Prevention and early diagnosis of frailty and functional decline

Tomasz Kostka
Medical University of Lodz, Poland
CONFLICT OF INTEREST DISCLOSURE

I have no potential conflict of interest to report

Tomasz Kostka
Medical University of Lodz, Poland
Definitions
Early diagnosis
Prevention
Definitions

Functional decline

Frailty
Physical performance (fitness)

1. Cardiorespiratory fitness, cardiorespiratory endurance, aerobic power, aerobic capacity, stamina
2. Muscle strength, power and endurance (muscular fitness)
3. Speed
4. Flexibility, balance...

Body composition (% body fat, BMI, WHR)
Age-related functional decline:

- physiological changes with ageing
- concomitant diseases
Aerobic capacity and age
Handgrip and age in 847 men aged 20-100 years.
Kallman et al., J Gerontol MED SCI 1990: 45, M82-M88.
\[ r^2 = 54.4 \]
\[ p < 0.001 \]

Correlations between functional status variables and muscle strength, power and $v_{opt}$

<table>
<thead>
<tr>
<th>Quantitative variable</th>
<th>$F_{ext} \cdot kg^{-1}$</th>
<th>$P_{max} \cdot kg^{-1}$</th>
<th>$v_{opt}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL (points)</td>
<td>r=0.08</td>
<td>r=0.41*</td>
<td>r=0.27</td>
</tr>
<tr>
<td>TUG test (s)</td>
<td>r=-0.32</td>
<td>r=-0.66***</td>
<td>r=-0.61***</td>
</tr>
<tr>
<td>Tinetti test (points)</td>
<td>r=0.26</td>
<td>r=0.64***</td>
<td>r=0.55**</td>
</tr>
<tr>
<td>6-MWT (m)</td>
<td>r=0.32</td>
<td>r=0.76***</td>
<td>r=0.59***</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quantitative variable</th>
<th>$F_{ext} \cdot kg^{-1}$</th>
<th>$P_{max} \cdot kg^{-1}$</th>
<th>$v_{opt}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL (points)</td>
<td>r=0.11</td>
<td>r=0.47*</td>
<td>r=0.46*</td>
</tr>
<tr>
<td>TUG test (s)</td>
<td>r=-0.52**</td>
<td>r=-0.83***</td>
<td>r=-0.77***</td>
</tr>
<tr>
<td>Tinetti test (points)</td>
<td>r=0.22</td>
<td>r=0.60**</td>
<td>r=0.69***</td>
</tr>
<tr>
<td>6-MWT (m)</td>
<td>r=0.38*</td>
<td>r=0.73***</td>
<td>r=0.71***</td>
</tr>
</tbody>
</table>

Major age-related diseases leading to functional decline and disability

Hypertension, CHD, CHF
Stroke
Diabetes
COPD, asthma
Osteoporosis, osteoarthritis
Dementia. AD, PD
Other…
Functional capacity

Age
Concepts of frailty

Frailty phenotype

Physical frailty, disability as an outcome of frailty

Frailty defined by deficit accumulation, overall state of health as a measure of frailty, overlaps with disability
Sarcopenia as the central biological substrate of physical frailty

PF & sarcopenia (PF&S) syndrome

Operationalization of the theoretical concept of PF&S


Functional capacity

Disability threshold

Age
Definitions

Early diagnosis

Prevention
Early detection/assessment of:
- **physical/biological** (at the physiological and molecular level)
- **psychological**
- **sociodemographic**
- **lifestyle**

biomarkers/risk factors/subclinical changes/deficits

is a prerequisite to the primary prevention of frailty
Appendicular lean body mass (ALM) cutpoints (ALM <19.75kg in men and <15.02kg in women) derived from a large, diverse sample of older adults identified lean mass thresholds below which older adults had a higher likelihood of weakness (defined as grip strength <26kg in men and <16kg in women).

Cut-points for low grip strength (<26kg men and <16kg women), low grip strength-to-body mass index (BMI) ratio (<1.00 men and <0.56 women) and low appendicular lean body mass (ALM)-to-BMI ratio (<0.789 men and <0.512 women) as candidate criteria for clinically relevant weakness and low lean mass for incident mobility impairment (gait speed ≤ 0.8 m/s).

Established Populations for the Epidemiologic Study of the Elderly (EPESE) performance battery: tests of balance, time to walk 8 ft, and time to rise from a chair 5 Times

Performance tests of lower extremity function accurately predict disability
Both the summary score and the gait speed alone allow for the estimation of risk of disability

A gait speed <0.8m/s; a timed-up-and-go test >10s; and a score of ≥3 on the PRISMA 7 questionnaire can indicate frailty.


Highlights
Frailty tool proliferation (identified 67 frailty instruments) is a challenge for selecting an assessment instrument. Instruments most used were frailty phenotype, deficit accumulation index, and VES-13.

### Sunfrail Tool

**Gender**  
- □ M  
- □ F  
- □ Yes

**Questions**

1. Do you regularly take 5 or more medications per day?  
   - □ Yes  
   - □ No

2. Have you recently lost weight such that your clothing has become looser?  
   - □ Yes  
   - □ No

3. Your physical state made you walking less during the last year?  
   - □ Yes  
   - □ No

4. Have you been evaluated by your GP during the last year?  
   - □ Yes  
   - □ No

5. Have you fallen 1 or more times during the last year?  
   - □ Yes  
   - □ No

6. Have you experienced memory decline during the last year?  
   - □ Yes  
   - □ No

7. Do you feel lonely most of the time?  
   - □ Yes  
   - □ No

8. In case of need, can you count on someone close to you?  
   - □ Yes  
   - □ No

9. Have you had any financial difficulties in facing dental care and health care costs during the last year?  
   - □ Yes  
   - □ No
The quickly and easily administered MNA-SF appears to be a good tool for predicting both under-nutrition and frailty in elderly hospitalised people.

Risk factors/biomarkers of frailty

Routine blood tests and standard physical measures (blood pressure)

Routine blood and urine tests

Higher TSH in men and lower TSH in women aged ≥65 years

Routine blood and special blood tests (eg, DNA)

“Omics”-based laboratory biomarkers
673 significant differentially expressed genes (128 upregulated and 545 downregulated) in sarcopenia patients of over 60 years of age.

Most of the upregulated genes were involved in metabolic processes.

The pooled OR of frailty for the lowest versus the highest level of vitamin D was 1.27 (95% CI=1.17-1.38, I(2)=59%), suggesting that low level of vitamin D was significantly associated with the risk of frailty.


After adjusting for BMI, the relationship of 25(OH)D < 10 ng/mL (vs ≥30 ng/mL) with incident frailty persisted, but was attenuated after further accounting for cardiometabolic diseases.

"inflamm-aging"

High levels of interleukin (IL)-6, IL-1, tumor necrosis factor-α, and C-reactive protein are associated in the older subject with increased risk of morbidity and mortality.

The low-grade inflammation characterizing the aging process notably concurs at the pathophysiological mechanisms underlying sarcopenia.

Higher serum levels of anti-inflammatory markers, and in particular IL-4 and IL-13, may play a protective role on FFM and performance maintenance in elderly subjects.

Frail subjects have lower levels of serum IGF-I and DHEA-S and higher levels of IL-6 than do non-frail, age-matched individuals.


Higher baseline levels of differential white cell counts (WCC), lower levels of dehydroepiandosterone sulphate (DHEAS) and higher cortisol:DHEAS ratio were all significantly associated with increased odds of frailty at 10-year follow-up.


Partial correlations in older women.

Partial correlations in older women.
Higher serum IGF-1 was independently associated with more muscle mass, higher BMD, and better handgrip performance in both genders.


Definitions
Early diagnosis
Prevention
Lifelong prevention
Midlife prevention
of age-related functional decline
Prevention of frailty and functional decline:

1. Physical activity
2. Nutrition
3. Prevention and treatment of concomitant disorders
Prevention of frailty and functional decline:

1. Physical activity
2. Nutrition
3. Prevention and treatment of concomitant disorders
All-cause mortality according to physical activity level in 16,936 absolvents of Harvard University.


Physical Activity and Public Health in Older Adults
Recommendation From the American College of Sports Medicine and the American Heart Association

Miriam E. Nelson, PhD, FACSM; W. Jack Rejeski, PhD; Steven N. Blair, PED, FACSM, FAHA; Pamela W. Duncan, PhD; James O. Judge, MD; Abby C. King, PhD, FACSM, FAHA; Carol A. Macera, PhD, FACSM; Carmen Castaneda-Sceppa, MD, PhD

*Circulation* 2007;116;1094-1105; originally published online Aug 1, 2007;
WHO 2010

Recommended levels of physical activity for health for 65 years old and above
Summary of ACSM/AHA physical activity recommendations for older adults.

Endurance exercise for older adults:

Frequency:

- for moderate-intensity activities, accumulate at least 30 or up to 60 (for greater benefit) min/day in bouts of at least 10 min each to total 150–300 min/week,
  or
- at least 20–30 min/day or more of vigorous-intensity activities to total 75–150 min/week,
  or
- an equivalent combination of moderate and vigorous activity.

Resistance exercise for older adults

**Frequency:**
At least 2 days/week

**Intensity:**
Between moderate- (5–6) and vigorous- (7–8) intensity on a scale of 0 to 10

**Type:**
Progressive weight training program or weight bearing calisthenics (8–10 exercises involving the major muscle groups of 8–12 repetitions each), stair climbing, and other strengthening activities that use the major muscle groups

Flexibility exercise for older adults:

**Frequency:**
At least 2 days/week

**Intensity:**
Moderate (5–6) intensity on a scale of 0 to 10

**Type:**
Any activities that maintain or increase flexibility using sustained stretches for each major muscle group and static rather than ballistic movements.

Balance exercise for frequent fallers or individuals with mobility problems

Activities that include the following:

- progressively difficult postures that gradually reduce the base of support (e.g., two-legged stand, semitandem stand, tandem stand, one-legged stand),

- dynamic movements that perturb the center of gravity (e.g., tandem walk, circle turns),

- stressing postural muscle groups (e.g., heel stands, toe stands), or reducing sensory input (e.g., standing with eyes closed).

There is support for the inclusion of power training for the healthy older adult. Muscle atrophy results from fiber denervation with loss of some fibers and atrophy of others, that is, especially fast twitch, with aging and inactivity. Age-related muscle atrophy is associated with reductions in strength and power, and reductions in power exceed decreases in maximal strength. Although most studies in the elderly examined heavy RT programs, power training may optimize functional abilities...
Physical exercise has beneficial effects for frail elderly on gait speed, physical functioning, mobility, falls, functional abilities, muscle strength, body composition, and frailty.


The multi-component exercise intervention composed by strength, endurance and balance training seems to be the best strategy to improve rate of falls, gait ability, balance, and strength performance in physically frail older adults.


Routine multicomponent exercise intervention should be prescribed to nonagenarians because overall physical outcomes are improved in this population.

Gardening as the dominant leisure time physical activity (LTPA) of older adults from a post-communist country. The results of the population-based PolSenior Project from Poland

Rafal Rowinski a, Andrzej Dabrowski b, Tomasz Kostka c,

a Faculty of Physical Education, Jozef Pilsudski University of Physical Education in Warsaw, Marymoncka 34, Warsaw, Poland

b Faculty of Physical Education and Sport in Biala Podlaska, Jozef Pilsudski University of Physical Education in Warsaw, Marymoncka 34, Warsaw, Poland

c Department of Geriatrics, Medical University of Lodz, Pl. Hallera 1, Lodz, Poland

Corresponding author at: Department of Geriatrics, Medical University of Lodz, Pl. Hallera 1, Lodz, Poland. Tel.: +48 42 639 3215; fax: +48 42 639 3218. tomaszkostka@wp.pl
### Table 2. Leisure time physical activities of respondents.

<table>
<thead>
<tr>
<th>Activity</th>
<th>No (%: n)</th>
<th>Yes (%: n)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walks farther from home or the place of accommodation</td>
<td>61.0%</td>
<td>39.0%</td>
<td>†‡§</td>
</tr>
<tr>
<td>Gymnastic exercise, aerobics, etc.</td>
<td>81.8%</td>
<td>18.2%</td>
<td>‡§</td>
</tr>
<tr>
<td>Riding a bicycle</td>
<td>62.7%</td>
<td>37.3%</td>
<td>†‡§</td>
</tr>
<tr>
<td>Running or jogging</td>
<td>98.4%</td>
<td>1.6%</td>
<td>*†</td>
</tr>
<tr>
<td>Swimming</td>
<td>93.7%</td>
<td>6.3%</td>
<td>*†‡§</td>
</tr>
<tr>
<td>Team games (volleyball, basketball, football, etc.)</td>
<td>99.2%</td>
<td>0.8%</td>
<td>*§</td>
</tr>
<tr>
<td>Tennis</td>
<td>99.6%</td>
<td>0.4%</td>
<td>*†‡</td>
</tr>
<tr>
<td>Table tennis</td>
<td>99.1%</td>
<td>0.9%</td>
<td>*§</td>
</tr>
<tr>
<td>Dancing</td>
<td>87.2%</td>
<td>12.8%</td>
<td>*†‡§</td>
</tr>
<tr>
<td>Gardening</td>
<td>35.4%</td>
<td>64.6%</td>
<td>†‡</td>
</tr>
</tbody>
</table>

Results of Chi-square test

* significant for gender (p<0.05) (“no” vs. “yes” answer or distribution of “yes” answers)
† significant for age cohort (p<0.05) (“no” vs. “yes” answer or distribution of “yes” answers)
‡ significant for size of the place of residence (p<0.05) (“no” vs. “yes” answer or distribution of “yes” answers)
§ significant for social class (p<0.05) (“no” vs. “yes” answer or distribution of “yes” answers)

Prevention of frailty and functional decline:

1. Physical activity

2. Nutrition and pharmacological interventions

3. Prevention and treatment of concomitant disorders
CONCLUSIONS:
The systematic review and meta-analysis revealed that malnutrition and physical frailty in community-dwelling older adults are related, but not interchangeable geriatric syndromes. Two out of 3 malnourished older adults were physically frail, whereas close to 10% of the physically frail older adults was identified as malnourished.
Nutritional supplementation is effective in the treatment of sarcopenia in old age, and its positive effects increase when associated with physical exercise.


Physical, nutritional, and cognitive interventional approaches were effective in reversing frailty among community-living older persons.


Multicomponent exercise intervention reverses frailty and improves cognition, emotional, and social networking in a controlled population of community-dwelling frail older adults.

European Union Geriatric Medicine Society (EUGMS), in cooperation with other scientific organizations, appointed an international study group to review dietary protein needs with aging (PROT-AGE Study Group).

To help older people (>65 years) maintain and regain lean body mass and function, the PROT-AGE study group recommends average daily intake at least in the range of 1.0 to 1.2 g protein per kilogram of body weight per day.

Both endurance- and resistance-type exercises are recommended at individualized levels that are safe and tolerated, and higher protein intake (ie, ≥ 1.2 g/kg body weight/d) is advised for those who are exercising and otherwise active.

Most older adults who have acute or chronic diseases need even more dietary protein (ie, 1.2-1.5 g/kg body weight/d). Older people with severe kidney disease (ie, estimated GFR <30 mL/min/1.73 m(2)), but who are not on dialysis, are an exception to this rule; these individuals may need to limit protein intake.

European Society for Clinical Nutrition and Metabolism (ESPEN) recommendations:

(a) for healthy older people, the diet should provide at least 1.0-1.2 g protein/kg body weight/day,

(b) for older people who are malnourished or at risk of malnutrition because they have acute or chronic illness, the diet should provide 1.2-1.5 g protein/kg body weight/day, with even higher intake for individuals with severe illness or injury,

(c) daily physical activity or exercise (resistance training, aerobic exercise) should be undertaken by all older people, for as long as possible.
Muscle protein synthesis enhancement:
Daily protein intake of 1.2-1.5 g/kg (0.4-0.5 g/kg per meal)
Increased proportion of leucine in a given dose of protein
Supplementation with n=3 polyunsaturated fatty acids
Physical activity prior to protein intake

Supplementation

- Vitamin D
- BCAA
- Leucine
- β-hydroxy-β-methylbutyrate (HMB)
- Creatine
## Summary of the effect of nutrition on sarcopenia in randomised, controlled studies meeting the inclusion criteria

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Number</th>
<th>Age, years, mean (SD) [range]</th>
<th>PEDro Score</th>
<th>Intervention (duration)</th>
<th>Outcomes measured</th>
<th>Main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flakoll et al.</td>
<td>Community-dwelling</td>
<td>57 (0/57)</td>
<td>76.7 [62–90]</td>
<td>8</td>
<td>ARG + HMB + LYS; PLA (12 weeks)</td>
<td>MM (BIA), MS (isometric leg strength, HS), PP (get up and go)</td>
<td>MS ($P \leq 0.05$) and PP ($P = 0.002$) significantly improved with ARG + HMB + LYS versus PLA. ARG + HMB + LYS did not significantly improve MM versus PLA.</td>
</tr>
<tr>
<td>Deutz et al.</td>
<td>Healthy individuals on bed rest</td>
<td>19 (4/15)</td>
<td>PLA: 67.1 (±1.7) HMB: 67.4 (±1.4) [60–76]</td>
<td>10</td>
<td>HMB; PLA Bed rest (10 days) + rehabilitation (8 weeks)</td>
<td>MM (DEXA), MS (KE, leg press), PP (SPPB, get up and go, 5-item PPB)</td>
<td>Bed rest caused a significant decrease in MM ($P = 0.02$) in the PLA group, but MM was preserved in the HMB group. Changes in MS and PP were not significant for HMB versus PLA.</td>
</tr>
<tr>
<td>Stout et al.</td>
<td>Community-dwelling</td>
<td>98 (49/49)</td>
<td>73 (±1 SEM) [≥65]</td>
<td>9</td>
<td>Phase I: HMB; PLA (24 weeks) Phase II: PLA + RET; HMB + RET (24 weeks)</td>
<td>MM (DEXA), MS (isokinetic leg strength, HS), PP (get up and go)</td>
<td>HMB alone significantly improved some, but not all measures of MS versus PLA. No significant changes were found in MM and PP with HMB versus PLA. Adding HMB to RET did not improve any parameters over RET alone.</td>
</tr>
<tr>
<td>Vukovich et al.</td>
<td>Community-dwelling</td>
<td>31 (15/16)</td>
<td>70 (±1)</td>
<td>10</td>
<td>HMB + RET; PLA + RET (8 weeks)</td>
<td>MM (DEXA, CT scan), MS (misc. upper and lower body strength press, flexion and extension measurements)</td>
<td>MM improved with HMB + RET versus PLA + RET, but not significantly ($P = 0.08$). MS did not improve with HMB + RET versus PLA + RET.</td>
</tr>
</tbody>
</table>
## Summary of studies involving creatine supplementation in older adults (Candow, 2011)

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Dosage</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bermon et al. 1998</td>
<td>Male/female (70 years)</td>
<td>CR: 20 g for 5 days</td>
<td>↔ lower-limb muscle volume</td>
</tr>
<tr>
<td></td>
<td>CR: 16; PL: 16</td>
<td>Maintenance: 3 g for 47 days</td>
<td></td>
</tr>
<tr>
<td>Brose et al. 2003</td>
<td>Male/female (68 years)</td>
<td>CR: 5 g, 98 days</td>
<td>↑ fat-free mass</td>
</tr>
<tr>
<td>Candow et al. 2008</td>
<td>Male (66 years)</td>
<td>CR: 0.1 g kg⁻¹, 30 days</td>
<td>↑ muscle hypertrophy</td>
</tr>
<tr>
<td>Chrusch et al. 2001</td>
<td>Male (71 years)</td>
<td>CR loading: 0.3 g kg⁻¹ for 5 days</td>
<td>↑ fat-free mass, strength</td>
</tr>
<tr>
<td></td>
<td>CR: 16; PL: 14</td>
<td>Maintenance: 0.07 g kg⁻¹ 79 days</td>
<td></td>
</tr>
<tr>
<td>Eijnde et al. 2003</td>
<td>Male (64 years)</td>
<td>CR: 5 g for 1 year</td>
<td>↔ fat-free mass</td>
</tr>
<tr>
<td>Gotshalk et al. 2008</td>
<td>Female (63 years)</td>
<td>CR: 0.3 g kg⁻¹ for 7 days</td>
<td>↑ fat-free mass, strength</td>
</tr>
<tr>
<td></td>
<td>CR: 15; PL: 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gotshalk et al. 2001</td>
<td>Male (65 years)</td>
<td>CR: 0.3 g kg⁻¹ for 7 days</td>
<td>↑ fat-free mass</td>
</tr>
<tr>
<td></td>
<td>CR: 10; PL: 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jakobi et al. 2001</td>
<td>Male (72 years)</td>
<td>CR: 20 g for 5 days</td>
<td>↔ force production</td>
</tr>
<tr>
<td>Rawson et al. 1999</td>
<td>Male (74 years)</td>
<td>CR: 20 g for 10 days</td>
<td>↔ fat-free mass</td>
</tr>
<tr>
<td></td>
<td>CR: 10; PL: 10</td>
<td>Maintenance: 4 g for 20 days</td>
<td></td>
</tr>
<tr>
<td>Tarnopolsky et al. 2007</td>
<td>Male/female (70 years)</td>
<td>CR: 5 g/days for 6 months</td>
<td>↑ fat-free mass, strength</td>
</tr>
</tbody>
</table>
Creatine vs. chest press strength

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Creatine Mean</th>
<th>Creatine SD</th>
<th>Creatine Total</th>
<th>Placebo Mean</th>
<th>Placebo SD</th>
<th>Placebo Total</th>
<th>Weight %</th>
<th>Std. Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aguair (2013)</td>
<td>14</td>
<td>17</td>
<td>9</td>
<td>9</td>
<td>5</td>
<td>9</td>
<td>8.7%</td>
<td>0.38</td>
<td>[-0.55, 1.31]</td>
</tr>
<tr>
<td>Bemben (2010)</td>
<td>42</td>
<td>13</td>
<td>10</td>
<td>33</td>
<td>6</td>
<td>10</td>
<td>8.9%</td>
<td>0.85</td>
<td>[-0.07, 1.78]</td>
</tr>
<tr>
<td>Bemben (2010) protein</td>
<td>38</td>
<td>20</td>
<td>10</td>
<td>36</td>
<td>17</td>
<td>10</td>
<td>9.9%</td>
<td>0.10</td>
<td>[-0.77, 0.98]</td>
</tr>
<tr>
<td>Bermon (1998)</td>
<td>1</td>
<td>1</td>
<td>8</td>
<td>0.6</td>
<td>0.4</td>
<td>8</td>
<td>7.6%</td>
<td>0.50</td>
<td>[-0.50, 1.50]</td>
</tr>
<tr>
<td>Brose (2003) men</td>
<td>30</td>
<td>20</td>
<td>7</td>
<td>22</td>
<td>12</td>
<td>7</td>
<td>6.7%</td>
<td>0.45</td>
<td>[-0.61, 1.52]</td>
</tr>
<tr>
<td>Brose (2003) women</td>
<td>15</td>
<td>14</td>
<td>6</td>
<td>13</td>
<td>7</td>
<td>6</td>
<td>5.9%</td>
<td>0.17</td>
<td>[-0.97, 1.30]</td>
</tr>
<tr>
<td>Candow (2008)</td>
<td>11</td>
<td>11</td>
<td>13</td>
<td>9</td>
<td>14</td>
<td>12</td>
<td>12.3%</td>
<td>0.15</td>
<td>[-0.63, 0.94]</td>
</tr>
<tr>
<td>Chrusch (2001)</td>
<td>19</td>
<td>13</td>
<td>16</td>
<td>16</td>
<td>11</td>
<td>14</td>
<td>14.6%</td>
<td>0.24</td>
<td>[-0.48, 0.96]</td>
</tr>
<tr>
<td>Hass (2007)</td>
<td>0.2</td>
<td>0.07</td>
<td>10</td>
<td>0.1</td>
<td>0.06</td>
<td>10</td>
<td>7.4%</td>
<td>1.47</td>
<td>[0.46, 2.48]</td>
</tr>
<tr>
<td>Tarnopolsky (2007) men</td>
<td>42</td>
<td>36</td>
<td>10</td>
<td>38</td>
<td>14</td>
<td>8</td>
<td>8.7%</td>
<td>0.13</td>
<td>[-0.80, 1.06]</td>
</tr>
<tr>
<td>Tarnopolsky (2007) women</td>
<td>36</td>
<td>10</td>
<td>10</td>
<td>31</td>
<td>7</td>
<td>10</td>
<td>9.4%</td>
<td>0.55</td>
<td>[-0.34, 1.45]</td>
</tr>
</tbody>
</table>

Total (95% CI)   109 104 100.0% 0.42 [0.15, 0.70]

Heterogeneity: Chi² = 6.81, df = 10 (P = 0.74); I² = 0%
Test for overall effect: Z = 3.01 (P = 0.003)

Candow, 2014
Creatine and carbohydrates

- Carbohydrate coingestion is important to optimize creatine effects on body composition, strength, and functional performance in older adults.

- Creatine should be coingested with a carbohydrate drink (for example with juice).

Pharmacological interventions targeting the underlying biology of sarcopenia

GH/IGF-1
DHEAS
Testosterone/androgens
Selective Androgen Receptor Modulators (SARMs)
TGFβ family members: myostatin, follistatin and GDF11
Myostatin antagonists
Becker et al. reported the improvement of power-demanding performance measures (stair climbing, five-chair rise, fast gait speed) in the older individuals after the treatment with the humanized monoclonal antibody LY2495655.

For less power-intensive performance-based measures (6-min walking distance, usual gait speed) and muscle strength no important treatment effects were observed.

<table>
<thead>
<tr>
<th></th>
<th>Myostatin (ng/ml)</th>
<th>Follistatin (pg/ml)</th>
<th>GDF11 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass (kg)</td>
<td>0.002</td>
<td>-0.070</td>
<td>-0.301*</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>0.022</td>
<td>-0.013</td>
<td>-0.354**</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>-0.043</td>
<td>0.083</td>
<td>-0.372**</td>
</tr>
<tr>
<td>Body fat %</td>
<td>-0.084</td>
<td>0.035</td>
<td>-0.458***</td>
</tr>
<tr>
<td>Fat free mass (%) (n=52)</td>
<td>0.073</td>
<td>-0.083</td>
<td>0.359**</td>
</tr>
<tr>
<td>Fat mass (kg) (n=52)</td>
<td>-0.071</td>
<td>0.006</td>
<td>-0.331**</td>
</tr>
<tr>
<td>Timed Up&amp;Go test (s)</td>
<td>-0.071</td>
<td>0.366**</td>
<td>-0.163</td>
</tr>
<tr>
<td>Handgrip strength L (kG)</td>
<td>-0.296*</td>
<td>-0.063</td>
<td>-0.080</td>
</tr>
<tr>
<td>P70% LP (kG)</td>
<td>-0.117</td>
<td>-0.279*</td>
<td>-0.250</td>
</tr>
<tr>
<td>P\textsubscript{max} (W)</td>
<td>-0.141</td>
<td>-0.387**</td>
<td>-0.186</td>
</tr>
<tr>
<td>P\textsubscript{max} ·kg\textsuperscript{-1} (W·kg\textsuperscript{-1})</td>
<td>-0.156</td>
<td>-0.405**</td>
<td>-0.049</td>
</tr>
<tr>
<td>ν\textsubscript{opt} (rpm)</td>
<td>-0.329*</td>
<td>-0.183</td>
<td>-0.220</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, ***p<0.001

Fife et a. Submitted
Prevention of frailty and functional decline:

1. Physical activity
2. Nutrition

3. Prevention and treatment of concomitant disorders
Frail and pre-frail older people corresponded to a substantial proportion of those with more CVD risk factors, especially diabetes mellitus, highlighting the need for preventive strategies in order to avoid the co-occurrence of CVD and frailty.


Abdominal obesity, insulin resistance, and inflammation were significantly associated with frailty, and the effect was independent of functional measurement and decline of skeletal muscle mass.

Cardiometabolic risk assessment:

- diet, smoking status, family history,

- fasting lipids (TC, triglycerides, HDL cholesterol, LDL Cholesterol, TC/HDL ratio)

- glucose

- blood pressure

- weight, height, waist and hip circumference (BMI, WHR)

- blood count, electrolytes, creatinine, eGFR, microalbuminuria
ACE inhibitor treatment may halt or slow decline in muscle strength in elderly women with hypertension and without CHF.


The I/I ACE genotype is associated with a lower risk of frailty and a lower frailty level relative to the D-carrying genotypes among older Han people.

The influence of Angiotensin System Blocking Medications (ASBMs) blockers on muscle function and Angiotensin Converting Enzyme (ACE) activity

<table>
<thead>
<tr>
<th></th>
<th>Women taking ACEI N=22</th>
<th>Women taking ARBs or ARBs +ACEI N=12</th>
<th>Women taking MCRA or MCRA+ACEI or MCRA +ARB N=10</th>
<th>Women taking no ASBMs N=51</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>73.6±4.7</td>
<td>70.8±4.4</td>
<td>73.1±3.9</td>
<td>71.5±4.4</td>
</tr>
<tr>
<td>Hand grip strength – left (kgf)</td>
<td>24.2±9.8</td>
<td>23.3±7.8</td>
<td>18.1±5.3</td>
<td>23.5±7.8</td>
</tr>
<tr>
<td>Hand grip strength – right (kgf)</td>
<td>25.6±9.1</td>
<td>24.4±7.0</td>
<td>22.7±6.5</td>
<td>25.5±7.9</td>
</tr>
<tr>
<td>$P_{\text{max}}$ (W)</td>
<td>217±88</td>
<td>221±52</td>
<td>233±44</td>
<td>230±65</td>
</tr>
<tr>
<td>$P_{\text{max}}$ (W·kg$^{-1}$)</td>
<td>3.11±1.20</td>
<td>3.25±0.88</td>
<td>3.38±0.95</td>
<td>3.49±1.05</td>
</tr>
<tr>
<td>$U_{\text{opt}}$ (rep/min)</td>
<td>65.2±11.7</td>
<td>69.6±8.4</td>
<td>67.0±13.3</td>
<td>69.2±9.1</td>
</tr>
<tr>
<td>ACE (U/L)</td>
<td>27.4±13.4</td>
<td>38.9±12.9</td>
<td>37.1±12.3</td>
<td>46.2±17.5*</td>
</tr>
</tbody>
</table>

The relationship between optimal shortening velocity ($U_{opt}$) and angiotensin converting enzyme activity in women not taking any ASBMs

\begin{center}
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
ACE activity (U/L) & Vopt (rep/min) \\
\hline
0 & 47 \\
20 & 57 \\
40 & 67 \\
60 & 77 \\
80 & 87 \\
100 & 97 \\
\hline
\end{tabular}
\end{center}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{plot.png}
\caption{Correlation between ACE activity and optimal shortening velocity.}
\end{figure}

Other diseases, e.g.:


COPD, dementia, depression…
Acute care of frail elderly patients in a CGA unit was independently associated with lesser loss of functional ability and lesser increase in frailty after 3 months.


Prevention of hospital-associated functional decline:
appropriate nutrition, early mobilisation, care of comorbidities (incontinence, decubitus)

Benefits of early rehabilitation in hospitalised older subjects
Summary

Early diagnosis and prevention of frailty and functional decline:

1. Building-up physiological potential throughout the lifetime
2. Identification of people at risk.
3. Identification and combatting of risk factors
4. Prevention and treatment of concomitant disorders
Thank you for your attention