The communication and dissemination activities for this pilot study will encompass a variety of channels to ensure broad outreach and engagement. These activities will include:

- Publishing research findings in high-impact (Q1 or Q2), peer-reviewed journals related to nutrition, public health, digital health technology, and machine learning

(e.g. Lancet Digital Health or BMC Digital Health, BMC Medical Research Methodology).

- Presenting at national and international conferences focused on nutrition, digital health, and wearable technology to share insights and gather expert feedback (e.g. we will present our first findings at the American Society for Nutrition Meeting 2024).
- Engaging with the public and specific target groups through workshops, webinars, and online platforms to raise awareness about the importance of accurate caloric intake monitoring.
- Utilizing social media channels to disseminate project updates, milestones, and results to a wider audience, fostering community engagement and dialogue.

#### 2.35.4. Target Audience

The target audience for this pilot study includes:

- Researchers and academics in the fields of nutrition, public health, digital health technology, and machine learning.
- Healthcare professionals, particularly nutritionists and dietitians, who may utilize the developed algorithm in their practice.
- Patients with specific dietary requirements, such as those with PKU, diabetes, or those on a ketogenic diet for polycystic kidneys.
- The general population interested in personal health, fitness, and lifestyle improvement through wearable technology.
- Industry stakeholders involved in the development and marketing of wearable devices and health apps.

#### 2.35.5. Objectives and Expected Impact

The objectives of the communication and dissemination activities are to:

- Increase the visibility and awareness of the FITMATE project and its contributions to improving dietary monitoring using wearable technology.
- Foster collaborations and partnerships with stakeholders in healthcare, technology, and patient advocacy to enhance the project's reach and applicability.
- Encourage the adoption of the developed algorithm by healthcare professionals and wearable technology providers, leading to improved patient outcomes and adherence to dietary recommendations.
- Inform policy-making and guidelines related to nutrition monitoring and management through evidence-based findings from the project.
- The expected impact includes:
  - Enhanced accuracy and objectivity in dietary monitoring, leading to better individual and public health outcomes.
  - Increased engagement and empowerment of patients in managing their dietary intake, particularly for those with special dietary needs.
  - Advancement in the integration of wearable technology with healthcare practices, contributing to the digital transformation of health monitoring.

### 2.35.6. Feedback and Evaluation

Feedback and evaluation of the pilot study will be systematically collected and analyzed through:

- Citation metrics and journal impact factors to assess the scientific influence of published research.
- Surveys and feedback forms from conference attendees, webinar participants, and workshop attendees to gauge the reception of the presented work.
- User feedback from pilot participants to evaluate the usability and effectiveness of the developed algorithm.
- Analytics from social media engagement to measure the reach and interaction of disseminated content.
- Post-implementation surveys and interviews with healthcare professionals to determine the practical application and benefits of the algorithm in clinical settings.

## 2.36. Task 5.6 - Prevention/mitigation of frailty in the continuum of care framework (responsible: Giuseppe Liotta - UNIROMA2)

### 2.36.1. Title

Developing of a social and health care integrated model to reduce the overcrowding of Emergency Room and inappropriate hospital admissions.

### 2.36.2. Abstract

Overcrowded Emergency Rooms (ER) represent a public health “Emergency” due to both inappropriate accesses and difficulties in accessing in-Hospital services, which is in turn related to the obstacles to inpatient discharge. These obstacles are partially due to the absence of effective out-of-hospital care where health and social professionals are working in separate silos because of the lack of integration of funds, procedures, tools, and measurable outcomes. The pilot aims to test a model of health and care integration starting from the ER Frequent Users (FU - patients who access the ER more than 4 times in a year) and supported by telemedicine and AI. Moreover, the pilot aims to set up an algorithm able to predict the risk of Length Of Stay (LoS) longer than the average for aged>65 inpatients in order to address intervention appropriate to prevent this event, involving community care services.

### 2.36.3. Description of Communication and Dissemination Activities

The aim of communication and dissemination activities of Task 5.6 is to communicate about a new model of management of hospital patients starting since the inpatients admission/Emergency dep. Access, in order to implement an activity plan able to avoid inappropriate use of hospital resources. Target of this communication are mainly hospital professionals and professionals working at community level. The communication will use publication on peer-reviewed journal as well as training course to be deployed at hospital and community level. Furthermore, the model developed during the project will be tested at community and hospital level in order to replicate it in case of encouraging results. The participation at national and international meeting will be useful to allow comparisons with other experiences.

Three papers will be sent within 2025 at some of the following journals:

- Annals of Emergency Medicine
- International Journal of Nursing Studies
- BMJ Open
- European Journal of Public Health
- Archives of Gerontology and Geriatrics
- BMC Health Service Research
- Journal of Medical Economy

Abstracts will be sent to the following meetings

- 17th EUPHA public health conference (Lisbona 12-14 November 2024)
- 57° congresso nazionale SItI (Palermo 23-26 ottobre 2024)

### 2.36.4. Target Audience

- Hospital personnel (MD, Registered Nurses, Health direction personnel, DPO, Ethical committee members)
- Social and health personnel involved in community care
- Policy makers at district, Local, regional and national level
- Public health researchers

### 2.36.5. Objectives and Expected Impact

It is expected that the model could be implemented by other institutions at hospital level in order to increase the integration of care. This is obviously related to meet the expectations which are the potential reduction of the patients' hospital length of stay and/or the frequency of ED accesses by Frequent Users or the number of Fus themselves.

### 2.36.6. Feedback and Evaluation

The involvement of other professionals will allow to better fine tuning the model. The type of feedback at research level (citations of published paper for example as well as the meeting at the conferences) will give us the idea of the effectiveness of communication, in order to refine the dissemination plan which is, at this stage, only a working hypothesis.



### 3. Conclusion and next steps

In this document, we present the communication and dissemination plan employed by the 36 pilot projects that compose the Spoke 3 research core within the DARE initiative. Each pilot project, although unique in its clinical focus, has adopted a systematic approach to advancing their respective domains through strategic dissemination and audience engagement. These activities will be pivotal in fulfilling the "third-mission" of transferring research products beyond academia, with efforts including social media engagement and broad public communications.

In the realm of communication and dissemination, the pilots predominantly favored scientific publications in peer-reviewed journals and presentations at national and international conferences to disseminate their findings. This approach aimed to reach a broad spectrum of stakeholders, including researchers, clinicians, and industry professionals. The pilot projects targeted diverse audiences, ranging from bioengineers and healthcare providers to policymakers and the general public, tailoring their communication strategies to the specific needs and interests of each group.

The objectives of the pilots were generally focused on engaging clinical and research partners, as well as regulators, to foster the adoption of innovative methodologies and technologies in clinical practice. The expected impact of these initiatives encompassed the enhancement of diagnostic capabilities, the refinement of therapeutic interventions, and the promotion of personalized medicine, all while considering the economic and social implications on healthcare systems.

Feedback and evaluation of the pilot projects' efforts were primarily assessed through quantitative measures such as citation counts, as well as qualitative feedback from peers during conferences and direct stakeholder interactions. The engagement of new stakeholders and the receptiveness to the methodologies introduced were also considered crucial indicators of success.

In conclusion, the last year has seen a concerted effort by the DARE pilot projects to advance their respective fields through rigorous scientific inquiry and effective



communication strategies. By targeting a wide array of stakeholders and focusing on the translation of research into practice, these projects have laid a foundation for significant clinical advancements. Looking forward, the continued evaluation and adaptation of these strategies will be vital in realizing the full potential of these innovative endeavors, ultimately contributing to the evolution of personalized healthcare and the betterment of patient outcomes.

At the time of writing, the development of the pilot studies is in line with the timing of the DARE project.