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Spoke 2 Deliverable
SP2.D3.1 Concept of models and definition of protocols

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SP2.D3.1 Concept of models and definition of protocols

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1. Publishable Summary

The present document provides a detailed description of the structure of the deliverable ***S2.D3.1 - Concept of models and definition of protocols,*** released by the team of experts involved in WP3.

In the first part, the main and specific objectives of the Four Tasks and five Pilot Projects that compose the WP3 are presented. The main objective, which is common to all the pilots, is to setting up digital solutions to obtain comprehensive sets of data related to lifestyle determinants and influencing the onset of chronic diseases for primary prevention. These digital solutions will include new and already existing web-based platforms, apps and wearable devices, and will be targeted to healthy populations aged 6 or more, also with some focus on transplanted individuals and people from the working sector.

Macro-activities of each task are evidenced, starting from preliminary searches of the scientific literature on the different topics treated; the identification of outcome indicators to be included in the data collection; the selection/development of questionnaires useful for digital surveys; the selection/development of platforms for data collection and for community trials; the selection/development of apps and wearables targeted to each kind of macro-population considered; the marketing evaluations through a real-world evidence approach.

In the second part of the report, issues related to the description of data sources for each Pilot, strategies of interaction of the new platforms with the Alma Health DB, logical models of digital functions, API libraries building and management protocols for the Pilot implementation and orchestration are examined. In particular, features of the developed web-based platforms are identified and one of the decentralized or federated operating models will be adopted. To monitoring and selecting the most promising transversal technologies used by all the Pilots, a collaborative approach among different teams was carried out.

2. List of abbreviations

CRFs: Case Report Forms

CTP: Community Trial Platform

FV: Fruits and vegetables

IPAQ: International Physical Activity Questionnaire

MET: Metabolic Equivalent of Task

MVPA: Moderate to Vigorous Physical Activity

NCD: Non-Communicable Disease

PA: Physical Activity

SB: Sedentary Behaviour

3. Introduction

3.1. Overviw

The present report is aimed at providing an overview of the basic concepts and methodological processes guiding the achievement of digital solutions to monitor and manage determinants of lifestyles in daily-life and occupational environments for primary prevention of chronic diseases.

3.2.Objectives of the deliverable

The overall objective of the deliverable is to identify the best procedures and tools for the collection of lifestyle information that are able to converge and nourish a huge Health database platform, through a collaborative approach among different experts.

3.2.1. Objectives of Task 3.1

With regard to the *setting up of a database system to monitor the impact of lifestyles on population health* (Task 3.1), the main objective of this first deliverable is to define all the digital tools and the procedures/protocols to collect lifestyle data on healthy and solid-organ transplanted populations for primary prevention.

Specific objectives include the following:

- Collection of scientific literature data on the tools to assess lifestyle data.
- List of lifestyle outcomes indicators.
- Selection of questionnaires and apps to collect self-reported lifestyle data within the Pilots.
- Revision of an already existing web platform to collect lifestyle data.
- Determination of the characteristics of the new app/s to develop.
- Selection of existing wearable devices to collect objective lifestyle data within the Pilots.
- Determination of the characteristics of the new wearable device/s to develop.

3.2.2. Objectives of Task 3.2

The Task 3.2 will allow to assess the effectiveness of innovative pre-primary and primary prevention interventions using digital tools on communities and selected targets, including vulnerable groups; evaluate the effectiveness of vaccination programs; evaluate the appropriateness of prevention paths and organizational models integrating prevention and primary care services and multidisciplinary specialist networks; assess the effectiveness of health literacy and empowerment actions through dedicated education and communication programs; assess the role of interventions aiming at modifying behavioral, socio-economic and environmental determinants of health; promote multi-professional interventions and an intersectoral collaboration between public health, civil society and the private sector to mobilize all available resources; interoperate different digital platforms for community trials.

In the present deliverable, all the characteristics of the interventions to be performed and procedures to be adopted are outlined.

3.2.3. Objectives of Task 3.3

Task 3.3 is aimed at supporting a better balance of work and life, ensuring a personal state of equilibrium to prevent psychological and health-related issues generated or exacerbated by problematic or unsustainable lifestyles. According to this aim, the main objective of the deliverable is to define procedures, protocols, and physiological sensors to monitor work-life balance, lifestyle, and mental health, with particular attention to psychological work-related issues, such as burnout, stress, anxiety, workaholism and depression.

The specific objectives include the following:

- Definition of synergies and collaborations with other DARE partners;
- Review of available self-reported measures to assess work-life balance;
- Review of available self-reported measures to assess psychosocial risks in the work environment;
- Review of available self-reported measures to assess psychological work-related issues, such as burnout, stress (including techno-stress), anxiety, workaholism and depression;
- Review of available self-reported measures to assess lifestyle (sleep, nutrition, physical activity, smoke and drug consumption);
- Definition and test of wearable sensors aimed at collecting physiological measures;

- Design of experimental protocols for the first data collection, including definition of target work contexts;
- Submission of protocols for ethical approval.

3.2.4. Objectives of Task 3.4

The main objective of Task 3.4 is using large-scale cohort studies to identify lifetime, environmental and occupational determinants of healthy ageing. Existing large-scale cohort data relative to elderly subjects from different European and non-European countries will be combined, updated and analysed through machine learning approaches to produce novel evidence on characteristics related to ageing and to ageing-related chronic diseases.

The present deliverable has the objective of defining the two stages in which the pilot will be carried out and the macro-activities that will be conducted.

3.3. WP3 Operational Architecture (Tasks)

WP3 has been organized in 4 Tasks and 5 Pilots.

LIST OF APPROVED PILOTS				
SPOKE	**WP**	**TASK**	**PILOT**	**ID-PILOT**
SPOKE2	WP3	T3.1	Monitoring lifestyles and health determinants in different settings and population targets through novel technological approaches for digital primary prevention.	S2-WP3-T3.1-P01
SPOKE2	WP3	T3.1	SHAPE program - Staying Healthy After a solid organ transplant: a digital Primary prEvention wellness program for non-communicable diseases (NCDs) and brain health	S2-WP3-T3.1-P02
SPOKE2	WP3	T3.2	Interoperable community trial platform.	S2-WP3-T3.2- P01
SPOKE2	WP3	T3.3	Preventing psychological issues related to work and lifestyles in the digital transition era	S2-WP3-T3.3-P01
SPOKE2	WP3	T3.4	Use large-scale cohort studies to identify lifetime, environmental and occupational determinants of healthy ageing	S2-WP2-T3.4-P01

3.3.1. Task 3.1 operational architecture

Task 3.1 presented n.2 Pilots:

Pilot 1 - *Monitoring lifestyles and health determinants in different settings and population targets through novel technological approaches for digital primary prevention*. This pilot is aimed at creating a *Lifestyle Database* based on digital technologies and at developing predictive models for primary prevention of non-communicable diseases (NCDs); therefore, already existing and novel digital tools will be tested to collect information on PA, sedentary behaviour (SB), physical fitness, diet, dependencies (smoke, alcohol, drug), sleep, metabolic and weight status, psychological, neurological and socio-economic- cultural-environmental aspects in different settings and target populations.

Pilot 2 - *SHAPE program - Staying Healthy After a solid organ transplant: a digital Primary prEvention wellness program for non-communicable diseases (NCDs) and brain health.* The aim of this Pilot is to implement a global strategy for primary prevention of NCDs, including diabetes, cancers, chronic respiratory disease and cognitive impairment, based on a multi-domain lifestyle approach among selected solid organ recipients (heart, liver, kidney, lung, pancreas and combined) with sustained remission of end-organ dysfunction; the intervention will consist in a digitalized holistic approach including nutritional guidance, physical exercise plan, cognitive training, social activities promotion ideas, sleep hygiene rules, alcohol/tobacco/substances abstinence campaigns and educational programs on vascular and metabolic risk factors.

The macro-activities of the deliverable conducted within the Task 3.1 are listed below.

a) Scientific literature of existing tools

A first activity useful for defining operational needs of the two Pilots is the identification of lifestyle indicators and existing digital tools for lifestyle data. To this end, different literature searches addressing lifestyle indicators and tools to collect lifestyle data and to change unhealthy behaviours were conducted.

The literature on physical activity digital tools confirmed the effectiveness of many of the worldwide used tools in monitoring and increasing physical activity or reducing sedentary behaviours, but also evidenced that digital platforms and systems allowing the monitoring

and the access to needed lifestyle data should be implemented [Panicker, 2022; Hutchesson, 2021].

Similarly, the literature reports an increase in the use of Dietary mobile applications useful for losing weight, managing chronic conditions and understanding dietary patterns and the quality of nutrient intake. Mobile (M)-health or Electronic (E)-health applications typically support users in tracking food and exercise and provide users with additional information to achieve personal goals.

Although various digital tools in migraine management have been described in the literature, including digital diaries and Internet/smartphone app-based surveys, their effectiveness has not been included in most studies.

Little is known on specific lifestyle tools for transplanted recipients to promote their long-term health.

b) Identification of outcome indicators

All the possible indicators of lifestyles have been considered and the following list has been drawn up as a result of collaborative searches and discussions.

Personal information:

socio-demographics - Gender, age, nationality, hometown, education, occupation, income, marital status, immigrant, family nucleus.

neonatal - Type of delivery, breast/artificial feeding, weaning.

clinical – Diagnosed diseases, hereditary or familiar diseases, symptoms, medications, supplements consumption, following any diet.

PA-related indicators:

acceleration, angular velocity, step count, sedentary time (sitting; laying; sleeping-time, quality);

METs (Metabolic Equivalent of Task), MVPA (Moderate to Vigorous PA), activity/sport time, activity/sport type, home activities time, mean to go to school/work, type of sitting activities (social networks, TV, PC, videogames, reading), leisure activities time/type.

Anthropometrics:

weight, height, waist circumference, hip circumference, waist to hip ratio, resistance, reactance and derived measures (eg. phase angle, total body water, body cell mass; body mass index; extracellular and intracellular water; free fat mass; fat mass).

Physiological/metabolic indicators:

heart rate, heart rate variability, ECG, stress levels, energy expenditure, resting metabolic rate, respiratory rate, blood pressure, VO2, CO2, blood oxygen saturation, body temperature, body composition (lean body mass, fat mass and hydration levels); glucose and lipid levels; gluten and lactose intolerance.

Food/nutrition-related indicators:

Nutrient intakes

Intake of macro- and micro-nutrients.

Food habits

Breakfast habits (weekly frequency, type, with/without other people, reason why skipping breakfast, duration).

Breaks-morning and afternoon (type).

Eating between main meals, fast food, eating out, type of FVs (organic, seasonal, …), vending machines products consumption, food choices main determinants.

Beverage type consumption (water, sweetened beverages, coffee, tea, energy drinks, wine, beer, other alcoholics).

Addictions indicators:

Smoking (quantity, type-cigarettes/e-cigarettes/pipe/etc).

Alcohol consumption (quantity, type).

Drugs use (quantity, type).

Eating disorders.

Internet addiction (screen time; access frequency; type of device – PC, smartphone, tablet, videogames; type of social networks – FB, twitter, tiktok, Instagram,…).

Migraine indicators:

Intensity

Pain location

Duration

Associated symptoms

Disability level

Possible triggers (e.g., stress, alcohol, sleep disorder, food, climate changes, menstruation)

Drugs taken

Drug efficacy

Transplant indicator:

Type of Transplant

c) Selection of standardized questionnaires for lifestyle data collection

Questionnaires on physical activity/sedentariness-related data

The most internationally used questionnaire to assess PA is the IPAQ (International Physical Activity Questionnaire). This tool measures the time per week spent on moderate or vigorous physical activity (MVPA) during different phases of lifetime (work, leisure, household tasks, etc.), and the final measure obtained is the MET (Metabolic Equivalent Task) used to classify subjects in levels of PA.

Different versions of this questionnaire exist (https://sites.google.com/view/ipaq/download), and they are based on:

- Length = IPAQ short version (7 items, PA over the last seven days); IPAQ long version (31 items, usual PA);
- Target age = adolescents, adults, elderly.
- Language = it is translated in many different languages, included Italian.

The IPAQ has already been used in a digital form included in a mobile application for monitoring physical activity of patients with cardiovascular diseases [Saran, 2014]. For the purpose of the Pilot, the IPAQ short form for adults (**IPAQ-SF**), and for adolescents (**IPAQ-A**) will be used after being included in the planned web platform to be compiled by sample populations.

Since a validated version of IPAQ for children is missing in the literature, the Physical Activity Questionnaire for older children (**PAQ-C**) will be used (Gobbi, 2016).

Another selected questionnaire is the **ASSO-PASQ** (Physical Activity and Sedentariness Questionnaire), a digitally-based questionnaire adapted from a previous questionnaire developed by the University of Palermo within the ASSO (Adolescents Surveillance System for the Obesity prevention) project [Tabacchi, 2016; Jemni, 2016], aimed at collecting PA and sedentary habits (sleep-duration, home activities, mean to move to/from work/school, leisure activities, sedentary time, sport type/frequency). Moreover, as the digital version of this questionnaire has already been developed, this will be updated by an expert programmer engineer.

Questionnaires on food/nutrition-related data

A digitally-based questionnaire **ASSO-FFQ** (Food Frequency Questionnaire) was previously developed and its validity and reliability assessed by the University of Palermo within the ASSO (Adolescents Surveillance System for the Obesity prevention) project [Filippi, 2014; Tabacchi, 2015] with the aim of collecting both macro- and micro-nutrient intakes in adolescents. This tool is included in the ASSO-NutFit software, requires on average 20 min to be compiled, and is structured in three sections (foods, beverages and dietary supplements) including 20 major groups: 12 food groups (fruit/vegetables/legumes, cereals/bread/substitutes, pasta/ rice/couscous, potatoes, sweets, cheeses/yogurt, fishery products, meat, eggs, fats/oils, savory foods, regional dishes); seven beverages groups (water, soft drinks, juice/milk- shakes, milk, tea, coffee, alcoholic drinks), and one dietary supplements group. Each main group is divided into different subgroups, for a total of 106 items. Data from ASSO-FFQ are automatically transformed into daily estimated energy and nutrient intakes by the ASSO-NutFit software.

This web-based questionnaire will be used, after proper revision, to collect data on nutrient intake in the Pilot. E.g., a revision of the Italian tables of nutrient composition will be conducted to update the database; the possibility of a shorter form (reduce the number of questions and consequently the time spent to compile) will be considered.

The food habits will be assessed by using another questionnaire developed within ASSO, the **ASSO-FHQ** (Food Habits Questionnaire) aimed at collecting information on meal habits (breakfast - weekly frequency, type, with/without other people, reason why skipping breakfast, duration; morning and afternoon breaks (type of food consumed);

lunch and dinner (type of food consumed); eating between main meals; fast food; eating out; type of FVs (organic, seasonal, …); vending machines products consumption; food choices main determinants; beverage type consumption (water, sweetened beverages, coffee, tea, energy drinks).

Questionnaires on addictions

The **ASSO-AddQ** (Addictions Questionnaire) will be used to collect information on smoking, alcohol, drugs, Internet and social networks. This questionnaire will be partly remodeled based on the ASSO-PASAQ questionnaire previously developed by the University of Palermo [Jemni, 2016].

Questionnaires on the use of digital devices

The development of a new questionnaire on the use of digital devices will be discussed.

Questionnaires on migraine-related data

The three-item "**ID Migraine**" migraine screener was found to be a valid and reliable screening instrument for migraine headaches [Brighina, 2008] with a sensitivity and specificity of about 80%. This questionnaire will be used to effectively identify migraine sufferers.

The **MIDAS** (Migraine Disability Assessment) questionnaire was developed as a reliable tool to measure headache-related disability and improve doctor-patient communication about the functional consequences of migraine. It is easy to complete and takes only a few minutes. The questionnaire is based on five disability questions that focus on lost time in three domains: schoolwork or work for pay; household work or chores; and family, social, and leisure activities. The obtained MIDAS score is highly correlated with physician judgments about the severity of illness and need for treatment: 0 to 5: MIDAS grade I, little or no disability; 6 to 10: MIDAS grade II, mild disability; 11 to 20: MIDAS grade III, moderate disability; 21 or higher: MIDAS grade IV, severe disability.

Questionnaires on personal (socio-demographic, clinical) data

The web-based **ASSO-PIQ** (Personal Information Questionnaire) was developed to collect data on demographic aspects (gender, age, nationality, hometown, education, occupation, income, marital status, immigrant, family nucleus); neonatal aspects (type of delivery, breast/artificial feeding, weaning); clinical outcomes (diagnosed diseases,

diseases in the family, health-related symptoms, medications, supplements consumption, following any diet) [Jemni, 2016].

After accurate revision, this questionnaire could be used to collect information on the Pilot populations.

Questionnaires on sleep quality

Three questionnaires have been selected:

- Mini sleep questionnaire (5 items – 7 frequencies) [Natale, 2014]
- µMCTQ (Munich ChronoType Questionnaire) ultra-short version (4 items) [Ghotbi, 2020]
- Morningness-Eveningness Questionnaire - reduced version (1 item) [Danielsson, 2019]

Questionnaires on psychological aspects

- The Italian version of the PWBS (Psychological Well-being Scale) [Ryff, 1995]
- The Italian version of the Depression Anxiety Stress Scale-21 (DASS-21) [Bottesi, 2015]

Questionnaires on cognitive aspects

Self-administered Montreal Cognitive Assessment (MoCA) [Sivan, 2023]

Questionnaires on life quality

The SF 12 Standard V1 [Ware, 1996].

d) Revision of an already existing web platforms to collect lifestyle data

The ASSO-NutFit Platform previously developed by the University of Palermo will be used in a first phase, after a detailed revision and update, for collection of data on PA, nutrition, and dependencies.

The application for the collection and management of information of interest is based on a common WEB interface, and is therefore accessible via the latest generation browsers. The data entered by the users are recorded on the MySQL relational database, in a database nicknamed master; this is accessible only from the developed application, and cannot be modified except during extraordinary maintenance, for safety reasons. The data in the master database is synchronized daily with that present in a database nicknamed slave, which contains a simplified and normalized image of the master database, and which is directly accessible for reading by a series of enabled users and stations.

Through the commercial software AccessMySqlConverter it is possible to acquire the data from the slave database and record it on a database in Microsoft Access format with the same structure, for the purposes of subsequent statistical processing.

This platform will be integrated with the ALMA Health DB platform.

e) Selection of existing wearable devices to collect objective lifestyle data

Physical Activity

Two existing wearables for PA monitoring have been identified:

Apple watch + accessory band AURA Strap 2 (https://auradevices.io/);

Fitbit sense 2 (https://www.fitbit.com/global/it/products/smartwatches/sense2).

These wearables will allow the collection of the following indicators: acceleration, angular velocity, step count, sedentary time (sitting; laying; sleeping-time, quality); METs (Metabolic Equivalent of Task), MVPA (Moderate to Vigorous PA), activity/sport time, activity/sport type, home activities time, mean to go to school/work, type of sitting activities (social networks, TV, PC, videogames, reading), leisure activities time/type; heart rate, heart rate variability, ECG, stress levels, energy expenditure, resting metabolic rate, respiratory rate, blood pressure, VO2, CO2, blood oxygen saturation, body temperature, body composition (lean body mass, fat mass and hydration levels).

Some aspects to be evaluated concern their cost and the features related to the access to raw data; the latter possibility would allow better implementation of data analysis techniques to extract quantitative indexes of PA.

Nutrition

1) wristband GoBe2 Healbe Corp (https://healbe.com/) is an automatic tracking of daily energy intake (calories) and macronutrient intake (grams of protein, fat, and carbohydrates). Dimitratos SM et al. Wearable Technology to Quantify the Nutritional Intake of Adults: Validation Study. JMIR Mhealth Uhealth. 2020 Jul 22;8(7):e16405. doi: 10.2196/16405.

2) MyFitnessPal, (https://www.myfitnesspal.com/it) via wearables watch it tracks fat, carbohydrates, protein, sugar, fiber, cholesterol, and vitamins. Monitoring, the logging of food, water, and nutrient intake and tracking of calorie consumption and calorie burning with exercise (Feinman, 2015).

2) HyperMotion500;

3) SugarBEAT (https://nemauramedical.com/nmrd-info/);

4) SenseCam (https://www.microsoft.com/en-us/research/project/sensecam/).

f) Determination of new Apps and Wearables to develop

Determination of the characteristics of the new App

A first version of the "Lifestyle App" will be developed for the purpose of data collection to be started in September 2024, on the basis of the already existing application named "ASSO Nut-Fit" previously developed by the University of Palermo [Tabacchi 2016].

This first version of the App will include the digital form of the selected/revised questionnaires previously mentioned. Prompt, alerts, virtual coaches and other features are envisaged, but their implementation will be decided in a second phase of the pilots.

Evaluation of the features of the new wearable device/s to develop PA/nutrition

The decision of developing N.1 wearable or maximum N.2 wearables (+ associated apps) for all population age groups was undertaken.

The new wearable/s device/s to be developed should assess the following variables: acceleration, angular velocity, step count, activity/sport type, sedentary time, sleep time and quality, heart rate, heart rate variability, ECG, stress levels, energy expenditure, resting

metabolic rate, respiratory rate, blood pressure, VO2, CO2, blood oxygen saturation, body temperature, body composition (lean body mass, fat mass and hydration levels).

Glucose concentration and cortisol levels are other two variables of interest. Some "patches" for their measurement, that are associated to the wearable, could be developed as well.

A faster alternative is to develop a simple bracelet (without digital screen) just to collect data within the Pilot on all the needed measures. The issue of the time needed to develop it has to be solved. Another concern to be discussed is that if we want to give feedback to users (for example an alarm for those values outside the normal ranges), it might be more useful to wear a smartwatch rather than a bracelet.

3.3.2. Task 3.2 operational architecture

Task 3.2 presented n. 1 Pilot: Interoperable community trial platform.

The prevention of communicable and non-communicable diseases requires a multidisciplinary approach involving different actors and sectors. An integrated approach is essential to implement community intervention strategies, oriented towards health promotion and healthy lifestyles, and willingness to change.

To obtain representative results through community trials or real-world evidence studies, it is necessary to deploy digital infrastructures that can facilitate the connection between all stakeholders.

Vaccination coverage for vaccines strongly recommended in the National and Regional Immunization Plans among high-risk population are generally lower than minimum target of adherence rates requested.

Risk factors for developing noncommunicable diseases are common in the general population. The ISTAT institute makes available, with the survey "Aspects of daily life", information on smoking habits, excess weight, alcohol consumption and sedentary lifestyle.

In this context, a digital infrastructure will be deployed to conduct community trials for assessing the effectiveness of preventive interventions, including digital tools for innovative primary prevention paths, and post marketing evaluations using a real-world evidence approach.

This digital function will be implemented within a Digital Prevention Research Center, conceived to support the local and the national health authorities in the upcoming framework of the National Prevention Hub.

The macro-activities of the pilot are:

- To conduct community trials in target population to assess the effectiveness of preventive interventions.
- To digitally follow up recruited individuals.
- To interoperate different digital platforms to merge data from trial studies to perform metanalysis.
- To perform post marketing evaluations on target population using a real-world evidence approach.

The Expected Result is to build up a person-oriented platform that allows all people to register personal data and obtain personalized information on lifestyle and actions to correct personal risk factors over time.

3.3.3. Task 3.3 operational architecture

Task 3.3 presented n. 1 Pilot:

Preventing psychological issues related to work and lifestyles in the digital transition era. The aim of this pilot is to prevent workers' psychological issues generated or exacerbated by work, an unsustainable work-life balance, and problematic lifestyles. The pilot is organized into two data collection actions.

The *first data collection* exploits data collected from self-reported questionnaires specifically designed for measuring lifestyles (with particular attention to sleep, nutrition, and physical activity), work-life balance, and psychological work-related issues (e.g., burnout, stress, depression) to identify the risk factors for the onset of psychological diseases.

The *second data collection* is aimed at exploiting physiological and behavioural data gathered from sensors and wearable devices, both during work and spare time, to predict the onset of psychological issues. Additional data will be collected through peripheral blood sampling for the quantification of systemic oxidative stress and inflammation, which are determined by lifestyle and play a key role in the pathogenesis of chronic diseases.

All the data will be analysed using machine learning techniques to build predictive models to identify people at risk of developing psychological diseases and to identify risk factors.

Macro-activities are presented below.

a) Definition of synergies and collaborations with other DARE partners.

Synergies and collaborations with other DARE partners have been established. We've held approximately ten meetings with different UNIBO and UNIPA partners for discussing the implementation of the Task 3.3 pilot, refining methodologies, and harmonizing the use of self-report measures and sensors (where possible) with other DARE Tasks.

b) Review of available self-reported measures to assess target constructs.

A deep review of the literature has been conducted to have a complete overview of the state-of-the-art self-report measures available to assess:

- work-life balance: we have identified 24 questionnaires. Between them, 4 have already been validated on Italian population.
- psychosocial risks in the work environment: we have analysed 13 different questionnaires and scales. From the literature analysis emerged that three main job stressors should be considered: "job demand", "job control" and "peer support".
- psychological work-related issues: the review has been focused on the self-assessment tool to measure burnout, stress, technostress, anxiety, workaholism and depression. We have analysed and considered 6 questionnaires measuring anxiety, 7 scales assessing stress levels, 12 questionnaires investigating work-related stress, 7 scales measuring burnout, 8 questionnaires as a measure of depression, 2 scales for workaholism, and 7 measures of technostress.
- lifestyle: the review has been focused on the self-assessment tool to measure sleep, nutrition, physical activity, smoke, and drug consumption. As concern sleep, we have analysed and considered 7 different instruments. For physical activity we have analysed the contents of 2questionnaires. As concerns nutrition, we have considered 3 questionnaires on food habits and quality of nutrition. Moreover, we reviewed 15

questionnaires to assess the consumption of alcohol, drugs, and nicotine, as well as general measures of well-being.

For each self-report measure we have recorded the following information: authors, year of first validation, availability of Italian psychometric validation, number of items, a description of the main construct measured, the content of specific subscales.

c) Design of experimental protocols for the first data collection, including definition of target work contexts.

The Task 3.3 is focused on healthy workers, with particular attention to senior workers, and very young workers on their first employment, with low education and training, or with low social skills. As concern the work contexts to be considered, we will include employees from different work sectors according to data reported in literature: a literature review by the EU-OSHA (2014) reports the most affected work sectors in terms of costs associated with psychosocial disorders and stress construction, education, health care and public administration. Moreover, in recent years the ever-increasing technologization and automation of work environments has been shown to be a potential source of stress, especially for senior workers [Spiess et al., 2021]. According to this evidence, we have defined the following target workers:

- "hard" workers (industry 5.0 employees and workers in the field of construction)
- public and private administrative staff (including university staff)
- school teachers
- health workers
- financial sector operators
- supermarket and mall clerks

Strict exclusion criteria of participants will be applied to avoid including subjects with established pre-existing pathologies. Moreover, for their peculiar lifestyle, shift workers will be not considered in the pilot studies.

As concerns the experimental protocol, for both the first and the second data collection 2 follow-ups are envisaged (at 3 or 6 and 12 months), to monitor the worker's mental health and identify those cases that developed a psychological condition (e.g., stress, depression) which is worthy of attention.

From the review of the standardized self-report measures available in the literature to assess the above-mentioned constructs (work-life balance, job stressors, psychological work-related issues, and lifestyle), a selection of these instruments has been done.

Measures have been selected according to the following criteria: i) questionnaires have to be standardized (psychometric properties should be available); ii) when possible, instruments validated on Italian population are preferred; iii) as the data collection will take place in the work context, great attention has to be placed on the number of items included in the protocol, to minimize the mortality of the sample; thus, questionnaires with a lower number of items were preferred. The final experimental protocol will include the following measures:

1. Socio-demographic data: gender, age, education, marital status, living arrangements, socio-economic status, having children, being a caregiver, having a chronic health condition, weight, height.
2. Occupational profile: job position, type of work, type of contract, working hours, possibility of remote working, distance from work, transportation used to reach the workplace.
3. Mental health: Depression Anxiety Stress Scale-21 (DASS-21; Henry & Crawford, 2005), Copenhagen Burnout Inventory (CBI; Kristensen et al., 2005).
4. Lifestyle: Mini Sleep Questionnaire (MSQ; Natale et al., 2014), Ultra-Short Version of the Munich Chronotype Questionnaire (μMCTQ; Ghotbi et al., 2020), Reduced Morningness-Eveningness Questionnaire (rMEQ; Adan & Almiral, 1991), International Physical Activity Questionnaires- Short Form (IPAQ-SF; Craing et al., 2003), Food Habits Questionnaire (ASSO-FHQ; developed within ASSO, see Task 3.1), some items of the Physical Activity, Smoking and Alcohol Questionnaire (ASSO-PASAQ; developed within ASSO, see Task 3.1).
5. Work-life balance: Work–family conflict and Family–work conflict scales (WFC and FWC; Netemeyer et al., 1996), Work-related rumination questionnaire (WRRS; Corpley et al., 2012), Recovery Experiences Questionnaire (REQ; Sonnentag & Friz, 2007), International Work Addiction Scale - short version (IWAS; Atroszko et al., 2023).
6. Work-related stressors: UK Health Safety Executive Stress Management Indicator Tool (HSE-IT; Edwards et al., 2008), Technostress creator scale (TSCS; Tarafdar et al., 2007), 1 question about the type of technologies used at work.

The final questionnaire will be implemented in an electronic form by using the Qualtrics platform. In the next months we plan to run first pilots with the aim to fine-tune the protocol.

d) Testing and definition of wearable sensors aimed at collecting physiological measures.

As concerns the second data collection, along with self-reported measures, we plan to collect physiological and behavioural measures by exploiting wearable technology. Participants will be asked to wear wearable sensors both during work and spare time

for about 5 days. Specifically, raw acceleration and heartbeat data were targeted as the fundamental physiological measures to be collected in order to derive indices and monitor the daily dynamics of physical activity, sleep, heart rate (HR), and heart rate variability (HRV), being all related to both work stress and mental health.

Different wearable devices have been tested to identify the ones most suitable for collecting the above-mentioned physiological parameters. Moreover, for each sensor, we analysed the trade-off between the accuracy of the measurements and the potential level of participants' acceptability of wearing the devices.

The following sensors have been considered and tested: Polar Verity Sense (i.e., consumer-grade arm band recording the acceleration and the photoplethysmographic (PPG) signal to be continuously Bluetooth-transmitted to the dedicated app), Polar H10 (i.e., consumer-grade chest strap recording the acceleration and the electrocardiographic (EKG) signal in a similar manner), RootiRx (i.e., medical-grade chest strap holter recording the acceleration and the EKG signal on its internal memory over up to seven days), Empatica EmbracePlus (i.e., research-grade wristband recording the acceleration and PPG signal, in addition to electrodermal activity and temperature on its internal memory over up to 48 hours) (https://www.empatica.com/en-eu/embraceplus/). According to our needs, after carefully considering all the features of the tested devices, we have chosen the Empatica EmbracePlus as the best tool to be used in the second data collection. Indeed, we evaluated the device as the most likely to be widely accepted by the target working populations (including construction work, where wearing chest straps might be unpractical) due to its small size, neutral design, and wrist-worn nature allowing for a quick device setting with minimal interactions with the user (i.e., not requiring participants to get undressed or clean their skin before positioning the sensor). Moreover, we positively evaluated the associated platform optimized for research, its CE certification as medical tool, and the output of raw signal recordings at satisfactory sampling rates. Particularly, the use of this device would allow for better harmonization of the data pre-processing pipelines used in this task (3.3) and task 4.3 of Spoke 2, in compliance with state-of-the-art algorithms for the scoring of physical activity and sleep/wake patterns. The event tagging button incorporated in the device is a further promising feature that would allow, for instance, instructing participants to signal specific events (e.g., beginning and end of the work

activity, bedtime, and wake-up time) while making the device more suitable for integration with experience sampling methods (i.e., short questionnaires sent via mobile app to associate the recorded signals with self-reported events or psychological states). Finally, we considered the EmbracePlus battery life and memory capacity (i.e., about 48 hours) as adequate for the desired protocol duration (i.e., about 5 consecutive days), provided that we replace participant devices each two days.

e) Submission of protocols for ethical approval.

We have started the process of approval from the local ethical committee of the first data collection foreseen by the Task 3.3 pilot. We are now in the phase of revision of protocols according to the ethical committee suggestions.

3.3.4. Task 3.4 operational architecture

Task 3.4 presented n. 1 Pilot: *Using large-scale cohort studies to identify lifetime, environmental and occupational determinants of healthy ageing*. This pilot is focused on the effect of environmental and occupational exposures, behavioural factors, diet and nutrition, genetics, and other biomarkers on health-related outcomes, such as cancer, cardiovascular diseases, and cognitive decline.

The analysis will be carried out in two stages. Stage 1 will be focused on a multilevel assessment of diet-related factors, including micro/macronutrients, foods, food groups, and food patterns. Stage 2 will be a parallel process based on the integration of additional variables aiding in the identification of patterns for healthy aging, including data regarding imaging and omics, environmental pollutants, social and cultural habits, and other contextual information.

In both stages, machine learning techniques will be adopted for data analysis.

Macro-activities are presented below.

a) Definition of collaborations with other DARE partners.

Collaborative efforts with other DARE partners have been initiated. Around twelve meetings with various partners have been conducted in different settings.

b) Establishment of contacts with cohorts and consortia of interest.

Our study is planned to be based on pooled data from cohorts participating in the "Consortium on Health and Ageing: Network of Cohorts in Europe and the United States" (CHANCES) project, which was funded by the European Commission between 2010 and 2015. Fourteen cohort studies participated in CHANCES, including over 680,000 subjects, from 23 European and three non-European countries. By the end of the project, 323 variables had been included and harmonized across studies, indicatively referring to: medical history of cancer, cardiovascular disease, diabetes and osteoporotic fractures, as well as nutrition, physical activity, tobacco smoking, drug use, alcohol consumption, reproductive health, socio-economic status, cognitive decline, and selected biomarkers related to ageing.

We have contacted the participating cohorts in CHANCES to join our project, and have so far encountered generally positive responses, with different levels of enthusiasm on behalf of the cohorts. Around half of the total number of cohorts therefore expressed their interest in collaborating with us on our Pilot. Some of the cohorts from CHANCES which agreed to participate (ESTHER Germany, Northern Sweden Health and Disease Study, Tromso) are now also part of the MORGAM Consortium, and they have expressed their preference in transferring their data directly through the MORGAM framework.

MORGAM (MOnica Risk, Genetics, Archiving and Monograph) is an international cooperative research initiative that focuses on unifying data from various population-based cohort studies. This study incorporates cohorts that were part of the standardized WHO MONICA risk factor surveys, along with other similar cohorts. These cohorts have been monitored for cardiovascular diseases and mortality. Initiated in the late 1990s, MORGAM aims to investigate how cardiovascular diseases develop in relation to both classic and genetic risk factors. From the mid-2000s onwards, MORGAM has expanded its research to include biomarker analysis from frozen sera, partially under the BiomarCaRE Project. The majority of the cohorts involved in MORGAM are based in Europe. These cohorts have baseline periods ranging from 1982 to 2014, and the longest of these have been followed for up to 30 years.

We have held three videocalls with the MORGAM coordinating center from the University Medical Center Hamburg-Eppendorf, in order to present our project and get

familiar with the cohorts participating in MORGAM. The coordinators have been very keen to collaborate with our project, and have invited us to submit a formal collaboration proposal in January, when they will start accepting new collaborations. We have already drafted a collaboration invitation and a project proposal, which will be submitted to MORGAM through Prof. Kee from the University of Belfast, our sponsor within the MORGAM consortium.

By including the additional MORGAM cohorts, the scope of our pooled analysis will expand, with much more data to count on for the machine learning training, leading to more robust statistical models, to a finer segmentation of the population and enabling the identification of more specific subgroups.

c) Definition of the analysis and main machine learning approaches.

The first stage of the analysis will focus on diet and nutrition. As opposed to the work already carried out within the five years of activity of CHANCES, where a-priori pre-defined dietary patterns such as the Mediterranean diet or the Healthy Diet Index have been investigated, the approach of this project will be based on descriptive machine learning techniques, in order to identify novel dietary patterns within the cohort populations, involving micro- and macro-nutrients, foods, and food groups.

More specifically, clustering algorithms, which can group individuals based on similar dietary food profiles, might be employed to identify the most common dietary patterns in the analyzed population, which might very well not fall into pre-existing diet definitions. Association rule discovery can be used to identify relationships between the identified dietary patterns or specific foods or nutrients and the onset of cardiovascular disease, cancer and cognitive decline, both as stand-alone conditions and through the integrated perspective of these conditions coexisting as comorbidities. Subgroup discovery could take the analysis further, by focusing on identifying specific subgroups within the cohort population that exhibit characteristics of interest in relation to the identified dietary patterns and disease outcomes; thanks to this approach, specific subgroups that may be particularly vulnerable or resistant to the investigated conditions could be revealed.

Phase 2 of the analysis will build upon the findings from Phase 1 and integrate additional variables to provide a comprehensive understanding of healthy ageing. This

phase will incorporate socio-economic factors, environmental pollutants, and available data related to biomarkers, imaging, and omics to explore more complex patterns of environmental exposure and their association with the three main outcomes of interest: cardiovascular disease, cancer, and cognitive decline.

The machine learning techniques presented before (such as clustering algorithms, association rule discovery and subgroup discovery) might be employed to handle the multidimensional nature of the data and identify intricate relationships between these variables and the onset of the diseases. The goal is to gain insights into the multifactorial nature of the combined effects of nutrition, environmental factors, and socio-economic determinants on healthy ageing outcomes.

Moreover, predictive models will be trained to assess the individual risk based on the discovered patterns.

Nevertheless, the approaches we have outlined will be contingent upon our review of the cohort data once it will be transferred to us. Our strategies may be adjusted or revised based on the nature and specifics of the data we actually receive, in order to account for the nature and extent of the actual usable pooled data.

d) Submission of protocols for ethical approval.

The initial steps for obtaining approval from the UniBO ethical committee for the data tranfer from our Task 3.4 partners have been initiated, in collaboration with the relevant UniBO legal offices, which have provided their input on the privacy-related aspects of the transfer.

4. Data Source Modelling

Data source census

SPOKE	WP	TASK	PILOT	ID-PILOT	DataSource	From	Available	Structured
SPOKE 2	WP3	T3.1	Monitoring lifestyles and health determinants in different settings and population targets through novel	S2-WP3-T3.1-P01	Lifestyle data	DASOE - Regione Sicilia	Y	Y
					Clinical data	FSE - Regione Sicilia	Y	Y
					Socio-demographic and lifestyle data	ISTAT - Families	Y	Y
					Pharmaceutical products purchase	Federfarma (Pharmacies)	Y	Y

			technological approaches for digital primary prevention.		Cancer data	Registro tumori - Regione Sicilia	Y	Y
					ASSO Nut-Fit web platform	University of Palermo	N	Y
SPOKE 2	WP3	T3.1	SHAPE program - Staying Healthy After a solid organ transplant: a digital Primary prEvention wellness program for non-communicable diseases (NCDs) and brain health	S2-WP3-T3.1-P02	Lifestyle data	DASOE - Regione Sicilia	Y	Y
					Clinical data	FSE - Regione Sicilia	Y	Y
					Socio-demographic and lifestyle data	ISTAT - Families	Y	Y
					Pharmaceutical products purchase	Federfarma (Pharmacies)	Y	Y
					Cancer data	Registro tumori - Regione Sicilia	Y	Y
					ASSO Nut-Fit web platform	University of Palermo	N	Y
SPOKE 2	WP3	T3.2	Interoperable community trial platform	S2-WP3-T3.2- P01	Clinical data	Local and hospital Health Agencies	Y	Y
					Clinical data	Clinical Trial Center at AOUPPA	Y	Y
					Pharmaceutical products purchase	Federpharma, Farmindustria	Y	Y
					Cancer data	SNCR (Sicilian network of cancer registries) – (Registro Tumori Palermo e Sicilia Orientale)	Y	Y
						Regional school office	Y	Y
						Scientific societies and healthcare integrated networks	Y	Y
						Private partners	Y	Y
						UNIPA	Y	Y
						UKE	Y	Y
						AOUPCT	Y	Y
						IRCCS	Y	Y
						Regione Sicilia	Y	Y
SPOKE 2	WP3	T3.3	Preventing psychological issues related to work and lifestyles in the digital transition era	S2-WP3-T3.3-P01	None (no data sources already available)	--	--	--
SPOKE 2	WP3	T3.4	Use large-scale cohort studies to identify lifetime, environmental and occupational determinants of healthy ageing	S2-WP3-T3.4-P01	CHANCES	CHANCES Consortium	Y	Y
					MORGAM	MOnica Risk, Genetics, Archiving and Monograph Project	Y	Y

5. Logical Data Architecture

In WP3, databases will be built both from already existing source databases and from the collection through the tools developed within the pilots. The already existing data will be obtained from platforms that are already available for managing population data when performing monitoring surveys and community trials. These web-based platforms for registering and updating data include the following features:

- centralized registration of people who will be enrolled in the research network;
- electronic case report forms (CRFs);
- information access profiles with user identification via username and password;
- data monitoring with activation of anonymization procedures and preparation of data quality controls;
- data extraction procedures.

The lifestyle platform developed within Task 3.1 and the Community Trial Platform (CTP) developed within Task 3.2 will involve the design of an adequate digital infrastructure to develop lifestyle monitoring systems and community and clinical trials to assess the effectiveness of digital tools.

These platforms will allow the management and monitoring of all regulatory, technical-administrative processes related to research; they will offer a complete and integrated application service, allowing all the actors involved (investigators, trial offices, surveillance institutions, ethics committee, management and administrative offices from the different research units, Universities, sponsors) in the monitoring of the research process. They will consist of application modules focused on aspects related to design, authorization, planning and scientific and economic reporting.

The data collected and managed within the individual integrated application modules for the management of processes and activities will flow into a research data warehouse. The data in the data warehouse will be accessed through a public institutional portal using synchronization methods or specific research tools to present reports and indicators to monitor, control and plan research activities.

The technologies implemented will be web-based. The digital platform will be based on server functions for the provision of services and on a central system for the monitoring activities of the sites involved.

All data will be imported/integrated in the Alma Health DB. The architecture will involve the definition of a specific middleware specialized in the integration of the different data sources and of an ETL bus for the subsequent transformation according to the provisions of the Alma Health DB architecture.

6. Concept of Digital Functions

Since three primary operating models (decentralized, federated and unified models) are used during digital transformations, the adoption of one of the *decentralized* or *federated* models is envisaged, to allow the various working groups to operate autonomously by pooling the various analysis tools that will be developed and then consenting an optimal flexibility in the implementation of the pilots. These models will allow: interactions between systems, through data sharing; easy use of different data sources (wearables, apps, etc.); and the possibility to scaling up the system, to remodulate or broaden it. Web platform authentication services or management of the scientific/informatic results will be envisaged.

7. Definition of Protocols

The implementation and orchestration processes of the pilots were carried out through the organization and meetings of working groups. For the aspects related to informatic and strictly technological issues, experts from the Spoke 1 are collaborating with pilot leaders of the WP3 of Spoke 2, with the main aim of monitoring and selecting the most promising transversal technologies for prevention in the DARE pilots.

A team work has been established including experts from all Tasks of WP3 for the evaluation of the wearable sensors use in DARE and possible synergies on this topic (which is present on various pilots).

Another group is working on the development of health apps for smartphones, and other synergies have been created to agree upon the use of questionnaires to be used in digital version.

Document standards will be defined, and so all authorization (e.g. ethic committee) and information aspects.

An Agile approach will be used, based on the **Agile project management framework**, that is one of the most used processes in project management.

8. API Library Model

An API library corresponding to each Pilot of the WP3 will be developed. Through these API libraries, the pilot's data and application functions will be available to other application components of the DARE architecture for reuse on other pilots or subsequent developments and evolutions of the technology. Each library will follow the typical hierarchical organizational model of the API libraries: the application functions will be classified for each individual pilot and will include access functions to individual data sources, correlation between different data sources, or simulation and modeling according to the different algorithms and analysis protocols that will be developed during the implementation phase of the individual pilots.

9. Conclusions

This document focuses on the identification of the best procedures and tools for data collection on lifestyle determinants from healthy populations aged 6 or more, including transplanted individuals and people from the working sector. Through a literature review and a collaborative approach between different experts, the indicators for the development of new and already existing web-based platforms, apps and wearable devices were defined. Decentralized or federated models will be used to: develop interactions between systems, through data sharing; easily use different data sources (wearables, apps, etc.); and scale up, remodulate or broaden the system. Web platform authentication services or management of the scientific/informatic results will be envisaged. Through API libraries, the pilot's data and application functions will be available to other application components of the DARE

architecture for reuse on other pilots or subsequent developments and evolutions of the technology.

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