

Publishable Summary

Work Package 2 (WP2) of the DARE project is a part of Spoke 3, titled 'Digitally-enabled secondary and tertiary prevention'. The overall scope is to make considerable progresses in current and novel "Personalization and Risk Stratification Tools". WP2 comprises now seven tasks, each with a single pilot study, all focusing in fact on secondary and tertiary prevention interventions supported by ICT infrastructures.

In summary, the targeted scopes and the relevant activities will be the following. In T2.1, the clinical validation of an original digital twin technology is searched to assess more precisely patient-specific risk of hip fracture in patients with primary osteoporosis. In T2.2, digital technologies will be developed to a) assess the risk of disease progression and support clinical management of patients with early osteoarthritis, and b) predict the risk of implant failure in patients with joint prostheses. In T2.3, an available digital tool for a personalized 3D pre-operative planning of knee osteotomy procedures for patient suffering of severe OsteoArthritis will be optimized and made accessible to a large population of hospitals and surgeons; the planning will also be enhanced with a comprehensive biomechanical analysis from instrumented gait-analysis. In T2.4, an artificial intelligence system based on X-ray images will be developed and exploited to assess the risk of pathological fracture in patients affected by metastatic carcinomas, very valuable for both prevention and decision making, i.e. surgical vs non surgical treatments. T2.5 wants to provide a new stroke risk score in patients with coronary artery disease based on specific features at CT imaging, including radiomics data and blood biomarkers, assuming this can enhance the therapeutic diagnostic and stroke prevention pathway. T2.6 wants to detect changes in brain, muscle, bone, cardiovascular system, hormonal milieu and body composition in community-dwelling older frail sarcopenic and healthy active individuals with sleep disorders, to gain a deeper understanding of the impact of sleep health on Mild Cognitive Impairment and cognitive frailty, sarcopenia and physical frailty, dementia and mobility-disability. T2.7 wants to assess the probability of the risk of falling in older persons, based on the reference prior and the individual likelihood estimated from multiple behavioural, anamnestic, anthropometric, and clinico-

haematological parameters; this will inform the generation of digital twins of postural stability from real-time updates on multimodal individual and population data.

These seven pilot studies employ a number of different methodologies, involve diverse groups of patients, take advantage of the most modern instruments and devices, and most of them are based on encouraging preliminary results. The investigators look in fact competent and experienced enough to guarantee a successful completion of all the pilots, eventually providing validated tools in support to secondary and tertiary prevention, in particular to stratify risks and to personalize therapies and treatments.

During the first 12 months of the project, the pilot concepts were defined more clearly and consistently within Spoke 3, also in fruitful collaborations with the Spoke 1 staff, in particular for the formulation of the necessary services and infrastructures, for the statistical analyses, and for the most appropriate indicators to measure the impact of all these new models and tools. All the seven pilots are intended to open new clinical and prevention pathways to improve both the quality of life of these patient populations and the effectiveness of relevant health services. At the time of writing a couple of these pilots have already received approval from the local Ethical Committee, and the other requests are now in preparation; also this process may imply eventually small changes, which however shall improve further the value of the studies.