

Frailty in the research framework: the good practices

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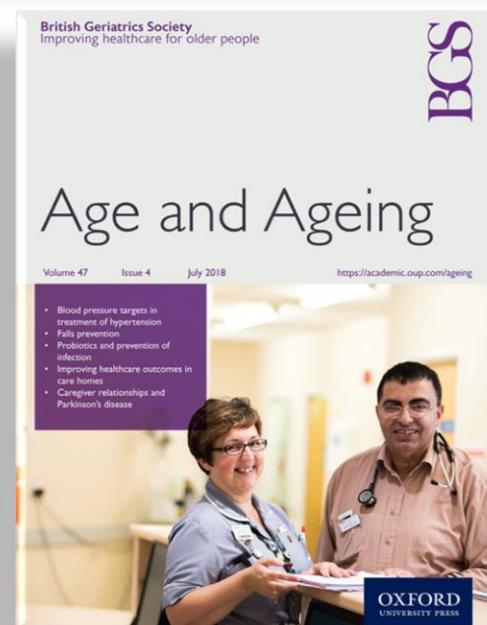
Frailty: mind the gap

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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.

Frailty is defined as a state of increased vulnerability resulting from aging and often disease associated decline in reserve and function across multiple physiologic systems such that the ability to cope with acute stressors is reduced

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

CHALLENGES IN THE IDENTIFICATION OF FRAILTY

Although there is a universal recognition of the frailty syndrome by most physicians caring for older people, there is still a lack of consensus on operational criteria to identify frail older subjects.

Comparing models of frailty: The Health and Retirement Study

Objectives: comparing 3 models of frailty, each representing a distinct theoretical vision (*il functional domains model*, *il burden model-frailty index*, *il biologic syndrome model-physical frailty*).

Design: cross-sectional

Participants: age \geq 65 years (N= 11,113), U.S. community-dwelling or NHs residents

Comparing models of frailty: The Health and Retirement Study

Conclusions

The different models of frailty, based on different theoretical models, identify different groups of elders.

The different models could represent different paths or trajectories of frailty, which determine adverse outcomes such as disability and finally death.

Frailty models

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

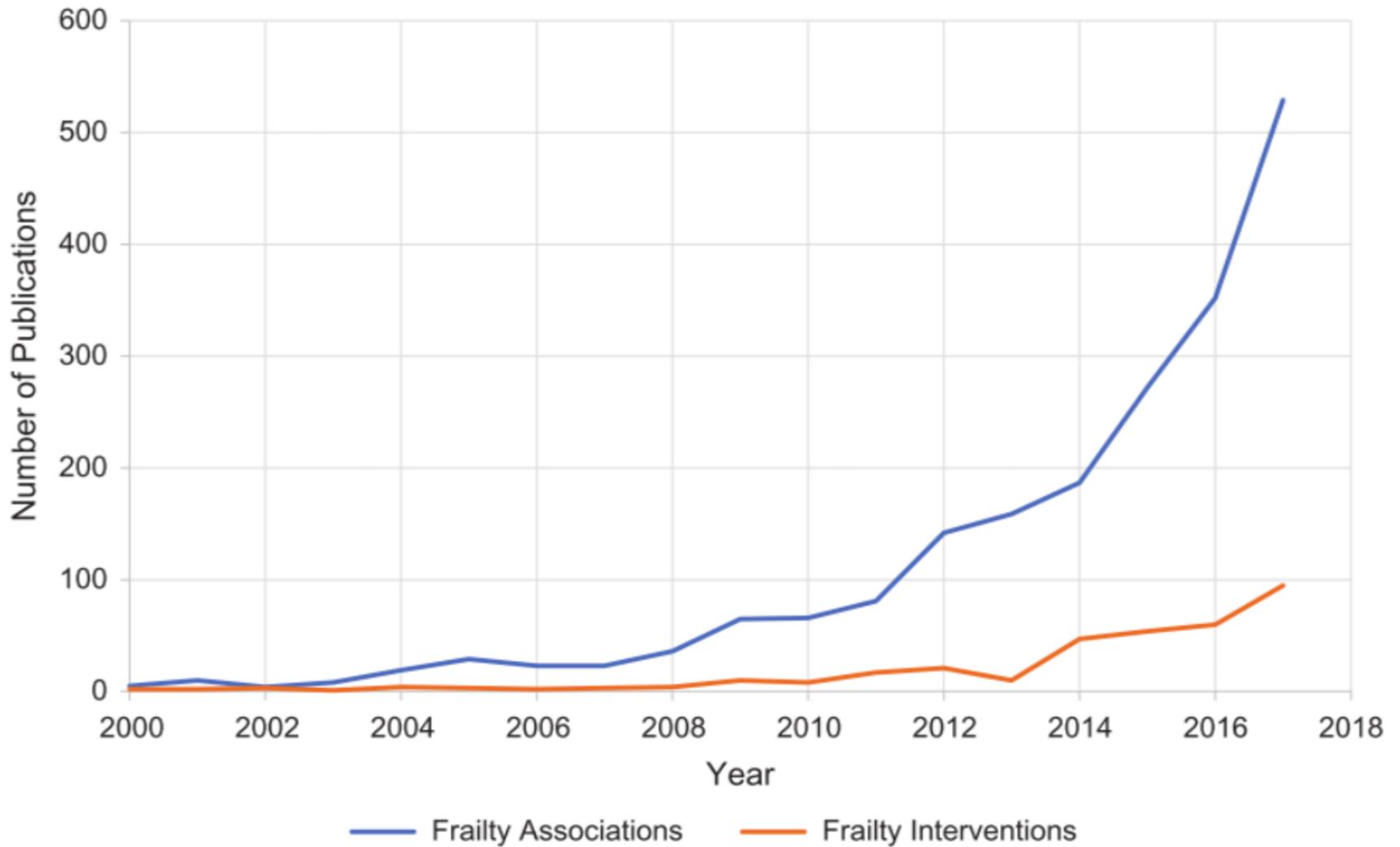
The empirical benefits of identifying and treating frailty remain unclear

Frailty is a strong predictor of 1-year and 5-year mortality and therefore may play a role in advance care planning and decision making.

It remains unclear the extent to which frailty is responsive to treatment of underlying disease and indicates the need for prioritizing treatment, and how much is not treatment responsive and might lead to recommending a conservative approach.

Better empiric research in this area is required in order to apply these tools to support appropriate treatment decisions but avoid unjustified rationing.

Mudge, Age Ageing.2018



Mudge, Age Ageing.2018



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Reflection paper on physical frailty: instruments for
baseline characterisation of older populations in clinical
trials

The concept of frailty

Better characterisation of the older population beyond age, following a standardized approach, might better inform the evaluation of efficacy and safety of medicines in the pre- and post-authorisation phase

Several frailty instruments have been tested and validated in epidemiological studies in the older population, while their applicability to other settings has been somewhat limited.

The concept of frailty

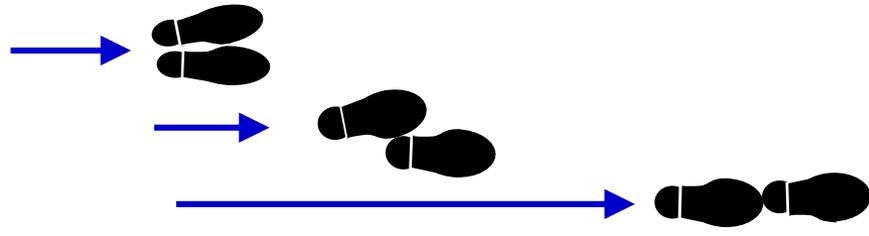
- It is recognised that a complete evaluation of frailty to support its management requires a multidimensional interdisciplinary Comprehensive Geriatric Assessment (CGA), which is the 'gold standard' in clinical practice.
- Domains assessed in a typical CGA include physical and cognitive function, nutritional status, multimorbidity, concomitant medications and socio-economic factors.
- However, the limitations that might hinder the incorporation of CGA into every clinical trial include the time required for the assessment and the expertise of a geriatrician for good reproducibility.

Short Physical Performance Battery (SPPB)

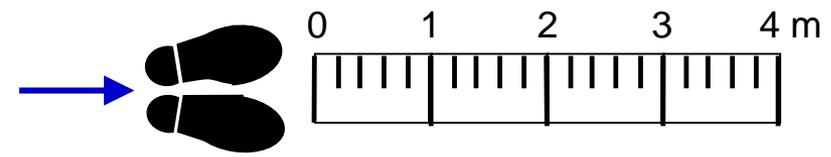
– Includes three tests:

- **Standing balance** (up to 10 seconds for each item)

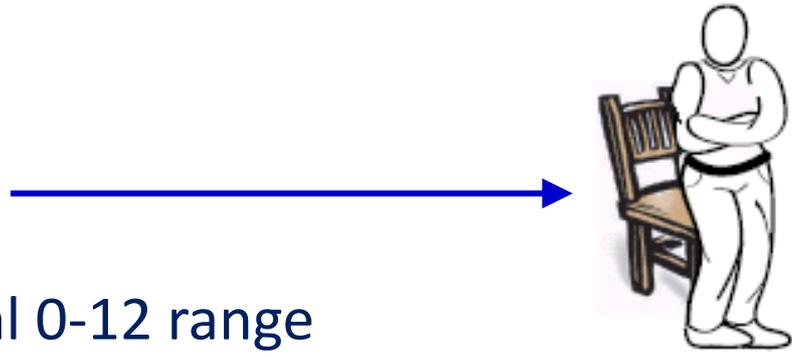
- Side-by-side
- Semi-tandem
- Tandem



- **Walking speed (4 meters)**



- **5 chair standing**



– Score 0-4 for each test, total 0-12 range

SPRINT-T work packages





Sprintt

CLINICAL TRIAL

The SPRINTT RCT clinical centres



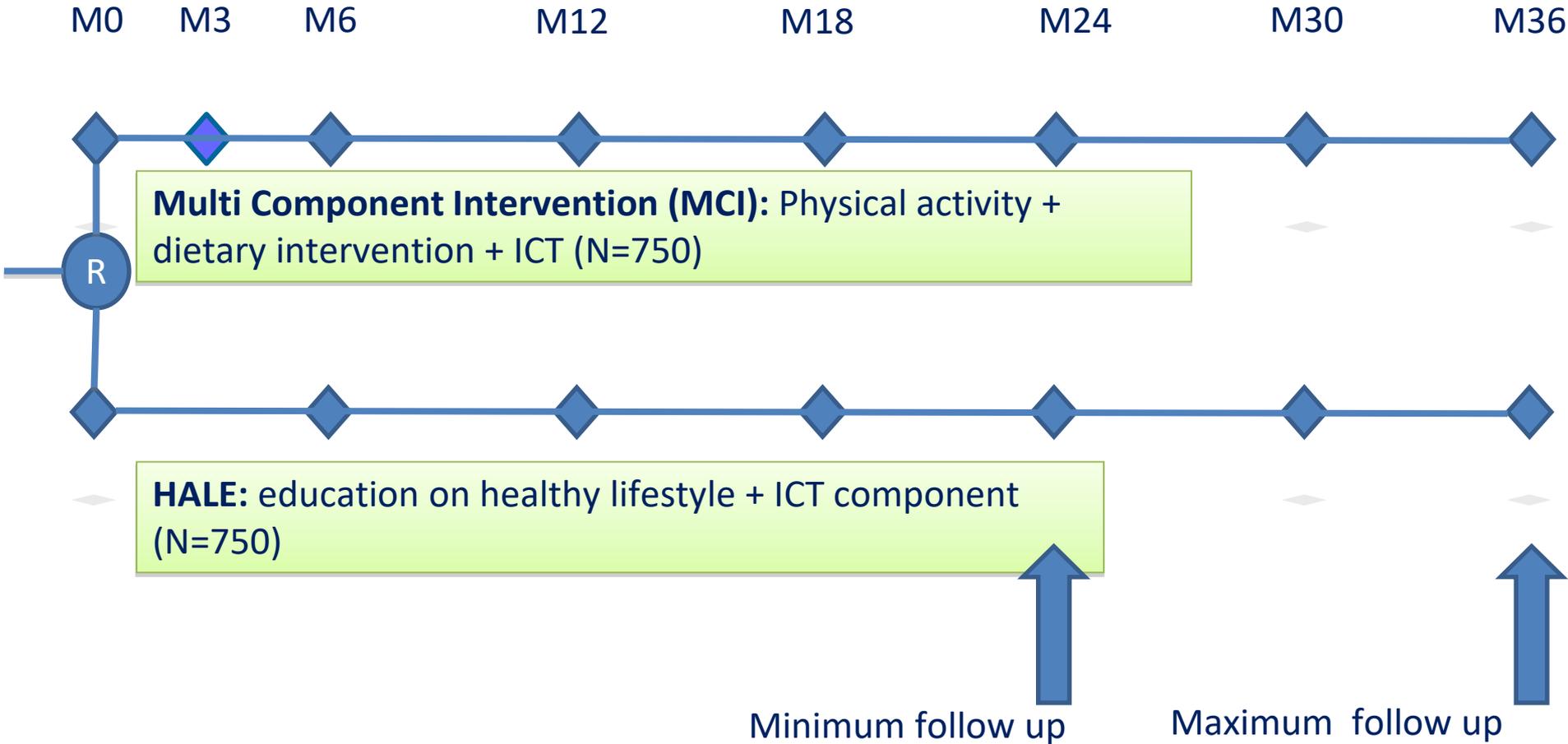
17 clinical sites
11 European countries

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 outline



Multi-component intervention (MCI)

Physical activity intervention

Structured exercise and physical activity (LIFE study protocol)

Nutritional assessment and dietary intervention

Personalised dietary recommendations (targets: 25-35 kCal/kg/day and 1.0-1.2 g protein/kg/day)

Health technology intervention

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

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.

SPRINTT RCT outcomes

Primary outcome

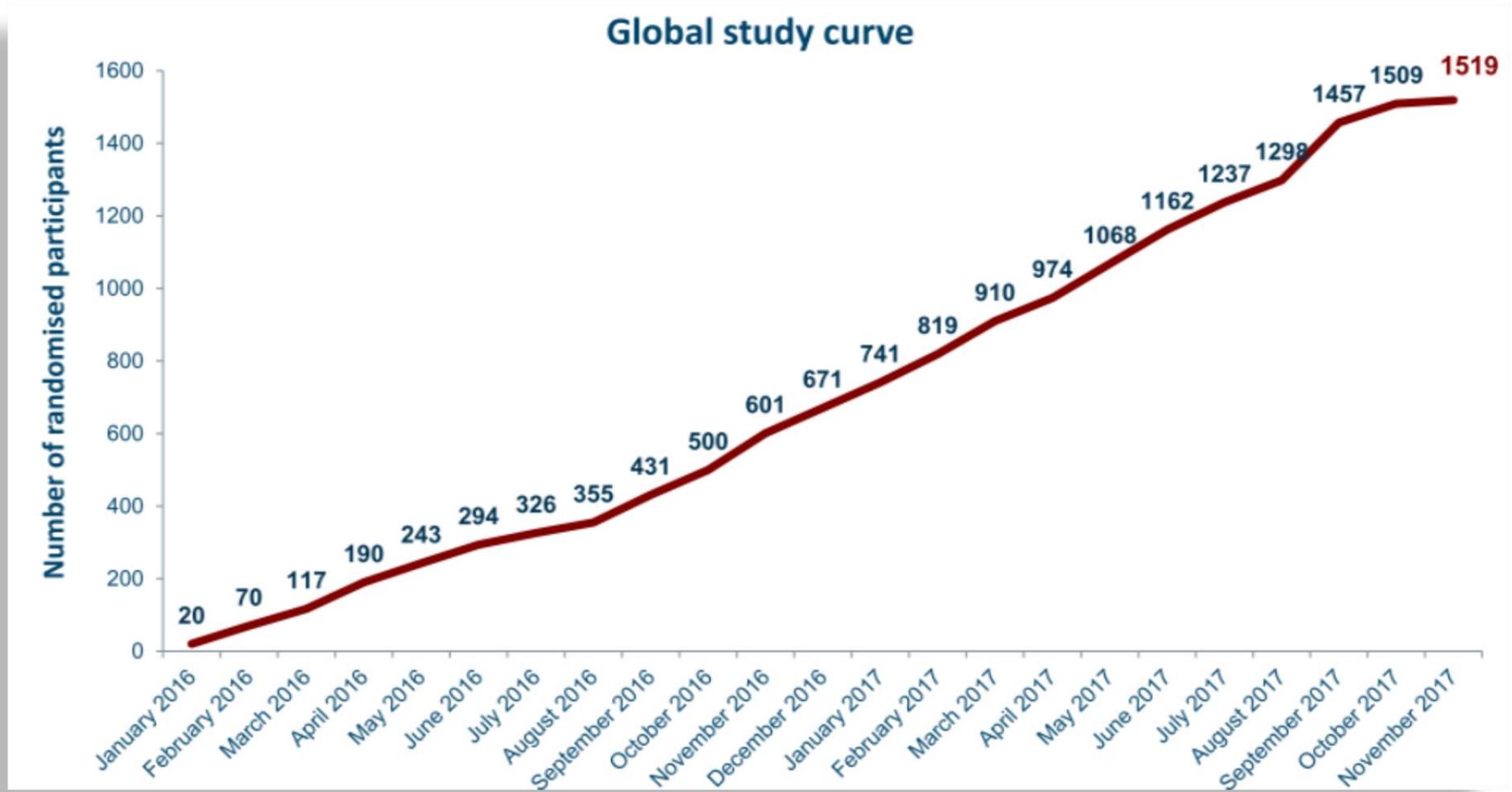
Incidence of mobility disability (inability to complete the 400-m walk test)

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)

SPRINTT BASELINE DATA

RCT recruitment curve



Baseline characteristics of SPRINTT participants

Characteristic	MCI (N=759)	HALE (N=758)
Age (years)	79.1 (5.9)	78.7 (5.7)
Female (%)	546 (71.9%)	540 (71.2%)
White (%)	670 (98.4%)	665 (98.2%)
Weight (kg)	70.7 (15.6)	70.9 (16.9)
BMI (kg/m ²)	28.6 (5.9)	28.6 (6.0)
≥ 30 kg/m ² (%)	276 (36.5%)	280 (37.0%)
SARC-F	2.9 (1.8)	3.0 (1.9)
≤4 (%)	628 (82.9%)	600 (79.2%)
SPPB total score	6.7 (1.4)	6.7 (1.4)
3-7 (%)	603 (79.4%)	599 (79.0%)
8-9 (%)	156 (20.6%)	159 (21.0%)
MMSE total score	27.9 (1.8)	27.9 (1.9)
400-m walk test (min)	8.7 (2.5)	8.7 (2.4)
DXA (local values)		
aLM (kg) (M/F)	21.0 (3.4) / 14.7 (1.9)	21.1 (3.6) / 14.8 (2.3)
aLM/BMI (M/F)	0.728 (0.086) / 0.528 (0.075)	0.723 (0.084) / 0.530 (0.078)

The empirical benefits of identifying and treating frailty remain unclear

- Physical activity and multicomponent interventions can reduce measures of frailty in community-living older people.
- It is unclear whether this improvement is unique to frail individuals (i.e. is a treatment effect on frailty per se) or is a universal consequence of physical activity participation.
- This is critical in understanding whether we should be specifically targeting frail or pre-frail individuals, or continuing a broad public health approach to the many benefits of physical activity participation.