UNIVERSITY OF BIRMINGHAM

The University of Nottingham

MRC-ARUK Centre for Musculoskeletal Ageing Research

Ensuring Adults are Fit for Old Age

ARUK-MRC Centre for Musculoskeletal Ageing Research

Translating Research Into Clinical Practice

Professor Tahir Masud

Examples of current ongoing Translational Research in the area

- Promoting Activity, Independence and Stability in Early Dementia (PrAISED)
- Developing and Evaluating a Chair Based Exercise Programme (CBE study)
- Nottingham Spinal Health (NoSH) Study
- Optimising Care Home Nutrition: Exploring the role of Leucine and Vitamin D
- Leucine and ACE Inhibitors as therapies for sarcopenia (The LACE trial)
- Incorporating Frailty, Sarcopenia and Nutritional Assessments in Osteoporosis Clinics

Promoting Activity, Independence and Stability in Early Dementia

(NIHR Programme Grant)

PrAISED

Promoting Activity, Independence and Stability in Early Dementia

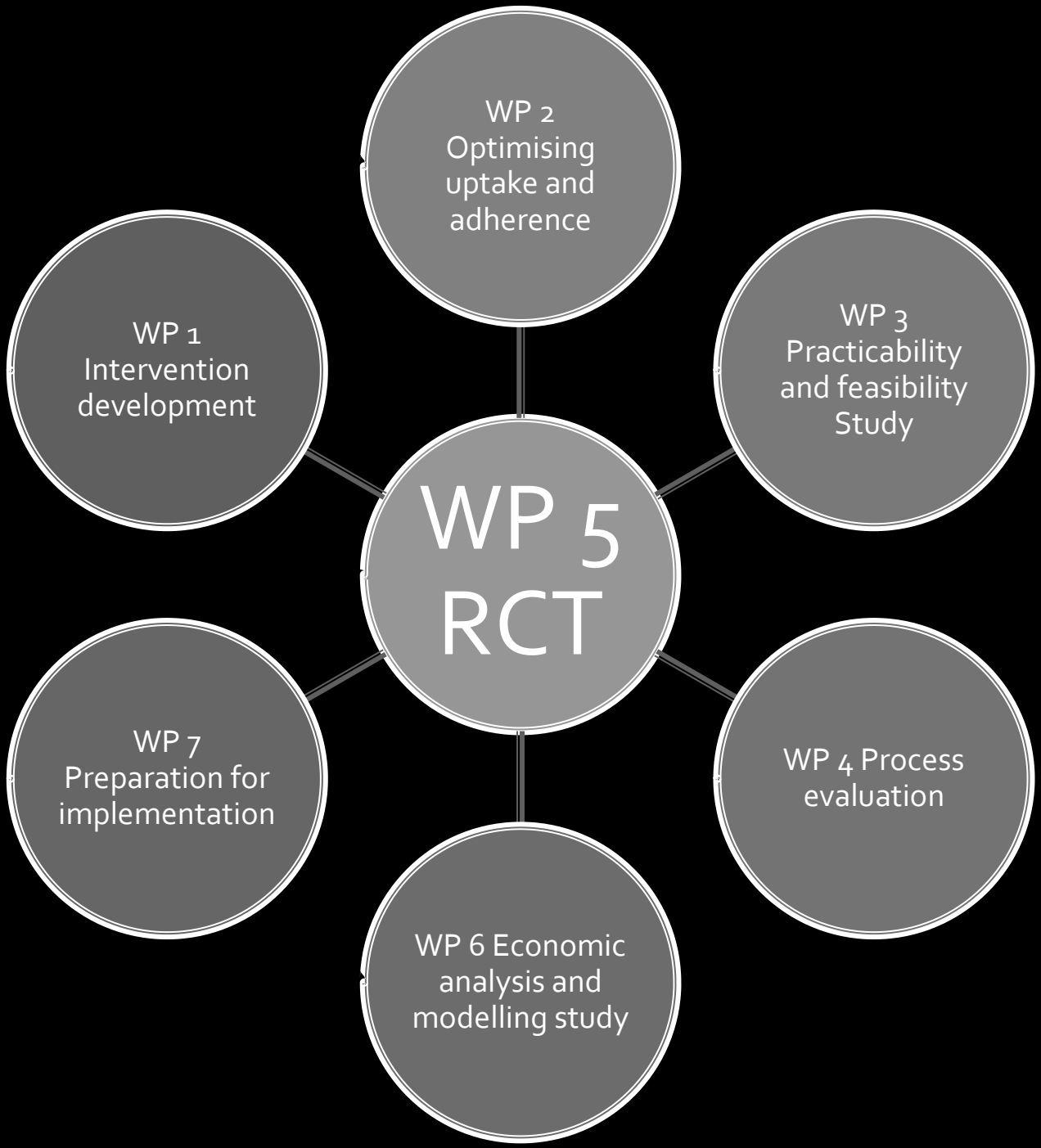
CI: Rowan Harwood

Co-Inv: Pip Logan, John Gladman, Veronika van der Wardt, Sarah Goldberg, Vicky Booth, Vicky Hood , Tahir Masud et al

To develop and test an intervention to enable people with mild dementia to stay independent for longer.

The multi- component intervention includes

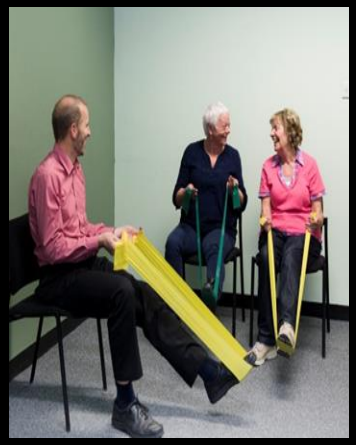
- Physiotherapy
- Occupational therapy
- Exercise psychology
- Risk enablement
- Education/information

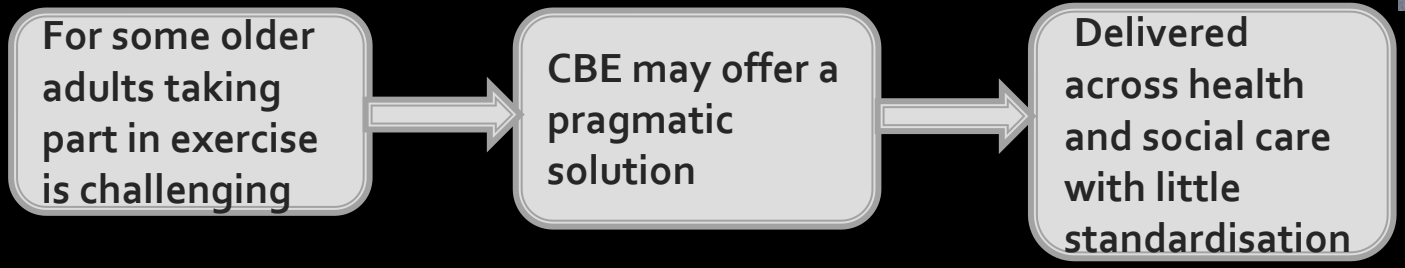

WP 2
Optimising uptake and adherence
WP 1
Intervention development
WP 3
Practicability and feasibility Study
WP 5
RCT
WP 7
Preparation for implementation
WP 4 Process evaluation
WP 6 Economic analysis and modelling study

Developing and Evaluating a Chair Based Exercise Programme

(NIHR RfPB Feasibility study)

Leads: Tahir Masud, Katie Robinson





- Developed a set of principles for chair based exercise programmes through an expert consensus development process

- Research for Patient Benefit feasibility trial to:
  - establish the parameters for a future definitive trial
  - explore if the CBE programme could be delivered in day centres, care home and community centres
  - explore what older people and care staff thought about the intervention

Main findings

- Difficulty delivering the intervention at a frequency and intensity to elicit physiological change
- Health conditions and fragile health status limited participation
- Older people wanted to try 'proper' standing and walking but care staff felt seated exercise was the most appropriate exercise in these settings

Nottingham Spinal Health (NoSH) Study

PI: Terence Ong

Co-investigator: Opinder Sahota, John Gladman, Nasir Quraishi

Funder: Dunhill Medical Trust Research Training Fellowship

AIM: Does an ortho-geriatric multidisciplinary model of care improve outcomes for patients admitted to hospital with vertebral fractures?

Currently in the development phase

- Review of scientific literature
- Analysis of patient characteristics and outcomes
- Modelling of care for future feasibility/pragmatic trial

Selected research output

- Ong T, et al. Characteristics and outcomes of hospitalised patients with vertebral fragility fractures: a systematic review. *Age Ageing* 2017. doi:10.1093/ageing/afx079
- Ong T, et al. Study protocol for the Nottingham Spinal Health (NoSH) Study: A cohort study of vertebral fragility fractures admitted to hospital. *EMRAN* 2017:12
- Walters S, et al. The prevalence of frailty in patients admitted to hospital with vertebral fragility fractures. *Curr Rheumatol Rev* 2016:12.244-247

Future research plan

- Vertebral augmentation in the management of hospitalised acute vertebral fractures
- The role of operative intervention for sacral-pelvic fractures

Optimising Care Home Nutrition: Exploring the role of Leucine and Vitamin D

Leads: Bethan Phillips, Adam Gordon

"CH residents experience greater multi-morbidity and polypharmacy than age-matched community dwellers, and have more prevalent malnutrition- 30% are malnourished with 56% at risk; in particular *protein energy malnutrition*.

The objective of this project aims to explore, *for the first time*, the effects of ***optimal protein intake and/ or amino acid (leucine) supplementation on muscle mass, function and metabolism*, in care home residents:**

AIM i) to establish current dietary provision and energy/ protein balance in CH residents;
AIM ii) to determine establish the optimal protein load in CH residents; and
AIM iii) to establish the efficacy of 6-months' "optimal" protein intake ± between-meal leucine supplementation on muscle mass, function and metabolic health in CH residents

AIM iii) to establish the efficacy of 6-months' "optimal" protein intake ± between-meal leucine supplementation on muscle mass, function and metabolic health in CH residents

Are Leucine supplements less satiating than protein supplements?

	Months			
	0	1	3	6
Muscle mass:	*	*	*	*
Body composition:	^			^
Muscle architecture:	~	~	~	~
Muscle function:	*	*	*	*
Muscle protein synthesis:	^			^
Appetite:	~		~	~

n=10: standard nutrition

n=10: optimal protein (informed by Aim ii)

n=10: optimal protein + Leucine

n=10 standard nutrition + Leucine

How does standard CH nutrition effect muscle 'health' over a 6-month period?

Which is the most favorable intervention strategy for muscle mass, function & metabolism?

- Muscle mass via BIA
- Body composition via DXA *(where possible)*
- Muscle architecture via leg muscle ultrasound
- Muscle function via SPPBT, TUG and handgrip *(where possible)*
- Muscle protein synthesis via D_2O and micro muscle biopsy***
- Appetite via questionnaires and meal tolerance test

***

- Baseline blood and saliva sample
- D_2O drink
- 3 hour saliva sample
- 6 hour <u>micro</u> muscle biopsy

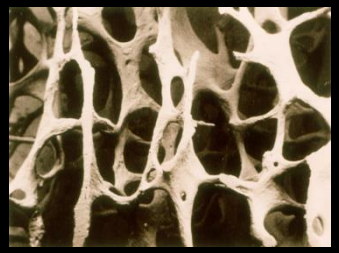
Leucine and ACEis in Sarcopenia (LACE) Trial

- Multicentre RCT (> 15 UK centres including Nottingham/Derby)
- CI: Miles Whitham (Dundee)
- 2 x 2 factorial design
  - Perindpopril 4mg + placaebo
  - Leucine tds + placaebo
  - Perindopril + leucine
  - Double placaebo
- Primary outcome - SPPB
- Secondary oiutcomes:
  - Muscle mass
  - Falls
  - QoL
  - Health economics

Incorporating Frailty, Sarcopenia & Nutritional Assessments in Osteoporosis Clinics

Tahir Masud
Mateen Arrain
Vicky Hood

FRACTURE
The link between osteoporosis and falls



Osteoporosis

Bone
Strengthening
Therapy

Fracture

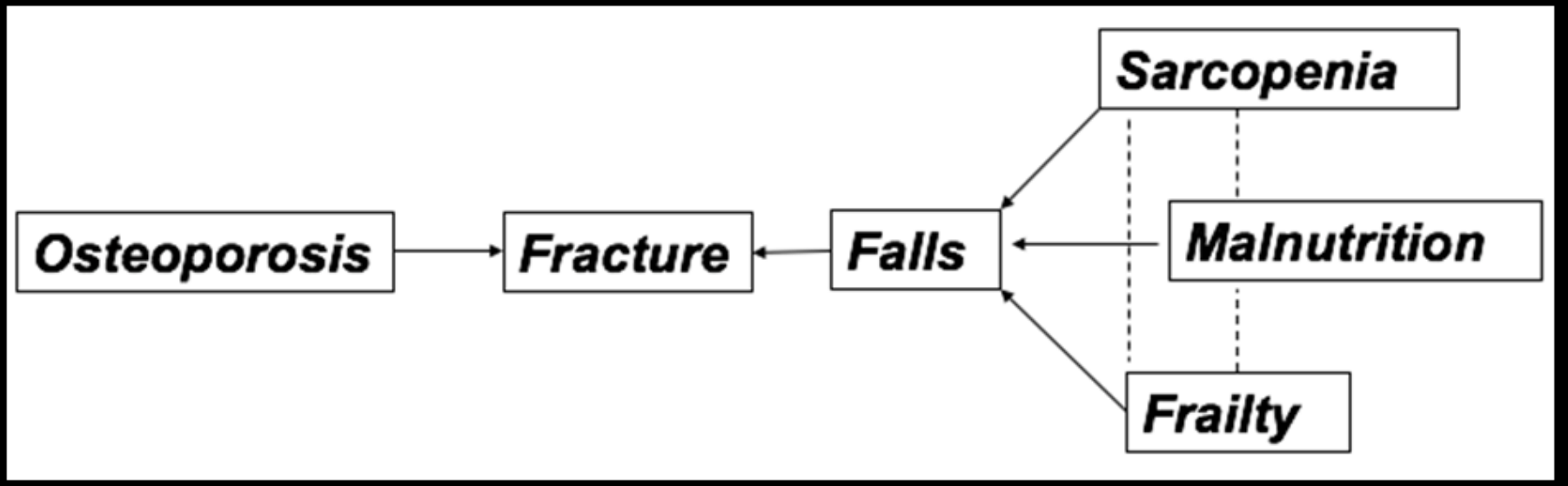
Falls

Identifying and
Reducing falls risk

(suboptimal) Nutrition

Sarcopenia

Frailty


Sarcopenia
Osteoporosis
Fracture
Falls
Malnutrition
Frailty

Frailty – Definition

Consensus Staement: Morley JE et al; J Am Dir Assoc 2013

‘. . .a medical syndrome with multiple causes and contributors that is characterised by diminished strength, endurance and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency and/or death.’

Operational definitions: 2 concepts

1. Accumulation of Deficits ("Rockwood")
   - concept of multisystem disorder
   - number of health deficits varies 30-70
   - defiicits – symptoms, signs, diseases, disabilities, lab results
   - Frailty Index (FI): 0-1
   - Frailty = FI > 0.25
   - eFI eg from GP data systems

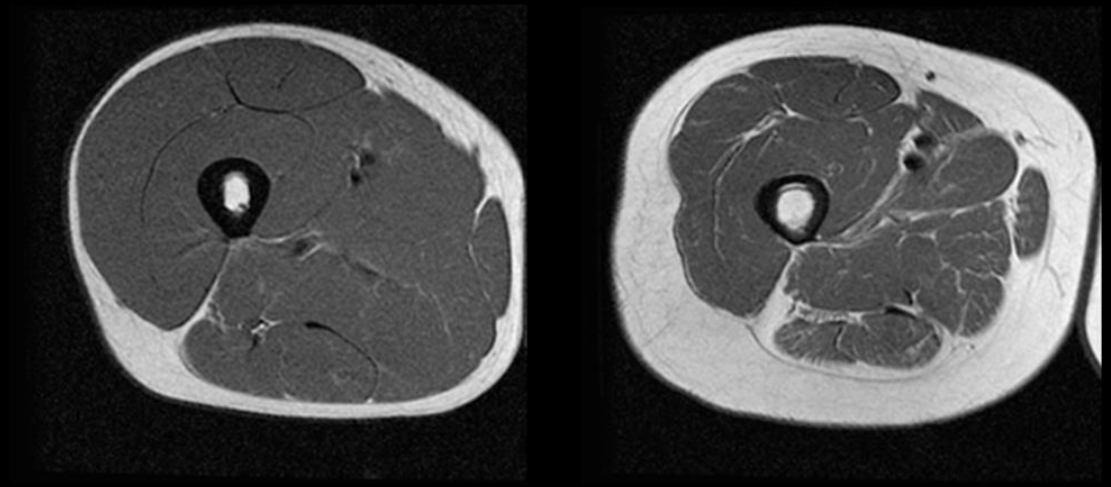
2. Physical Frailty Phenotype (PFP) ("Fried")
   - Weakness .....Grip strength
   - Slow walking speed .....Timed walk
   - Low physical activity ..... .Kcals / week
   - Weight loss (unintentional) .....10 lbs or >5% / year
   - Exhaustion .....Self Report

Frail = 3+, Prefrail = 1-2

Other PFP tools: Frail Scale, Gerontopole Frailty Screening Tool

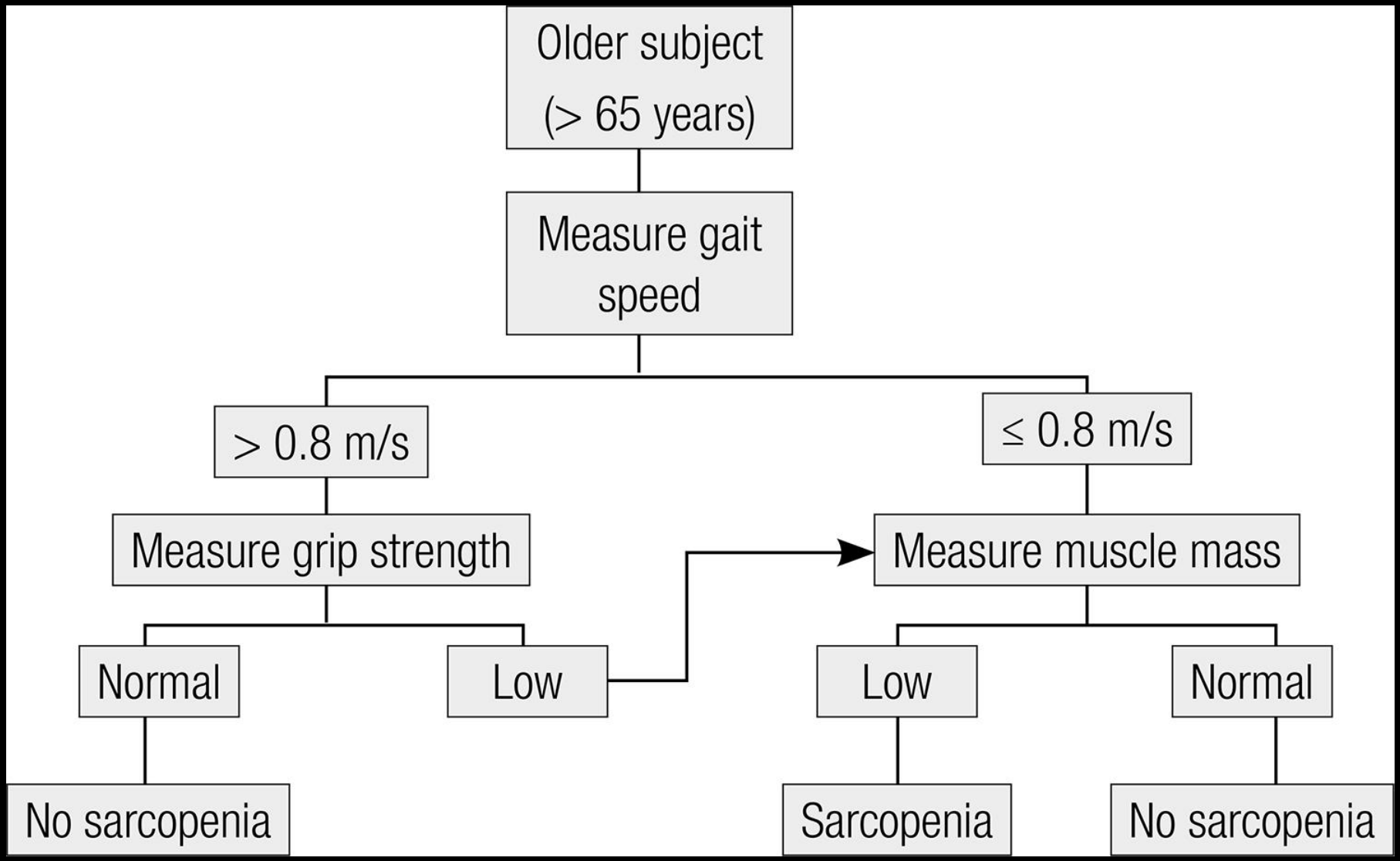
Sarcopenia

- Loss of muscle mass and function (strength or performance)
- Prevalence increases with age
- Associated with disability, morbidity, frailty and mortality
- Prevalence varies according to definition
  - Japan 13% in older population (mean age 75 yrs)
  - Uk 4.6% men, 7.9% women (mean age 67 yrs) (Patel)



Age 25 Age 63

EWGSOP algorithm for diagnosing sarcopenia



Cruz-Jentoft et al Age Ageing 2010

Groningen Frailty Indicator

Physical components	
Are you able to carry out these tasks single-handedly and without any help? (The use of help resources, such as a walking stick, walking frame, or wheelchair, is considered to be independent.)	
1. Shopping	
2. Walking around outside (around the house or to the neighbors)	
3. Dressing and undressing	
4. Going to the toilet	
5. What mark do you give yourself for physical fitness? (scale 0 to 10)	
6. Do you experience problems in daily life because of poor vision?	
7. Do you experience problems in daily life because of being hard of hearing?	
8. During the past 6 months have you lost a lot of weight unwillingly? (3 kg in 1 month or 6 kg in 2 months)	
9. Do you take 4 or more different types of medicine?	
Cognitive component	
10. Do you have any complaints about your memory?	
Social component	
11. If you are at work, with your family, or at church do you believe that you are part of the social network?*	
12. Do other people pay attention to you?*	
13. Will other people help you if you are in need?*	
Psychological component	
14. In the past 4 weeks did you feel downhearted or sad?*	
15. In the past 4 weeks did you feel calm and relaxed?*	
Scoring:	
Questions 1–4:	Yes = 0; No = 1
Question 5:	0–6 = 1; 7–10 = 0
Questions 6–9:	No = 0; Yes = 1
Question 10:	No = 0; Sometimes = 0; Yes = 1
Questions 11–13:	Never = 1; Sometimes = 1; Often = 0; All the time = 0†
Question 14:	Never = 0; Seldom = 0; Sometimes = 1; Often = 1; Very often = 1; All the time = 1†
Question 15:	Never = 1; Seldom = 1; Sometimes = 1; Often = 1; Very often = 0; All the time = 0†

*Psychosocial items were slightly rephrased compared with the previous published self-report version.[22]
†Likert scales were adapted compared with the previous published self-report version.

Mini Nutritional Assessment

MNA®

[redacted]

Last name: First name:

Sex: Age: Weight, kg: Height, cm: Date:

Complete the screen by filling in the boxes with the appropriate numbers. Total the numbers for the final screening score.

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake ☐

B Weight loss during the last 3 months
0 = weight loss greater than 3 kg (6.6 lbs)
1 = does not know
2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs)
3 = no weight loss ☐

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out ☐

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no ☐

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems ☐

F1 Body Mass Index (BMI) (weight in kg) / (height in m)^2 ☐
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater ☐

IF BMI IS NOT AVAILABLE, REPLACE QUESTION F1 WITH QUESTION F2.
DO NOT ANSWER QUESTION F2 IF QUESTION F1 IS ALREADY COMPLETED.

F2 Calf circumference (CC) in cm
0 = CC less than 31
3 = CC 31 or greater ☐

Screening score ☐☐
(max. 14 points)

12-14 points: ☐ Normal nutritional status
8-11 points: ☐ At risk of malnutrition
0-7 points: ☐ Malnourished

Save
Print
Reset

Baseline Characteristics n=63

Age [years, mean (SD)]	77.6 (7.5)
Age Range [years]	60-93
Women [number (%)]	56 (88.9%)
Height [cm, mean (SD)]	159.0 (9.0)
Weight [kg, median (IQR)]	59.1 (50.8-70.4)
Body Mass Index [kg/m^2, median (IQR)]	22.2 (19.9-27.8)
Gait Speed [m/s, median (IQR)]	0.8 (0.5-1.1)
Grip Strength in women [kg, mean (SD)]	16.9 (6.2)
Grip Strength in men [kg, mean (SD)]	27.0 (7.1)
Muscle mass in women [kg/m^2, median (IQR)]	6.20 (5.65-6.70)
Muscle mass in men [kg/m2, median (IQR)]	8.00 (6.20-8.80)
Groningen Frailty Indicator score [median (IQR)]	5.0 (3.0-8.0)
Mini-Nutritional Assessment-SF [median (IQR)]	13.0 (11.0-15.0)
Calf Circumference [cm, median (IQR)]	33.7 (31.3-36.2)
Physical Activity Levels [number (%)]	
0 < once a month	20 (31.7)
1 between once a week and once a month	0 (0)
2 ≥ once a week and < 5 times per week	30 (47.6)
3 ≥ 5 times per week	13 (20.6)

Results

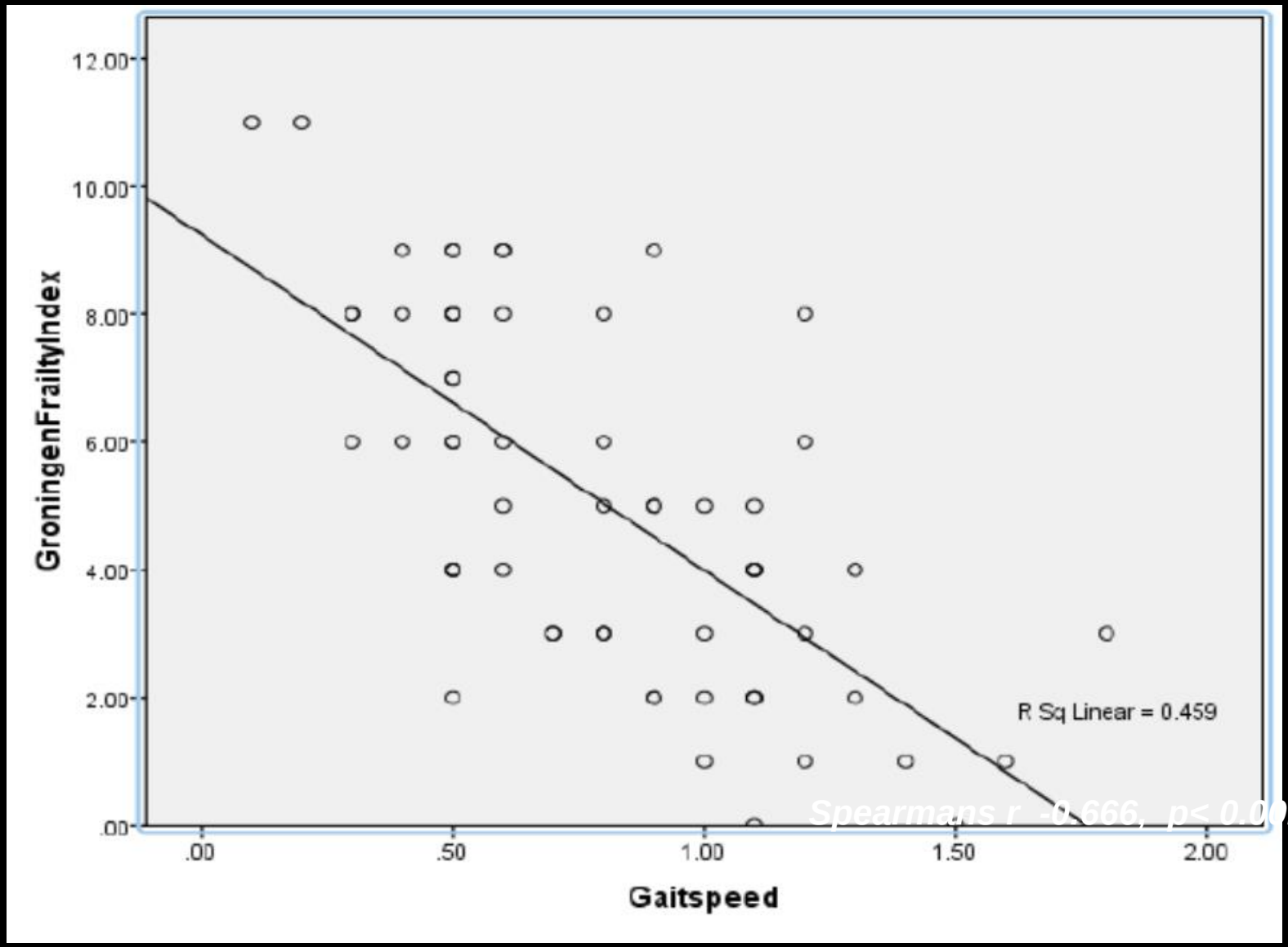
Prevalence

Sarcopenia	*41.0%*
Frailty	*66.7%*
Malnutrition	*7.9%*
Malnutrition or at risk of malnutrition	*28.6%*


Frailty
Sarcopenia
19
14
5
3
0
1
0
14
Malnourished

Predictors of Frailty (Logistic Regression)

Independent variable	Wald Statistic	Exp β [OR] (95%CI)	P
Age (years)	0.38	1.04 (0.92 – 1.18)	0.548
Gait Speed (m/s)	**5.78**	**0.026 (0.001 – 0.511)**	**0.016**
MNA-SF score	3.04	0.78 (0.58 – 1.03)	0.081
Physical Inactivity (categorical)	2.20	6.29 (0.55 – 71.61)	0.138
Grip strength (categorical)	2.25	3.98 (0.66 – 24.14)	0.134


GroningenFrailtyIndex
12.00
10.00
8.00
6.00
4.00
2.00
.00
.00
.50
1.00
1.50
2.00
Gaitspeed
R Sq Linear = 0.459
Spearmans r -0.666, p< 0.001

	Normal Gait speed (> 0.8 m/s)	Slow Gait Speed (≤ 0.8 m/s)	
Not Frail (GFI < 4)	16	5	21
Frail (GFI ≥ 4)	11	29	40
	27	34	61

(Pearson Chi squared = 13.23, Fisher's exact test p< 0.001)

Table 4: *Two by two table of normal/low gait speed with frail/not frail.*

The two by two table shows a statistically significant relationship between slow gait speed and frailty status. In patients who had a slow gait speed 85.3% were frail, and in those with a normal gait speed 40.7% were frail. In frail patients 72.5% had a slow gait speed, whereas in non-frail patients only 23.8% had a slow gait speed.

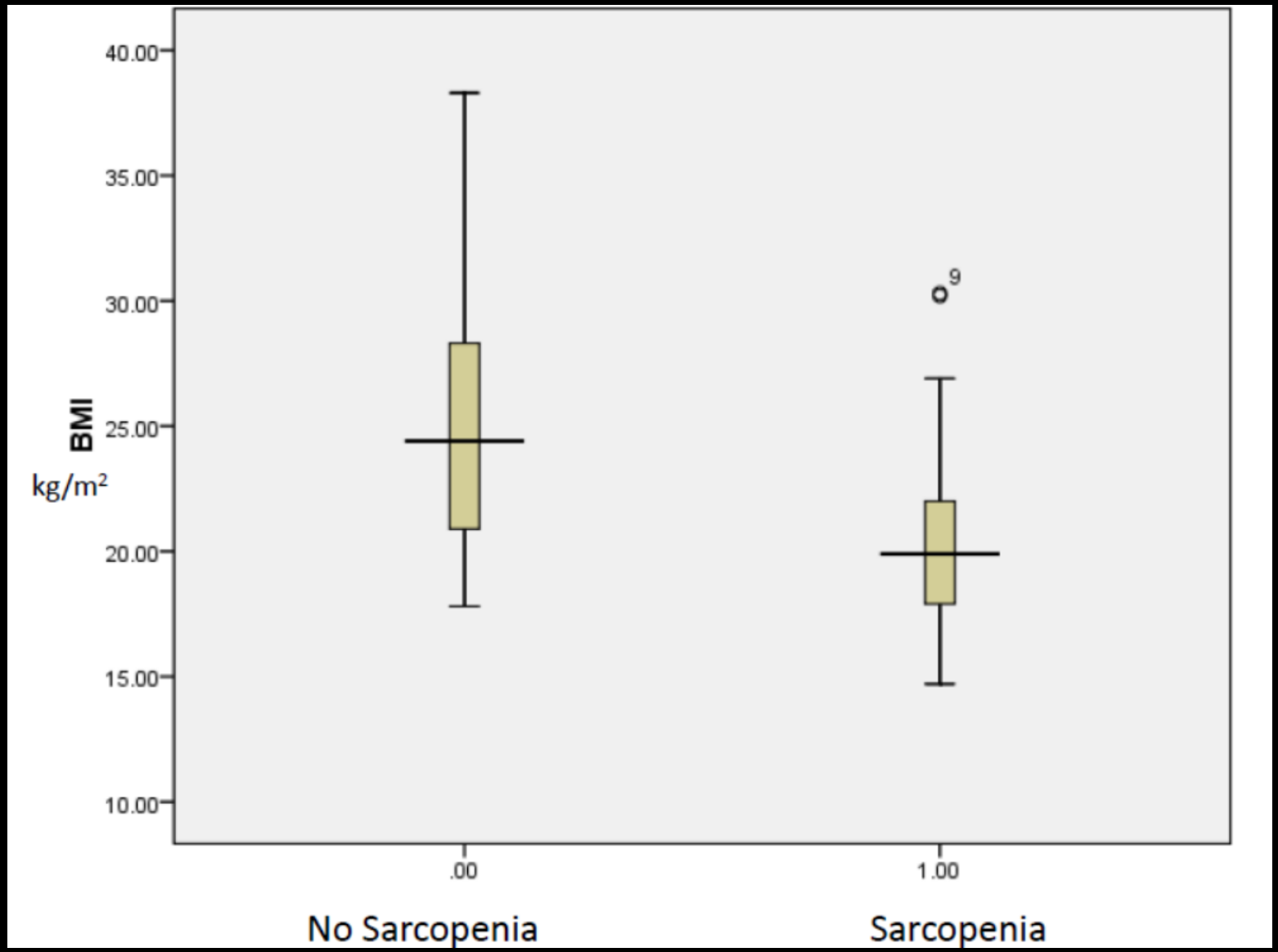
Predictors of Sarcopenia (Univariate Logiostic regression)

Independent Variable	Wald statistic	Exp β [OR] (95%CI)	P
Age (years)	0.21	1.00 (0.93 – 1.07)	0.885
Sex	2.71	4.31 (0.76 – 24.52)	0.100
Height (cm)	0.02	1.00 (0.95 – 1.07)	0.877
Weight (kg)	4.84	0.96 (0.92 – 0.99)	0.028
BMI (kg/m^2)	8.36	0.80 (0.69 – 0.93)	0.004
Frailty (GFI)	3.80	1.23 (1.00 – 1.52)	0.051
MNA-SF score	7.92	0.72 (0.58 – 0.91)	0.005
Calf Circumference (cm)	7.21	0.77 (0.64 – 0.93)	0.007
Physical Inactivity	2.92	2.89 (0.88 – 0.35)	0.087

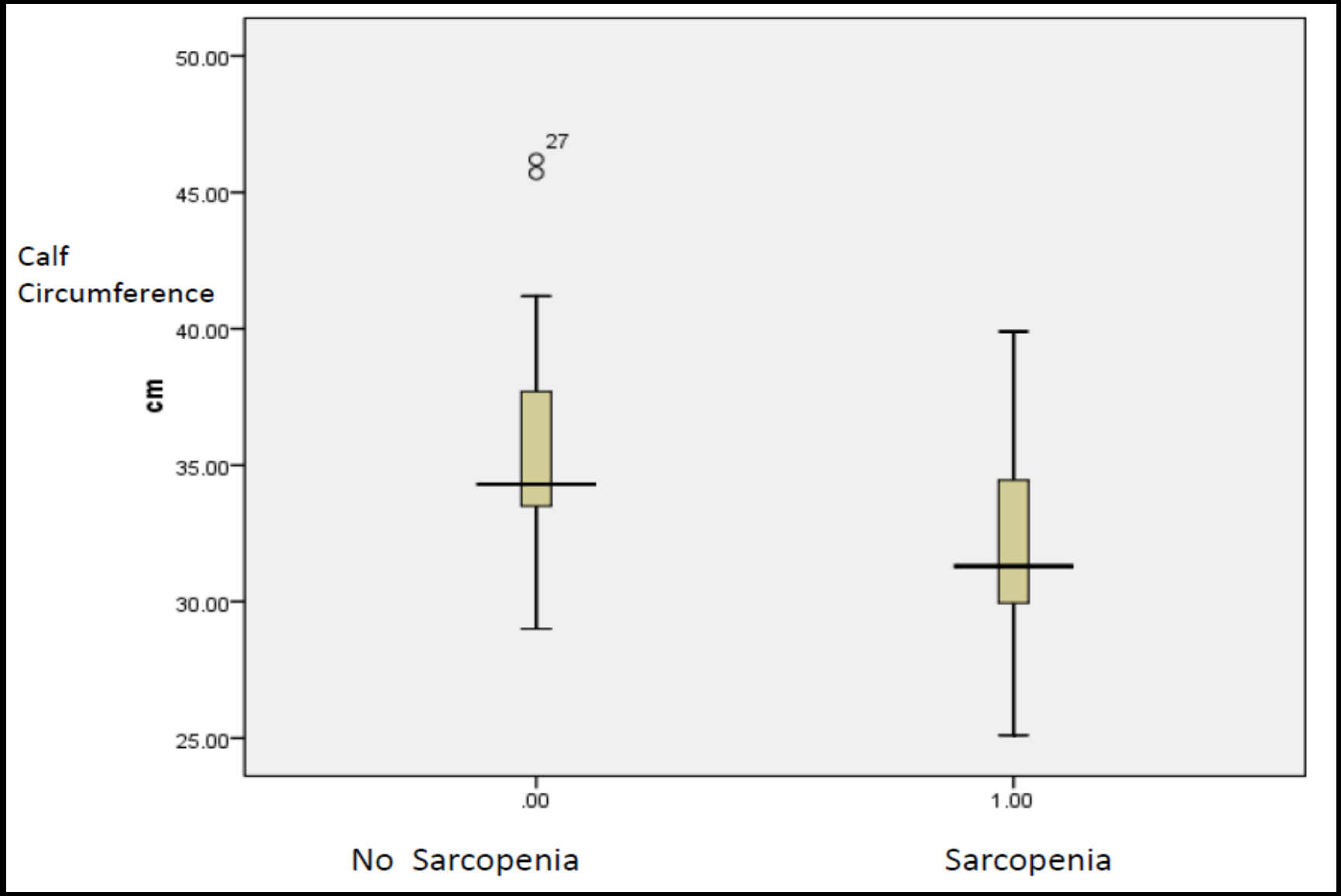
Multivariate logistic regression model (forward stepwise method) only

- ***BMI (log likelihood 14.33, P <0.001) and***
- ***Physical inactivity (log likelihood 5.15, p=0.027)***

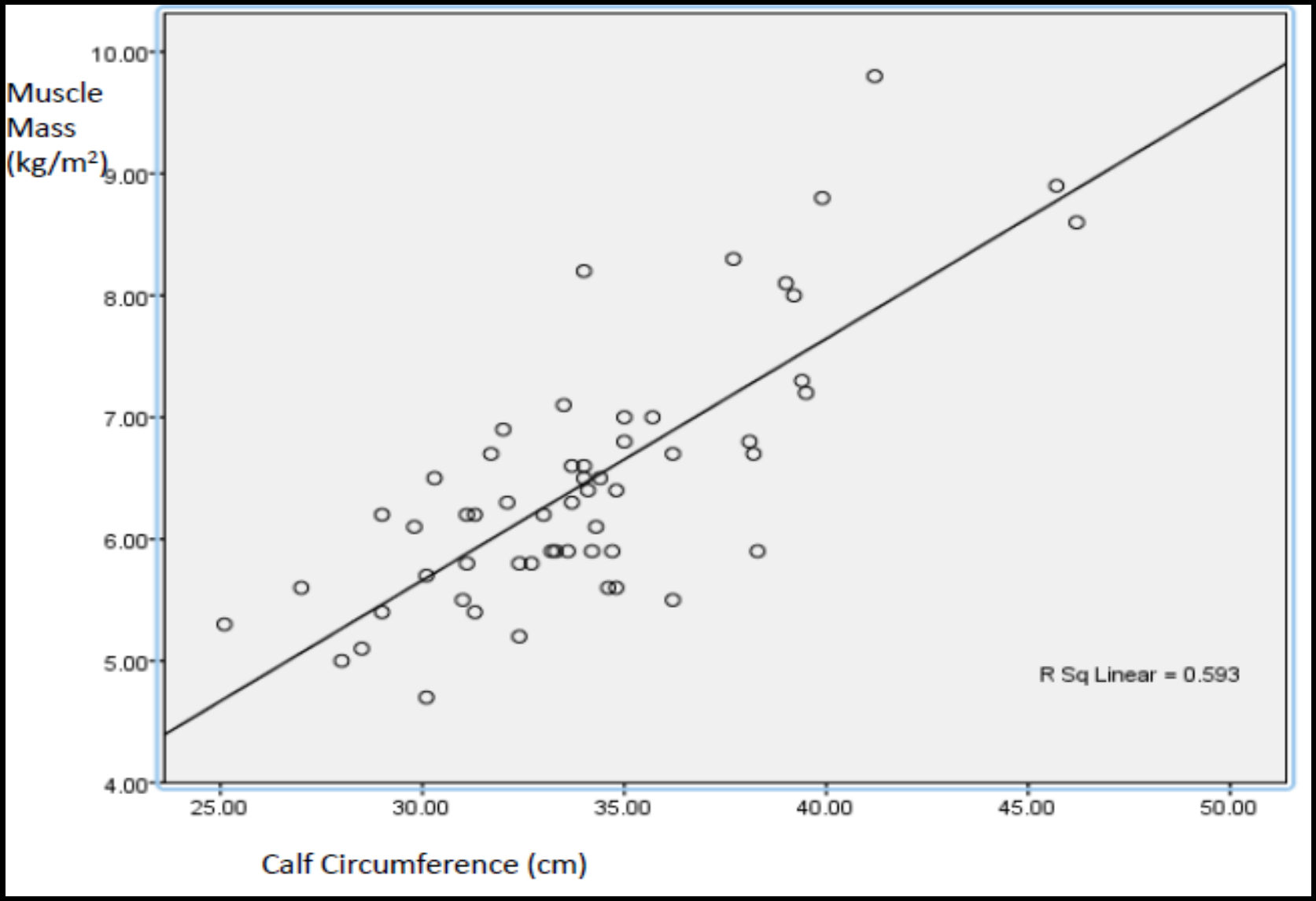
remained independently predictive of sarcopenia



Mann Whitney U=175, p<0.001].



Mann Whitney U= 195, p=0.002



Pearson's r 0.77, p< 0.001

Conclusions

- Assessments for frailty, sarcopenia and malnutrition can easily be incorportaed in busy osteoporosis clinics
- Bio-impedance is a practical and easy to use tool to measure muscle mass in busy clinics
- Gait speed shows potential as an easy to use surrogate test for sarcopenia
- Calf Circumference shows potential as a surrogate for muscle mass

- The ultimate goal of all health related research is to apply it to people
- Translational Research is the vital progression from basic science research