THE SPRINTT PROJECT:
TOWARD A “NEW” GERIATRIC MEDICINE
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
From the disease-centred paradigm to a holistic approach for the care of older people

• During aging, 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.

• “Traditional” interventions that target single diseases and use “conventional” endpoints have limited efficacy in older, multimorbid and functionally impaired people.

• The functional status is a critical target for interventions to restore robustness, improve the quality of life, and (possibly) extend survival.
Disability, more than multimorbidity, predicts mortality in advanced age

No disability - no comorbidity
No disability - comorbidity (2 diseases)
No disability - comorbidity (3+ diseases)
Disability - no comorbidity
Disability - comorbidity (2 diseases)
Disability - comorbidity (3+ diseases)

Survival rate

Years

Landi et al., J Clin Epidemiol 2010

Innovative Medicines Initiative
Multimorbidity, disability, and mortality in community-dwelling older adults

“Multimorbidity predicts 5-year mortality but the effect might be mediated by disability”. “(...) after adjusting for functional status, the effect of multimorbidity was no longer significant”.

St John et al., Can Fam Physician 2014
Effect of a moderate physical activity intervention on the onset of major mobility disability and persistent mobility disability

Pahor M et al., JAMA 2014
Frailty and sarcopenia are common causes of physical function impairment.
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.
Pathophysiology

-Frailty-

1. **Phenotype Model:** is based on 5 characteristics which, when present, predict worse clinical outcomes.

Subjects with 3 or more characteristics (e.g. unintentional weight loss, reduced muscle strength, reduced gait speed, self reported exhaustion and low energy expenditure) are considered frail.

People with none of the 5 indicators are considered robust older people. Those with one or two characteristics are intermediate or pre-frail group.

Young J., British Geriatric Society, 2014
Clegg A., Clinical Medicine, 2011
## Models of frailty: THE PHENOTYPE MODEL

<table>
<thead>
<tr>
<th>Characteristics of frailty</th>
<th>Cardiovascular Health Study Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Shrinking: Weight loss</td>
<td>• Baseline: &gt; 10 lbs lost unintentionally in prior year</td>
</tr>
<tr>
<td>• Weakness</td>
<td>• Grip strength lowest 20% (by gender, BMI)</td>
</tr>
<tr>
<td>• Poor endurance: Exhaustion</td>
<td>• Exhaustion (self-reported)</td>
</tr>
<tr>
<td>• Slowness</td>
<td>• Walking time/15 feet: lowest % (by gender: height)</td>
</tr>
<tr>
<td>• Low activity</td>
<td>• Kcals/week: lowest 20%</td>
</tr>
<tr>
<td></td>
<td>Males: &lt; 283 Kcals/week</td>
</tr>
<tr>
<td></td>
<td>Females &lt; 270 Kcals/week</td>
</tr>
</tbody>
</table>

Models of frailty: 
THE PHENOTYPE MODEL

ADVANTAGES

• Extensive validation in epidemiological and, to a lower extent, in clinical samples. The Fried criteria are among the most commonly used criteria.
• Multi-stage model, differentiating pre-frailty from frailty

LIMITATIONS

• Unidimensional approach, with lack of any measure of cognition and mood
• Difficult application in routine clinical practice, e.g. lack of adaptation of the criteria to the older European population
• Equipment and trained measurers required
• Problem of assessing performance in the frailest individuals.
2. **Cumulative Deficit Model**: Rockwood and colleagues developed a summary measure of deficit accumulation across many different levels: functional, clinical, and physiological.

It was designed to quantifying the theorized impact of aggregate disease and illness burden: it is a multidomain evaluation for frailty in older people.

Rockwood and colleagues compiled a Frailty Index based on impairments in cognitive status, mood, motivation, communication, mobility, balance, bowel and bladder function, activities of daily living, nutrition and social resources, as well as a number of comorbidities (70 items).
List of variables used by the Canadian Study of Health and Aging to construct the 70-item CSHA Frailty Index

<table>
<thead>
<tr>
<th>Changes in everyday activities</th>
<th>Mood problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck problems</td>
<td>Feeling sad, blu, depressed</td>
</tr>
<tr>
<td>Poor muscle tone in neck</td>
<td>History of depressed mood</td>
</tr>
<tr>
<td>Bradykinesia, facial</td>
<td>Tiredness all the time</td>
</tr>
<tr>
<td>Problems getting dressed</td>
<td>Depression (clinical impression)</td>
</tr>
<tr>
<td>Problems with bathing</td>
<td>Sleep changes</td>
</tr>
<tr>
<td>Problems carrying out personal grooming</td>
<td>Restlessness</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>Memory changes</td>
</tr>
<tr>
<td>Toiletting problems</td>
<td>Short-term memory impairment</td>
</tr>
<tr>
<td>Bulk difficulties</td>
<td>Long-term memory impairment</td>
</tr>
<tr>
<td>Rectal problems</td>
<td>Changes in general mental functioning</td>
</tr>
<tr>
<td>Gastrointestinal problems</td>
<td>Onset of cognitive symptoms</td>
</tr>
<tr>
<td>Problems cooking</td>
<td>Clouding or delirium</td>
</tr>
<tr>
<td>Sucking problems</td>
<td>Paranoid features</td>
</tr>
<tr>
<td>Problems going out alone</td>
<td>History relevant to cognitive impairment or loss</td>
</tr>
<tr>
<td>Impaired mobility</td>
<td>Family history relevant to cognitive impairment or loss</td>
</tr>
<tr>
<td>Musculoskeletal problems</td>
<td>Impaired vibration</td>
</tr>
<tr>
<td>Bradykinesia of the limbs</td>
<td>Tremor at rest</td>
</tr>
<tr>
<td>Poor muscle tone in limbs</td>
<td>Postural tremor</td>
</tr>
<tr>
<td>Poor limb coordination</td>
<td>Intention tremor</td>
</tr>
<tr>
<td>Poor coordination, trunk</td>
<td>History of Parkinson’s disease</td>
</tr>
<tr>
<td>Poor standing posture</td>
<td>Family history of degenerative disease</td>
</tr>
<tr>
<td>Irregular gait pattern</td>
<td>Seizure, partial complex</td>
</tr>
<tr>
<td>Falls</td>
<td>Seizure, generalized</td>
</tr>
<tr>
<td></td>
<td>Syncope or blackouts</td>
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<tr>
<td></td>
<td>Headache</td>
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<tr>
<td></td>
<td>Cerebrovascular problems</td>
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<tr>
<td></td>
<td>History of stroke</td>
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<td></td>
<td>History of diabetes mellitus</td>
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<tr>
<td></td>
<td>Arterial hypertension</td>
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<td></td>
<td>Peripheral pulses</td>
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<tr>
<td></td>
<td>Cardiac problems</td>
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<td></td>
<td>Myocardial infarction</td>
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<td></td>
<td>Arrhythmia</td>
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<td>Congestive heart failure</td>
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<td></td>
<td>Lung problems</td>
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<td></td>
<td>Respiratory problems</td>
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<td></td>
<td>History of thyroid disease</td>
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<td>Thyroid problems</td>
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<tr>
<td></td>
<td>Skin problems</td>
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<tr>
<td></td>
<td>Malignant disease</td>
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<td></td>
<td>Breast problems</td>
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<td></td>
<td>Abdominal problems</td>
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<td></td>
<td>Presence of snout reflex</td>
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<td></td>
<td>Presence of the palmomental reflex</td>
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<td></td>
<td>Other medical history</td>
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<td></td>
<td>Other medical history</td>
</tr>
</tbody>
</table>
Models of frailty: The cumulative deficit model for frailty (Rockwood)

This **Frailty Scale** classifies patients at four levels, going from fitness to frailty:

1. those who walk without help, perform basic activities of daily living (eating, dressing, bathing, bed transfers), are continent of bowel and bladder, and are not cognitively impaired;

2. bladder incontinence only;

3. one (two if incontinent) or more of needing assistance with mobility or activities of daily living, has CIND, or has bowel or bladder incontinence;

4. two (three if incontinent) or more of totally dependent for transfers or one or more activities of daily life, incontinent of bowel and bladder, and diagnosis of dementia.
Mildly frail persons are already disabled

Models of frailty: The cumulative deficit model for frailty (Rockwood)

### Clinical Frailty Scale

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Very Fit</td>
<td>People who are robust, active, energetic and motivated. These people commonly exercise regularly. Even so, they are among the fittest for their age.</td>
</tr>
<tr>
<td>2 Well</td>
<td>People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.</td>
</tr>
<tr>
<td>3 Managing Well</td>
<td>People whose medical problems are well controlled, but are not regularly active beyond routine walking.</td>
</tr>
<tr>
<td>4 Vulnerable</td>
<td>While not dependent on others for daily help, often symptoms limit activities. A common complaint is being “slowed up”, and/or being tired during the day.</td>
</tr>
<tr>
<td>5 Mildly Frail</td>
<td>These people often have more evident slowing, and need help in high order (ADLs: finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.</td>
</tr>
<tr>
<td>6 Moderately Frail</td>
<td>People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.</td>
</tr>
<tr>
<td>7 Severely Frail</td>
<td>Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 months).</td>
</tr>
<tr>
<td>8 Very Severely Frail</td>
<td>Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.</td>
</tr>
<tr>
<td>9 Terminally Ill</td>
<td>Approaching the end of life. This category applies to people with a life expectancy &lt;6 months, who are not otherwise evidently frail.</td>
</tr>
</tbody>
</table>

### Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common symptoms in mild dementia include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In moderate dementia, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In severe dementia, they cannot do personal care without help.
Models of frailty:
The cumulative deficit model for frailty (Rockwood)

ADVANTAGES
• Extensive validation in epidemiological and, to a lower extent, in clinical samples
• It seems to measure risk of adverse outcomes more precisely than the Fried scale
• Multidimensional approach
• Sound mathematical properties

LIMITATIONS
• Difficult application in routine clinical practice
• Time consuming
• Lack of an underlying unifying pathophysiological model
• No clear identification of a pre-disability stage
-Frailty-

- The phenotype model
- The cumulative deficit model
- Short Physical Performance Battery (SPPB)
- Prisma 7 questionnaire
- Walking speed (gait speed)
- Timed up and go test (TUGT)
- Self-Reported Health
- GP assessment
- Multiple medications (polypharmacy)
- The Groningen frailty indicator questionnaire

Young J., British Geriatric Society, 2014
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
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
Sarcopenia - Clinical features

**Clinical features**

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

Age-related sex hormones, apoptosis, mitochondrial dysfunction

Immobility, physical activity, zero gravity

endocrine System corticosteroids, GH, IGF-1, abnormal thyroid function, insulin resistance

Neurodegenerative diseases motor neurone lesion

Malnutrition / malabsorption

cachexia
Identifying an at-risk older population
-Sarcopenia-

European Working Group on Sarcopenia in Older People
EUGMS, ESPEN, IANA, IAGG - 2010

REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People
Alfonso J. Cruz-Jentoft, Jean Pierre Baeyens, Jürgen M. Bauer, Yves Boirie, Tommy Cederholm, Francesco Landi, Finbarr C. Martin, Jean-Pierre Michel, Yves Rolland, Stéphane M. Schneider, Eva Topinková, Maurits Vandewoude, Mauro Zamboni

Age and Ageing 2010; 39: 412–423
doi: 10.1093/ageing/afq034
Published electronically 13 April 2010
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Identifying an at-risk older population
-Sarcopenia-

EWGSOP

“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.”

• Diagnosis is based on documentation of criterion 1 plus criterion 2 or 3:

1. Reduced muscle mass

2. Reduced muscle strength

3. Reduced physical performance
EWGSOP- Sarcopenia Algorithm

Older people (> 65 years)

Walking speed measures

Walking speed measures:
- > 0.8 m/s
  - Hand-grip measures
    - Normal
    - Reduced
      - No sarcopenia
  - Reduced
    - Sarcopenia

Walking speed measures:
- ≤ 0.8 m/s
  - Muscle mass measures
    - Reduced
    - No sarcopenia

Cruz-Jentoft A.J. et al, Age and Ageing 2010
Identifying an at-risk older population
-Sarcopenia-

EWGSOP

Hypothetical stages of sarcopenia

<table>
<thead>
<tr>
<th>Stage</th>
<th>Mass mm</th>
<th>Strength mm</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-sarcopenia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarcopenia</td>
<td></td>
<td></td>
<td>Or</td>
</tr>
<tr>
<td>Severe Sarcopenia</td>
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</tbody>
</table>
Special Article

The FNIH Sarcopenia Project: Rationale, Study Description, Conference Recommendations, and Final Estimates

Stephanie A. Studenski, Katherine W. Peters, Dawn E. Alley, Peggy M. Cawthon, Robert R. McLean, Tamara B. Harris, Luigi Ferrucci, Jack M. Guralnik, Maren S. Fraga, Anne M. Kenny, Douglas P. Kiel, Stephen B. Kritchevsky, Michelle D. Shardell, Thuy-Tien L. Dam, and Maria T. Vassileva

Table 3. Recommendations for Cutpoints for Weakness and Low Lean Mass in Men and Women

<table>
<thead>
<tr>
<th>Cutpoint</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weakness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommended: grip strength (GSMAX)</td>
<td>&lt;26 kg</td>
<td>&lt;16 kg</td>
</tr>
<tr>
<td>Alternate: grip strength adjusted for BMI (GSMAX\textsubscript{BMI})</td>
<td>&lt;1.0</td>
<td>&lt;0.56</td>
</tr>
<tr>
<td><strong>Appendicular lean body mass</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommended: ALM adjusted for BMI (ALM\textsubscript{BMI})</td>
<td>&lt;0.789</td>
<td>&lt;0.512</td>
</tr>
<tr>
<td>Alternate: ALM</td>
<td>&lt;19.75 kg</td>
<td>&lt;15.02 kg</td>
</tr>
</tbody>
</table>

Notes: ALM = appendicular lean mass; BMI = body mass index.
Every participant (recruited at the UCSC as part of previous study) was sarcopenic according to one-to-four operational definitions (mean 2.54) proposed in the past by Janssen et al., Baumgartner et al., and Newman et al. (crude and fat-adjusted models).

<table>
<thead>
<tr>
<th>Definition of sarcopenia based on FNIH criteria</th>
</tr>
</thead>
</table>

- **N:** 37 (women 78.4%)
- **Age:** 77.9 (SD 0.2) years
- **BMI:** 23.9 (SD 0.1) kg/m²

<table>
<thead>
<tr>
<th></th>
<th>Detected</th>
<th>Undetected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude ALM</td>
<td>78.4%</td>
<td>21.6%</td>
</tr>
<tr>
<td>ALM(_{BMI})</td>
<td>43.2%</td>
<td>56.8%</td>
</tr>
<tr>
<td>ALM(_{BMI}) and crude ALM</td>
<td>37.8%</td>
<td>42.2%</td>
</tr>
<tr>
<td>ALM(_{BMI}) or crude ALM</td>
<td>83.8%</td>
<td>16.2%</td>
</tr>
<tr>
<td>Crude ALM for BMI &lt;25 kg/m²</td>
<td>83.8%</td>
<td>16.2%</td>
</tr>
<tr>
<td>ALM(_{BMI}) for BMI ≥25 kg/m²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Agreement: 54.7%
Agreement: 100%
## Identifying an at-risk older population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Research</th>
<th>Clinical practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle mass</td>
<td>Computed tomography (CT)</td>
<td>BIA</td>
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<tr>
<td></td>
<td>Magnetic resonance imaging (MRI)</td>
<td>DXA</td>
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<tr>
<td></td>
<td>Dual energy X-ray absorptiometry (DXA)</td>
<td>Anthropometry</td>
</tr>
<tr>
<td></td>
<td>Bioimpedance analysis (BIA)</td>
<td></td>
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<tr>
<td></td>
<td>Total or partial body potassium per fat-free soft tissue</td>
<td></td>
</tr>
<tr>
<td>Muscle strength</td>
<td>Handgrip strength</td>
<td>Handgrip strength</td>
</tr>
<tr>
<td></td>
<td>Knee flexion/extension</td>
<td></td>
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<tr>
<td></td>
<td>Peak expiratory flow</td>
<td></td>
</tr>
<tr>
<td>Physical performance</td>
<td>Short Physical Performance Battery (SPPB)</td>
<td>SPPB</td>
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<tr>
<td></td>
<td>Usual gait speed</td>
<td>Usual gait speed</td>
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<tr>
<td></td>
<td>Timed get-up-and-go test</td>
<td>Get-up-and-go test</td>
</tr>
<tr>
<td></td>
<td>Stair climb power test</td>
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</tbody>
</table>
How to assess physical performance in people with PF&S
In the absence of targeted interventions, 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

Sarcopenia and physical frailty: two sides of the same coin

Matteo Cesari¹²*, Francesco Landi³, Bruno Vellas¹², Roberto Bernabei³ and Emanuele Marzetti³

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

Lower limbs performance test
Robustness

- SPPB ≥10/12
- No sarcopenia
- No mobility disability

Probable few benefits from interventions against disability

Disability

- SPPB between 3/12 and 9/12
- Sarcopenia
- No mobility disability

Possible interventions for preventing disability

Disability

- SPPB <3/12
- Sarcopenia (cachexia?)
- Mobility disability

Possible interventions for treating disability

Exhaustion of endogenous reserves for restoring robustness

Limit posed by the SPPB impairment

Limit posed by the mobility disability
Setting the SPPB range

- The identification of non-disabled older persons exposed to increased vulnerability to stressors will rely on 2 key elements, which are the components of the proposed PF&S operationalisation:

1. Target organ deterioration (i.e., low muscle mass as measured by DXA = sarcopenia)

2. Clinical signs and symptoms of physical frailty (i.e., weakness, slow walking speed and poor balance) objectively measured through the SPPB and corresponding to a summary score between 3 and 7

3. Absence of major mobility disability

- A convenience sample of 300 individuals with SPPB 8 and 9 will also be enrolled since these persons, although presenting a lower risk of incurring in adverse health outcomes, may still benefit from a multicomponent preventive intervention.
Use of usual gait speed as primary outcome

Pros

• Usual gait speed is a general marker of wellbeing ("vital sign")

• Key part of SPPB responsiveness

• Large geriatric literature links slow gait speed to morbidity and mortality

• Easy to apply in clinical settings

• Excellent screening tool for identifying at-risk populations

• Less challenging than long-distance walk tests
The 400-meter walk test as the primary outcome

Four-hundred meters (roughly ¼ mile) is a distance commonly used to measure self-reported mobility disability and believed to be required for independence with daily tasks (e.g., public transportation, grocery shopping).


Inability to complete a 400-m walk is associated with negative outcomes (mortality, cardiovascular events, incident disability) and higher healthcare costs.


Subjects who complete the walk in >15 minutes have an extremely slow pace (<0.45 m/sec), which makes their walking capacity of little utility in daily life.


An average older adult can cover a 400-meter distance in about 6 minutes.

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
The SPRINTT RCT clinical centres

17 clinical sites
10 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) Heart of England NHS Foundation Trust (Birmingham, UK)
14) Aston University (Birmingham, UK)
15) University of Iceland (Reykjavík, Iceland)
16) University of Helsinki (Helsinki, Finland)
17) Maastricht University Medical Center (Maastricht, The Netherlands)

* Centralised backup site
The eligibility criteria in this study are aimed at identifying persons who are physically frail and sarcopenic, that is have the clinical and biologicall 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 of 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 based 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 randomized 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
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)
• Cancer requiring treatment in the past 3 years, except for non-melanoma skin cancers or cancer that have an excellent 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, history of cardiac arrest, presence of implantable defibrillator, or uncontrolled angina)
• 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
• Current enrolment in another RCT involving lifestyle, nutrition, or pharmaceutical interventions

• Other medical, psychiatric, or behavioral factors that in the judgment 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 concerning 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 of the participant’s eligibility 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 of 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. Nevertheless, 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 (systolic 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 arrhythmia, new Q waves within the past 6 months or ST-segment depression (> 3mm) on the ECG
- Myocardial infarction, major heart surgery (i.e. valve replacement or coronary bypass graft), stroke, deep vein thrombosis, or pulmonary embolism in the past 6 months
- Use of growth hormone, estrogens, progesterone or testosterone supplementation in the past 3 months
SPRINTT RCT
ESTABLISHING ELIGIBILITY

• Eligibility is established 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 verifying the eligibility is the body composition evaluation by DXA SCAN.
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

**Multi Component Intervention (MCI):** Physical activity + dietary intervention + ICT (N=750)

**HALE:** education on healthy lifestyle + ICT component (N=750)

Minimum follow up  Maximum follow up
**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 behaviourally.
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

<table>
<thead>
<tr>
<th>Intervention staff contacts for the PA group</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week</strong></td>
<td><strong>Centre-based PA</strong></td>
<td><strong>Home-based PA</strong></td>
</tr>
<tr>
<td>Adoption (weeks 1-52)</td>
<td>2 times each week</td>
<td>1 time/week (weeks 1-4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 times/week (weeks 4-8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Up to 3-4 times/week (weeks 8-52)</td>
</tr>
<tr>
<td>Maintenance (weeks 53 – end of the trial)</td>
<td>2 times each week</td>
<td>Up to 3-4 times/week</td>
</tr>
</tbody>
</table>

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]).
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, 45-minute 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.
“The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under Grant Agreement n° 115621, resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7 / 2007-2013) and EFPIA companies’ in kind contribution”.