THE SPRINTT PROJECT: TOWARD A "NEW" GERIATRIC MEDICINE

Funding

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Why GPs should be interested in the SPRINTT?

The SPRINTT project offers the opportunity to investigate the presence of physical frailty and sarcopenia and to have access to state of the art treatments for this conditions. All people enrolled in the RCT will be followed for 3 years by a specialized team of health care professionals. They will undergo medical visits and exams at no cost (e.g. blood analysis, DXA, electrocardiogram). People participating in the intervention group will take part in a multicomponent intervention including exercise classes, nutritional counseling and ICT support.

GPs have an extremely important role. Based on utilizing the knowledge and trust engendered by repeated contacts with patients, they can identify potential candidates who can be referred to the research center. They can mutually discuss the study progress and results with their patients and the research team. Finally, this project aims at developing an intervention that can be applied in primary care Hence, the involvement of GPs and family doctors is fundamental.

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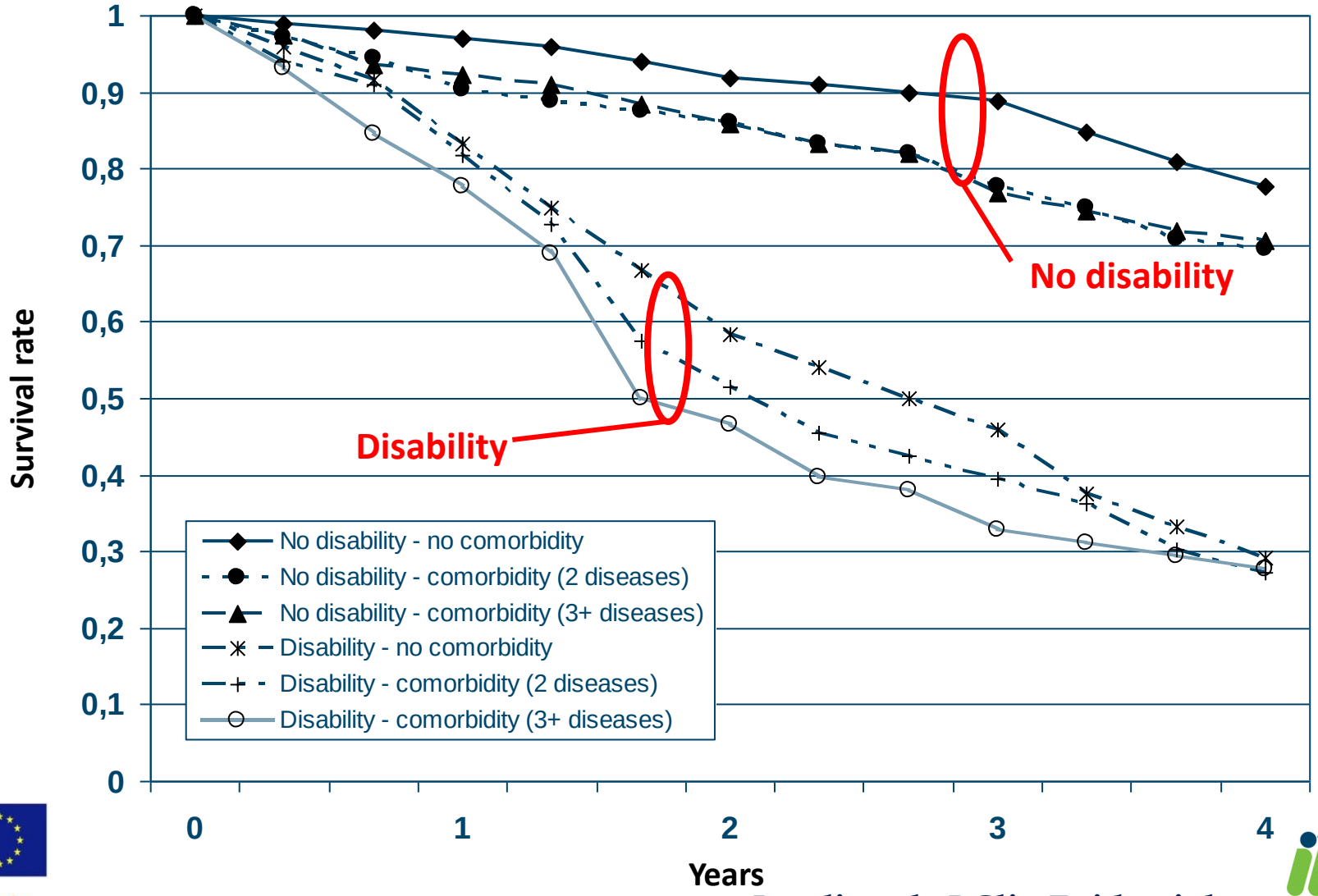
Introduction - 1

From a disease-centred paradigm to a holistic approach for the care of older people

- During ageing the decline in homeostatic reserves may lead to functional impairment, loss of independence and mortality, regardless of disease conditions.

- In older adults, functional impairment is a stronger predictor of adverse health outcomes than the comorbidity burden.

Disability rather than multimorbidity predicts mortality at advanced age



Landi et al., J Clin Epidemiol 2010

Frailty and sarcopenia as a cause of physical function impairment

Frailty and sarcopenia are common causes of physical function impairment.

Identifying an at-risk older population: FRAILTY

- **Frailty** is a common geriatric syndrome associated with aging

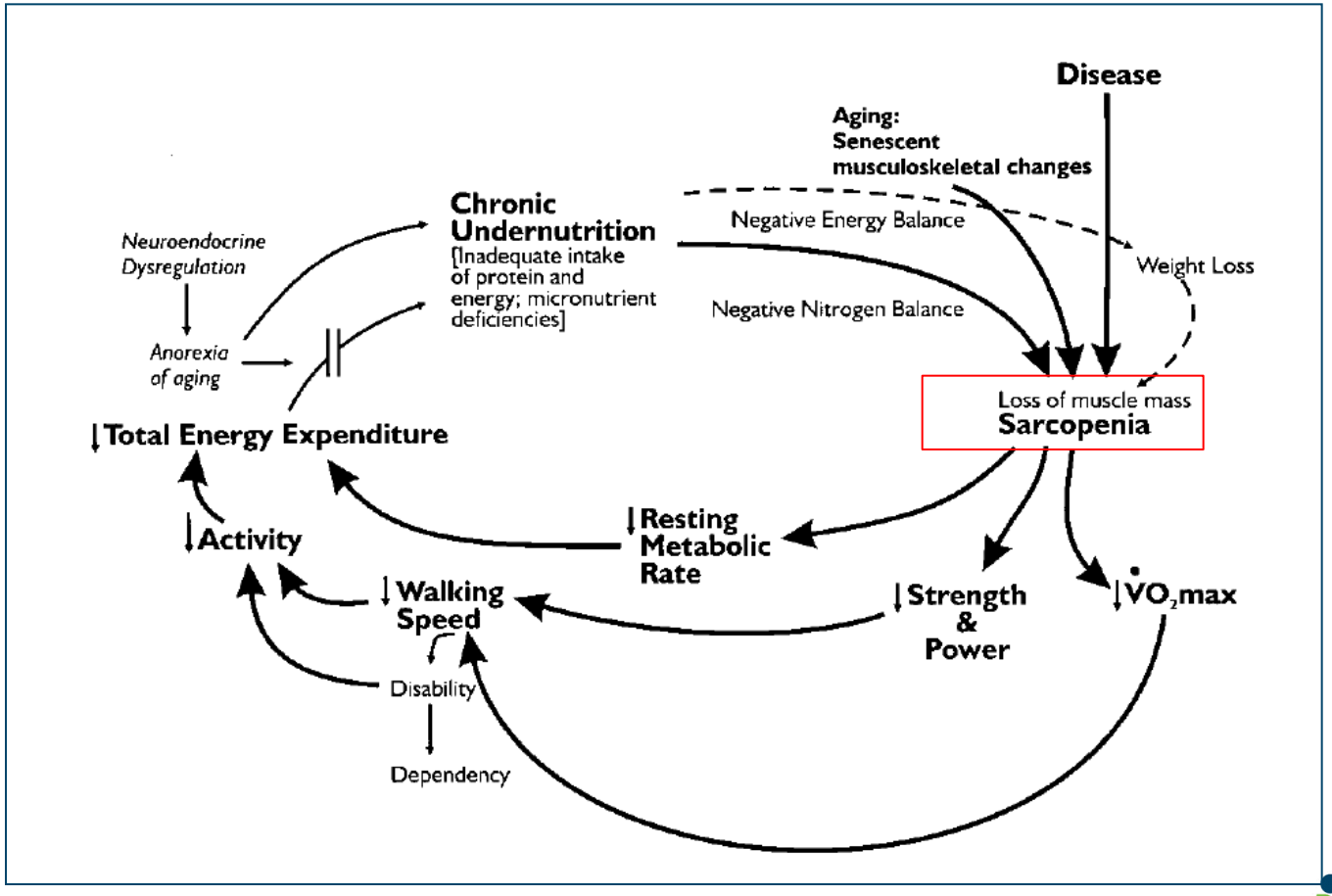
- Around 10% of people aged over 65 years have frailty, rising to between a quarter and half of those aged over 85 years.

Based on a recent consensus definition, frailty is a ***"multidimensional syndrome characterized by decreased reserve and diminished resistance to stressors…."***.

Frailty is associated with increased risk of adverse events such as: functional decline, disability, repeated falls, reduction of the quality of life, repeated hospitalizations, nursing home admission and increased risk of death.

Identifying an at-risk older population -Frailty-

Pathophysiology



Fried et al., J Gerontol A Biol Sci Med Sci 2001

Identifying an at-risk older population -Frailty-

The common clinical presentations of frailty can themselves be used to alert health and social care professionals to the possible presence of frailty:

- Falls
- Immobility or change in mobility
- Delirium
- Urine or fecal incontinence
- Susceptibly to side effects of medications.

They often mislead carers and emergency personnel, because an apparently straightforward symptom can mask a serious underlying illness.

Turner G., Age and Ageing, 2014

Identifying an at-risk older population: SARCOPENIA

Ageing of skeletal muscle is characterized by a progressive decrease in muscle mass.

"Sarcopenia is a syndrome characterized by the progressive and generalized loss of skeletal muscle mass and strength with increased risk of adverse outcomes, such as physical disability, poor quality of life and death."

Its diagnosis is based on criterion 1 plus criterion 2 or 3 :

1. Reduced muscle mass
2. Reduced muscle strength
3. Reduced physical performance

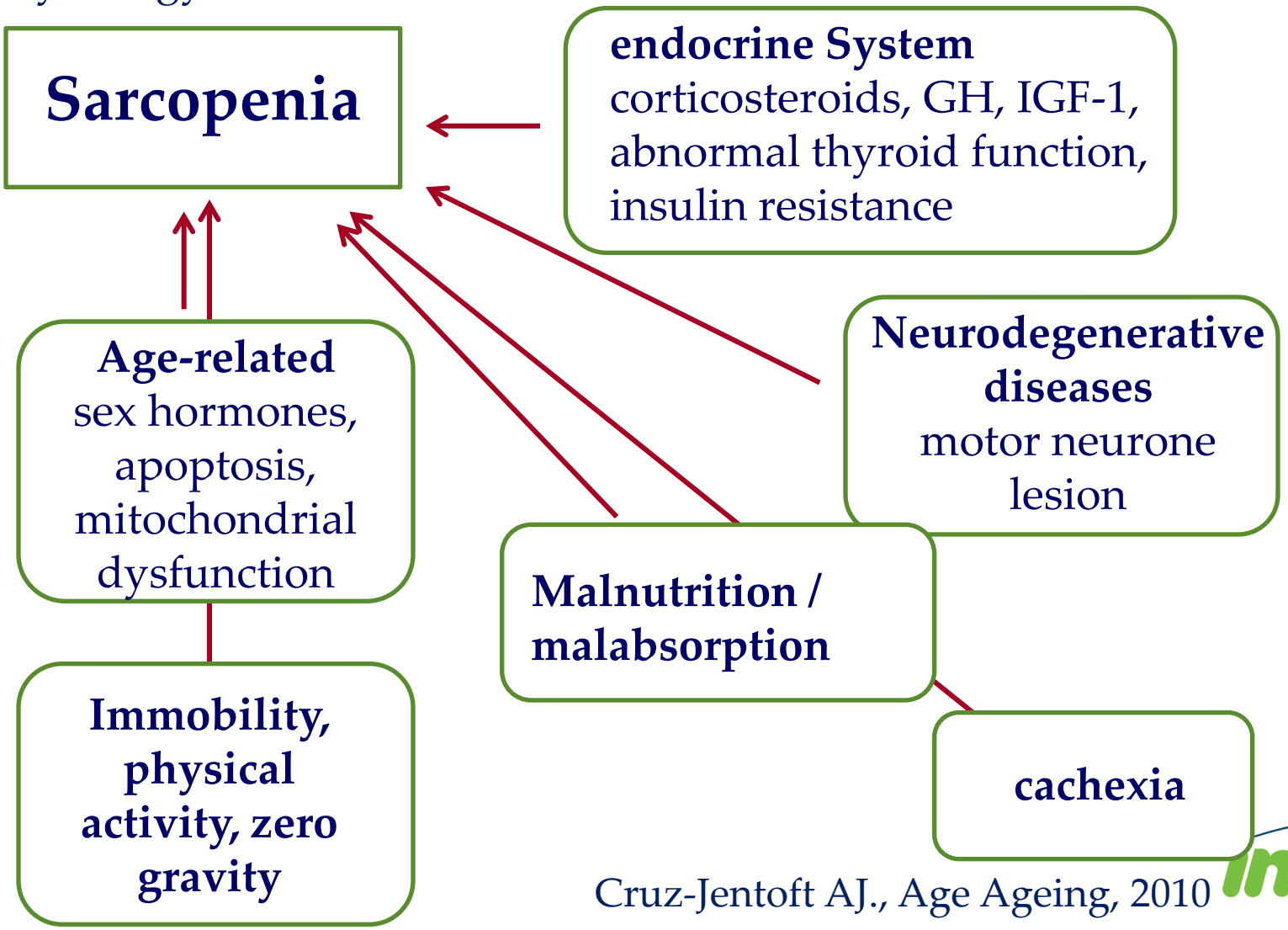
Identifying an at-risk older population -Sarcopenia-

Clinical features

- Impaired physical performance - mobility - functional status
- Reduced balance, risk of falling and fractures
- ↑Risk of drugs side effects
- Altered thermoregulation
- ↑ Mortality

Identifying an at-risk older population -Sarcopenia-

Pathophysiology



Cruz-Jentoft AJ., Age Ageing, 2010

Identifying an at-risk older population

In the absence of targeted interventions, the progression of sarcopenia and frailty is marked by increased morbidity, disability, frequent and often inappropriate healthcare use, nursing home admission, and poor quality of life.

Identifying an at-risk older population

frontiers in
AGING NEUROSCIENCE

OPINION ARTICLE
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Sarcopenia and physical frailty: two sides of the same coin

Matteo Cesari[1,2], Francesco Landi[3], Bruno Vellas[1,2], Roberto Bernabei[3] and Emanuele Marzetti[3]*

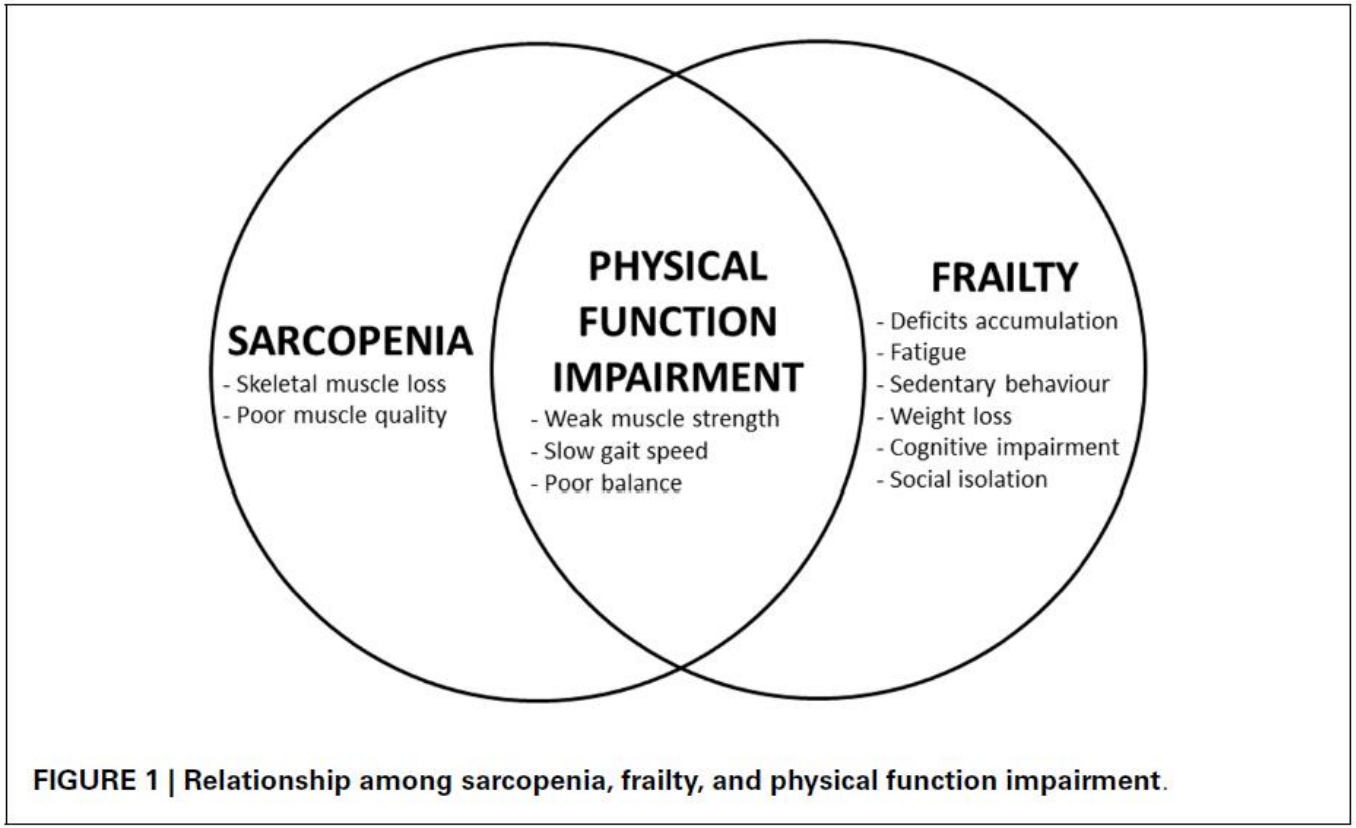

FIGURE 1 | Relationship among sarcopenia, frailty, and physical function impairment.

SPRINTT study objectives

1. Provide a clear operationalisation of the currently vague concept of physical frailty

2. Identify a precise target population with unmet medical needs

3. Evaluate the effectiveness of a multi-component intervention in preventing mobility disability in an older population at risk of disability

4. Identify and validate diagnostic and prognostic biomarkers for physical frailty & sarcopenia

SPRINTT
Sarcopenia & Physical fRailty IN older people: multi-component Treatment strategies

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CLINICAL TRIAL

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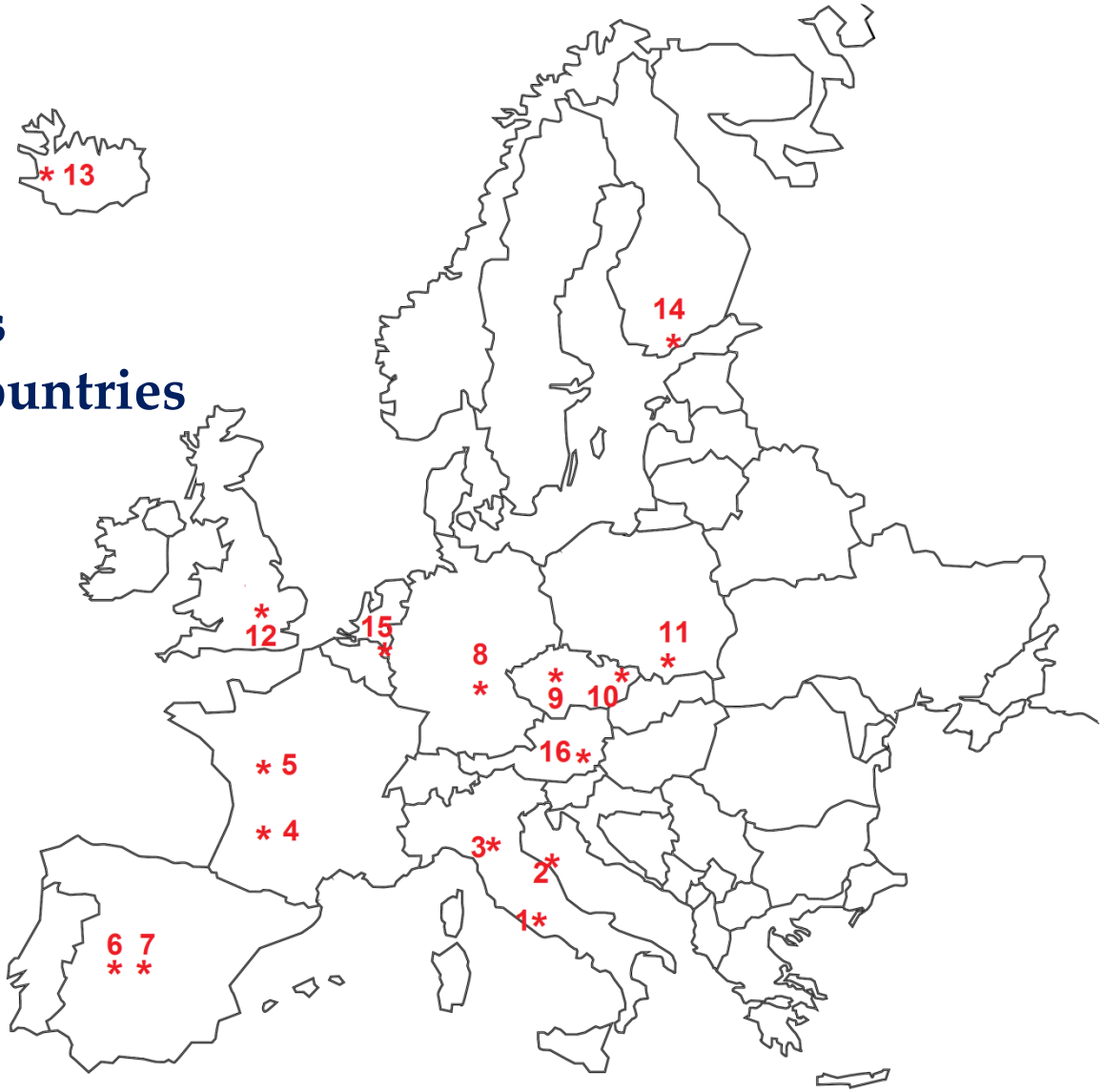
The SPRINTT RCT clinical centres

16 clinical sites
11 European countries



SPRINTT RCT participating centres

1) Catholic University of the Sacred Heart School of Medicine (Rome, Italy)
2) IRCCS-INRCA (Ancona, Italy)
3) University of Parma (Parma, Italy)
4) CHU Toulouse (Toulouse, France)
5) CHU Limoges (Limoges, France)
6) Getafe University Hospital (Madrid, Spain)
7) Hospital Universitario Ramón y Cajal (Madrid, Spain)
8) Friedrich-Alexander Universität Erlangen-Nürnberg (Nürnberg, Germany)
9) Charles University (Prague, Czech Republic)
10) Salesians Hospital (Opava, Czech Republic)
11) Jagiellonian University Medical College (Krakow, Poland)
12) Diabetes Frail (Luton, UK)
13) University of Iceland (Reykjavík, Iceland)
14) University of Helsinki (Helsinki, Finland)
15) Maastricht University Medical Center (Maastricht, The Netherlands)
16) Medical University of Graz (Graz, Austria)

SPRINTT RCT ELIGIBILITY CRITERIA

- The eligibility criteria in this study are aimed at identifying persons who are physically frail and sarcopenic, that is have the clinical and biological hall marks of functional limitation (as assessed by a battery of physical performance tests and DXA)
- Candidates for the SPRINTT RCT will also be non-disabled as documented by their ability to walk 400m without sitting or the help of another person. Targeting this subset f the population makes it possible to recruit a non-disabled but at risk population for a clinical trial of disability and prevention
- The eligibility criteria to be adopted in SPRINTT are very similar to those already implemented in the recently concluded LIFE study. This will not only allow the positioning of SPRINTT on the solid bases of LIFE, but also possible future comparisons across the 2 population and adopted interventions.

SPRINTT RCT INCLUSION CRITERIA

- Age ≥70 years
- Able to complete the 400-m walk test within 15 minutes without sitting down, the help with other person, the use of a walker, or stopping for more than 1 minute at time
- Short Physical Performance Battery (SPPB) score between 3 and 9
- Presence of low muscle mass according to results from a dual energy X-ray absorptiometry (DXA) scan (FNIH criteria)
- Willingness to be randomised to either intervention group

SPRINTT RCT
EXCLUSION CRITERIA - I

- Unable or unwilling to provide informed consent
- Plans to relocate out of the study area within the next 2 years
- Nursing home residence
- Current diagnosis of schizophrenia, other psychotic or bipolar disorder
- Consumption of more than 14 alcoholic drinks per week

  One alcoholic drink (equal to 14.0 grams of pure alcohol) corresponds to: 36 cc of beer (5% alcohol content), 24 cc of malt liquor (7% alcohol content), 15 cc of wine (12% alcohol content), 4.5 cc of distilled spirit or liquor (40% alcohol content)
- Difficulty communicating with the study personnel due to speech, language, or (non-corrected) hearing problems
- MMSE lower than 24/30
- Severe arthritis (e.g., awaiting joint replacement) that would interfere with the ability to participate fully

SPRINTT RCT
EXCLUSION CRITERIA - II

The exclusion criteria proposed in SPRINTT are mainly aimed at:

1. Excluding persons with specific clinical conditions that may render the intervention unsafe (i.e., severe diseases, unstable health status)

2. Avoiding the inclusion of individuals whose adherence to the protocol might be low due to clinical (e.g. cognitive impairment, dialysis) and non-clinical (e.g. plans to relocate reasons)

SPRINTT RCT
EXCLUSION CRITERIA - III

- Cancer requiring treatment in the past 3 years, except for non-melanoma skin cancers or cancer that have an excellen prognosis (e.g., early stage breast or prostate cancer)

- Lung disease requiring regular use of supplemental oxygen

- Inflammatory conditions requiring regular use of oral or parenteral corticosteroid agents

- Severe cardiovascular disease (including New York Heart Association [NYHA] class III or IV congestive heart failure, clinically significant valvular disease, hystory of cardiac arrest, presence of implantable defibrillator, or uncontrolled angina)

SPRINTT RCT EXCLUSION CRITERIA - III

- Upper and/or lower extremity amputation
- Peripheral arterial disease Lériche-Fontaine 3 or 4
- Parkinson's disease or other progressive neurological disorder
- Renal disease requiring dialysis
- Chest pain, severe shortness of breath, or occurrence of other safety concerns during the baseline 400-m walk test
- Current participation in a structured PA program, physical therapy or cardiopulmonary rehabilitation

SPRINTT RCT
EXCLUSION CRITERIA - IV

- Current enrolment in another RCT involving lifestyle, nutrition, or pharmaceutical interventions

- Other medical, psychiatric, or behavioral factors that in the judjment of the principal investigator may interfere with the study participation or the ability to autonomously follow either the MCI or the HALE programmes

- Other illness of such severity that life expectancy is expected to be less than 12 months

- Clinical judgment concering safety or non- compliance

SPRINTT RCT

TEMPORARY SUSPENSION OF THE SCREENING PROCEDURES - I

- Candidates may have conditions that would preclude participation in the study that could resolve. Therefore, a set of criteria temporary suspending the procedures for validation og the participant's elegibility is defined. Participants presenting such conditions may be re-contacted later during the recruitment period for completing the evaluation on a second time

- Older people excluded for one the temporary medical conditions can be rescreened a period that is considered clinically relevant by the local study physician

- The participant will maintain the same informed consent form and will not change his/her participant ID. Neverthless, all the eligibility validation) will be checked

- This approach will maximize the efficacy of the recruitment strategies and (in parallel) avoiding double versions of signed informed consent forms and participant's ID for the same individual

SPRINTT RCT

TEMPORARY SUSPENSION OF THE SCREENING PROCEDURES - II

- Uncontrolled hypertension (systoloc blood pressure > 200 mmHg, or diastolic blood pressure > 100 mmHg)
- Uncontrolled diabetes with recent weight loss, diabetic coma, or frequent hypoglycemia
- Hip fracture, hip or knee replacement, or spinal surgery in the past 6 months
- Serious cardiac conduction disorder (e.g. third degree heart block), uncontrolled arrhytmia, new Q waves within the past 6 monts or ST-segment depression (> 3mm) on the ECG
- Myocardial infarction, major hearth surgery (i.e. valve replacement or coronary bypass graft), stroke, deep vein thrombosis, or pulmonary embolism in the past 6 month
- Use of growth hormone, estrogens, progesterone or testosterone supplementation in the past 3 months

SPRINTT RCT
ESTABLISHING ELIGIBILITY

•Eligibility is estabilished in a multi-step process maximizing cost-effectiveness of the screening procedures.

•The first step could be an at-distance (telephone and /or mail) screen to assess specific inclusion and exclusion criteria.

•This is followed by an onsite assessment, including the administration of the SPPB, the 400m walk test, the MMSE, and an interview.

•Finally, the potential participant receives an examination by the study physician, physician assistant or nurse practitioner, who determines if conditions are present that meet exclusion criteria

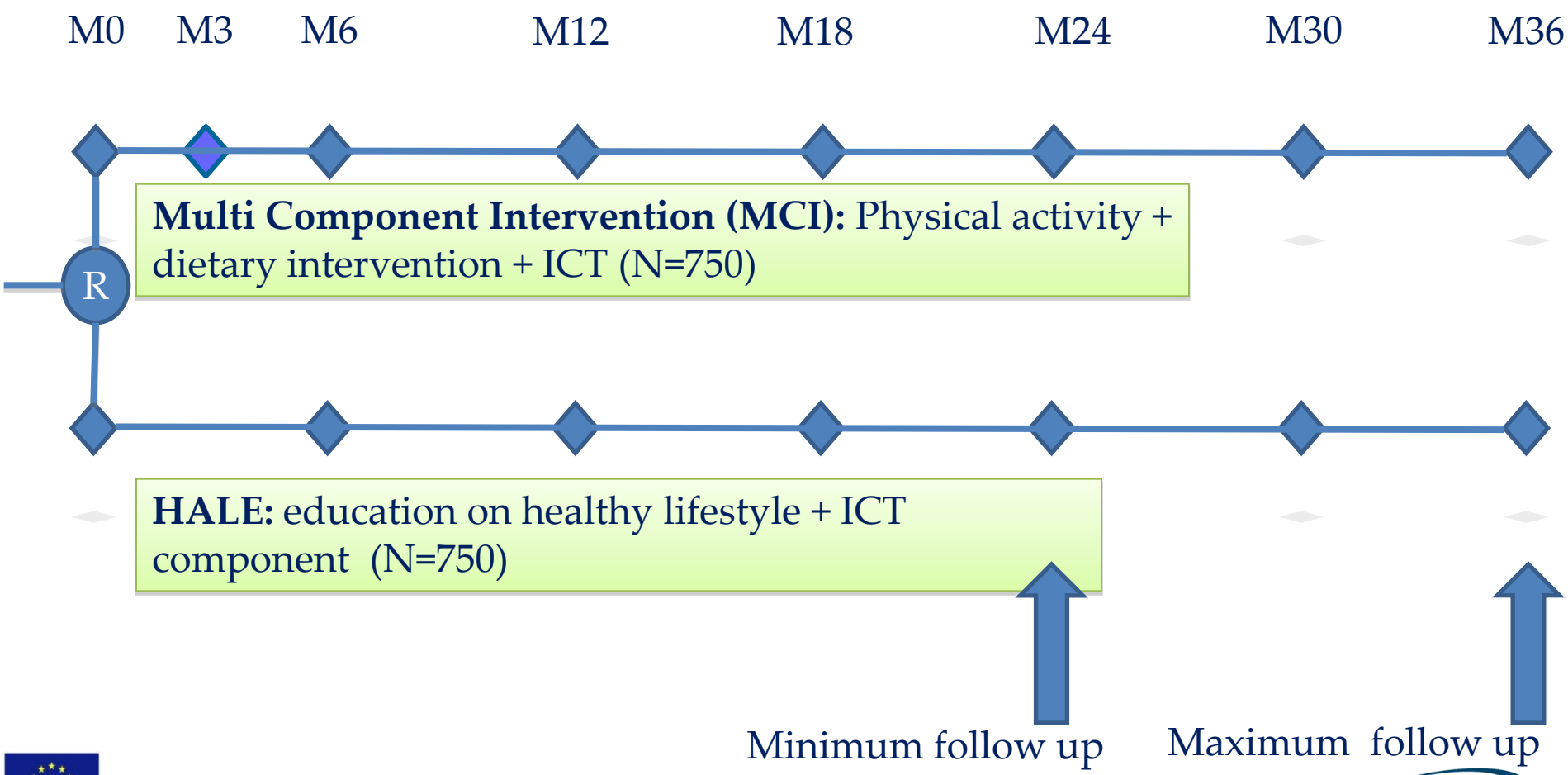
•The last step in the process verifyng the eligibility is the body composition evaluation by DXA SCAN

SPRINTT RCT

Identikit: How an alleged SPRINTT participant may look like

- 70+ year-old
- Underweight or overweight
- Uses a cane to get around and/or has a very slow pace
- Walks slowly and/or wobbly
- Needs help to rise from a chair
- Not short of breath or on oxygen while walking
- Holds the handrails when walking up or down stairs

SPRINTT RCT outline



SPRINTT RCT outcomes

Primary outcome

Incidence of mobility disability (inability to complete the 400-m walk test)

Secondary outcomes

- Changes in physical performance (i.e., SPPB, handgrip strength)
- Body composition modifications
- Incidence of falls
- Changes in nutritional status
- Changes in functional status (i.e., ADL, IADL, PAT-D)
- Changes in cognitive function and mood
- Changes in healthcare services utilisation
- Changes in quality of life (i.e., EuroQoL-5D, Participant-Reported)

Multi-component intervention (MCI)

Physical activity intervention

Structured exercise and physical activity (LIFE study protocol)

Nutritional assessment and dietary intervention

Personalised dietary recommendations

Health technology intervention

Remote monitoring of daily physical activity, walk speed, reinforcement of intervention adherence

Multi-component intervention (MCI)

Physical intervention

The PA intervention will be of moderate intensity and consists of aerobic, strength, flexibility, and balance training. Walking will be the primary mode of PA for preventing/postponing the outcome of major mobility disability.

The target duration of walking will be 150 min per week. This goal will be gradually approached on the basis of the Borg's scale, taking into account perceived exertion. Other forms of endurance activity (e.g. stationary cycling) may be utilised on a limited basis when regular walking is contraindicated either medically and behaviurally.

Multi-component intervention (MCI)

Physical intervention

Moreover, two times per week, following a bout of walking, participants will be instructed during the initial phase of the programme to complete a 10-min routine focused on strengthening exercises for lower extremity muscle groups by using variable weight ankle weights. This will be followed by a brief lower extremity stretching routine.

Balance training will be introduced during the adoption phase of the programme as a complement to the aerobic and strength components. The intervention will also involve encouraging participants to increase all forms of PA throughout the day (e.g., leisure sports, gardening, etc.).

Multi-component intervention (MCI)

Physical activity and ICT intervention

Intervention staff contacts for the PA group		
Week	***Centre-based PA***	***Home-based PA***
Adoption (weeks 1-52)	2 times each week	1 time/week (weeks 1-4) 2 times/week (weeks 4-8) Up to 3-4 times/week (weeks 8-52)
Maintenance (weeks 53 – end of the trial)	2 times each week	Up to 3-4 times/week

The total amount of PA will be monitored on a continuous basis by the AdamoWatch . At specified timeframes (at baseline and every 6 months) and on-demand by the investigator, the study staff will monitor the adherence to PA using such information and provide personalised feedback/tips to the participant. As back-up plan and in support of the AdamoWatch, investigators will also have results of actimetry from the ActivPAL™ device (measured at baseline and every 6 months [±2 weeks]).

Multi-component intervention (MCI)

Nutritional assessment and dietary intervention

SPRINTT mostly aims at achieving two predefined nutritional targets:

- a daily total energy intake of 25 to 30 kcal/kg body weight;
- an average protein daily intake at least in the range of 1.0 to 1.2 g per kilogram of body weight.

Moreover, vitamin D supplementations will be recommended to participants in both groups in whom serum levels of 25OH-vitamin D are deficient or insufficient, in accordance with their primary care physician.

As recommended by the American Geriatrics Society Consensus Statement on Vitamin D for Prevention of Falls and Their Consequences, a serum 25 hydroxyvitamin D (25-OH-D) concentration of 30 ng/mL (75 nmol/L) should be a minimum goal to achieve in older adults, particularly in frail older people who are at higher risk of falls, injuries, and fractures.

Multi-component intervention (MCI)

Nutritional assessment and dietary intervention

• In each study centre, the local dietician/nutritionist (D/N) will train each participant randomised to the MCI group on how to complete a 3-day dietary record. The 3-day dietary record will be collected from each participant in the intervention group at baseline and every 12 months.

• The macro- and micronutrient composition of the diet will be determined locally by the D/N through the use of nutritional software or national dietary databases, consistently with standard assessments conducted in clinical practice. This assessment will then support the elaboration of personalised nutritional recommendations by the local D/N, in agreement with national and international guidelines (as currently done in the standard clinical practice).

• The local D/N will regularly monitor the adherence to dietary prescription, eventually proposing additional *in itinere* assessments according to clinical needs.

Control group

Healthy Aging Lifestyle Education (HALE) programme

Regular meeting in small groups (twice a month, 45minute each).

The programme will be based on workshops on "successful aging" and a short instructor-led programme (5-10 min) of upper extremity stretching exercises at the end of each class.

The rationale for this "placebo exercise" activity is that it helps foster adherence to this arm of the study and increases the perceived benefit of the HALE workshop series to the participants without directly affecting the study outcomes.

How GPs can help us?

- Giving information to outpatients about the SPRINTT project

- Sending to our recruiting centers patients that could be potentially recruited to the SPRINTT clinical trial

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CLINICAL TRIAL

SPRINTT
Sarcopenia & Physical fRailty IN older people: multi-component Treatment strategies

If you want to know more on physical frailty and sarcopenia, please refer to the next power point presentation

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Disclaimer

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SPRINTT project website

www.mysprintt.eu