Alterning lifestyle to improve nutritional status in older adults

Exercise interventions to prevent and treat frailty

D. Schöne (DE)
Exercise interventions to prevent and treat frailty

ESPEN congress, The Hague, 10th September 2017

Daniel Schoene, PhD
Disclosure for Daniel Schoene

In compliance with COI policy, ESPEN requires the following disclosures to the session audience:

<table>
<thead>
<tr>
<th>Category</th>
<th>No relevant conflicts of interest to declare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shareholder</td>
<td></td>
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<tr>
<td>Grant / Research Support</td>
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<tr>
<td>Consultant</td>
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<td>Employee</td>
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<td>Paid Instructor</td>
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<td>Speaker bureau</td>
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<tr>
<td>Other</td>
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</table>
Learning objectives

● Know the effectiveness of different types of physical exercise in preventing and treating frailty

● Know the impact of combining nutritional and exercise interventions in preventing and treating frailty
Frailty Consensus: A Call to Action

John E. Morley MB, BCh a, *, Bruno Vellas MD b,c, G. Abellan van Kan MD b,c, Stefan D. Anker MD, PhD d,e, Juergen M. Bauer MD, PhD f, Roberto Bernabei MD g, Matteo Cesari MD, PhD b,c, W.C. Chumlea PhD h, Wolfram Doehner MD, PhD d,i, Jonathan Evans MD j, Linda P. Fried MD, MPH k, Jack M. Guralnik MD, PhD l, Paul R. Katz MD, CMD m, Theodore K. Malmstrom PhD a,n, Roger J. McCarter PhD o, Luis M. Gutierrez Robledo MD, PhD p, Ken Rockwood MD q, Stephan von Haehling MD, PhD r, Maurits F. Vandewoude MD, PhD s, Jeremy Walston MD t

“...A medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency and/or death...”
Manini & Pahor, Br J Sport Med 2009;43:28
<table>
<thead>
<tr>
<th>Selected components of physical fitness</th>
<th>Definition</th>
<th>Subcomponent</th>
<th>Example for relevance</th>
<th>Example activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endurance</strong> → also <strong>Aerobic exercise</strong></td>
<td>Ability to perform movements of body’s large muscles in rhythmic manner for sustained periods</td>
<td>Power: ability to exert force in short time</td>
<td>Determinant of exercise capacity; VO2 max indicates functional reserve</td>
<td>Brisk walking, running, cycling, swimming</td>
</tr>
<tr>
<td><strong>Strength</strong> → also <strong>resistance exercise</strong></td>
<td>Ability to exert force by contracting against resistance</td>
<td></td>
<td></td>
<td>Lifting weights (external or body weight); work against resistance (resistance bands)</td>
</tr>
<tr>
<td><strong>Flexibility</strong></td>
<td>Ability to perform movements with specific/extended range of motion around a joint</td>
<td></td>
<td>ADLs, such as clothing and reaching</td>
<td>Stretching exercises</td>
</tr>
<tr>
<td><strong>Precision/coordination</strong></td>
<td>Ability to integrate sensory, central nervous and motor components to correct movement</td>
<td>Balance/postural stability: ability to maintain the center of gravity within the base of support</td>
<td>Risk of falling</td>
<td>Tai Chi, dancing</td>
</tr>
</tbody>
</table>
Training principles

- **ADAPTATION** – refers to the body's ability to adjust to increased or decreased physical demands. Regularity required
- **USE/DISUSE** - use it or lose it → Detraining
- **OVERLOAD** – greater than normal stress or load is required
- **PROGRESSION** – if overload occurs too slowly, improvement is unlikely, but overload that is increased too rapidly may result in injury or muscle damage
- **SPECIFICITY** – You get what you train for
- **RECOVERY** – adequate rest is needed to maximize improvements
- **INDIVIDUAL DIFFERENCES** - unique individuals with slightly different response to exercise
## Dose of exercise

<table>
<thead>
<tr>
<th>Dose components</th>
<th>Definition</th>
<th>Measured how</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>number of times an exercise/activity is performed</td>
<td>sessions, episodes, or bouts per week</td>
</tr>
</tbody>
</table>
| **Intensity**   | refers to the rate at which the activity is being performed or the magnitude of the effort required to perform an activity or exercise | - METs  
- VO2 max  
- %HR max  
- perceived exertion → Borg scale  
- amount of weight or resistance |
| **Time**        | length of time for each bout of any specific activity | Duration (aerobic): minutes  
Volume (strength): 2-3 sets with 2-3 minutes break |
| **Type**        | Mode of exercise performed | e.g. continuous walking, functional multi-joint strength exercises |
PA and prevention of frailty
PA and frailty development

- reduction in PA level may cause a reduction in physiologic reserves and *vice versa*

→ related to frailty etiology, component and a correlate of the frailty syndrome

Prevention of frailty

PA in general throughout lifetime is likely important to prevent frailty in old age.

Physical inactivity exacerbates age-related impairments in physiologic systems. Those impairments will likely result in the accumulation of functional limitations and disability over time.

Exercise as preventive factor for frailty

- Health ABC study, $N = 2,964$, follow-up 5y, 70-79 years, initially no difficulties mobility and ADLs

Table 4. Odds of Incident Moderate or Severe Frailty by Physical Activity Category ($N = 2,964$)

<table>
<thead>
<tr>
<th>Volume</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR$^a$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1.33 (1.08–1.64)</td>
<td>1.03 (0.83–1.28)</td>
</tr>
<tr>
<td>Recommended</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>$p$ for trend</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intensity</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR$^a$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedentary</td>
<td>1.30 (0.90–1.88)</td>
<td>1.10 (0.75–1.63)</td>
</tr>
<tr>
<td>Light</td>
<td>1.58 (1.19–2.08)</td>
<td>1.48 (0.88–1.59)</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.94 (0.68–1.30)</td>
<td>0.91 (0.65–1.28)</td>
</tr>
<tr>
<td>Vigorous</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>$p$ for trend</td>
<td>.002</td>
<td>.22</td>
</tr>
</tbody>
</table>

Table 5. In the Moderately Frail, Odds of Incident Severe Frailty by Physical Activity Category ($N = 410$)

<table>
<thead>
<tr>
<th>Volume</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR$^a$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1.26 (0.75–2.13)</td>
<td>0.97 (0.55–1.70)</td>
</tr>
<tr>
<td>Recommended</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>$p$ for trend</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intensity</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR$^a$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedentary</td>
<td>2.28 (0.95–5.48)</td>
<td>1.47 (0.58–3.73)</td>
</tr>
<tr>
<td>Light</td>
<td>2.03 (0.94–4.35)</td>
<td>1.31 (0.58–2.95)</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.76 (0.26–2.20)</td>
<td>0.66 (0.22–1.98)</td>
</tr>
<tr>
<td>Vigorous</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>$p$ for trend</td>
<td>.009</td>
<td>.19</td>
</tr>
</tbody>
</table>

Notes: OR = odds ratio; CI = confidence interval.
$^a$Adjusted for age, sex, race, education, marital status, smoking status, drinking status, waist circumference, and count of diagnoses.

PA is associated with ADLs

- low vs medium/high PA level reduces the risk of incident BADL disability as well as for the progression of BADL disability

OR 0.51 (95%CI 0.38 to 0.68; p.<001)  OR 0.55 (95%CI 0.42 to 0.71; p.<001)
PA recommendations for older adults

- at least 150 minutes of moderate-intensity aerobic PA throughout the week or at least 75 minutes of vigorous-intensity
- Aerobic activity should be performed in bouts of at least 10 minutes duration.
- For additional health benefits, older adults should increase their moderate-intensity aerobic physical activity to 300 minutes per week, or engage in 150 minutes of vigorous-intensity aerobic physical

- Muscle-strengthening activities, involving major muscle groups, should be done on 2 or more days a week.

- Older adults, with poor mobility, should perform physical activity to enhance balance and prevent falls on 3 or more days per week.

WHO 2011; ACSM/AHA 2007
Exercise to treat frailty
Frailty as an outcome

Ng et al. Am J Med. 2015; 128:1225

Frailty mod Fried participants
female, 81y pre-frail, frail; 70y pre-frail, frail; 71.4y robust, pre-frail, frail 77y

Exercise strength, gait strength, balance strength, aerobic, balance strength, flexibility
dose 12wk, 2wk, 60min; moderate 12wk, 2wk, 90min + 12wk home-based, daily; moderate 12wk, 3wk, 60min; hard 12mo, 1-3/wk, 40-60min + home-based, 3/wk from wk 9; moderate, hard assess/follow-up 3mo/7mo

Results
- frailty score - reversal rate 39.4 vs 15.2%
- frailty score - reversal rate 41.3 vs 15.0%
- frailty score - reversal rate 45/42/40 vs 27/26/31%

p-value for average effect = 0.02
p-value for average effect = 0.004
Improved function

Meta-analytic evidence:
- Ex vs inactive controls

- BBS score improved average of 1.69 (95% CI, 0.56–2.82)
- ADL improved; mean difference of 5.33 (95% CI, 1.01–9.64)
- normal gait speed (MD=.07m/s; 95% CI, .04–.09)
- fast gait speed (MD=.08m/s; 95% CI, .02–.14)
- SPPB (MD=2.18; 95% CI, 1.56–2.80)

- The evidence comparing different modalities of exercise is scarce and heterogeneous

Exercise and components of physical frailty

- Most studies did not include an operational definition of frailty
- Evidence that exercise interventions are feasible and safe for frail older individuals
- Exercise appears to be more beneficial in earlier stages of frailty
- Optimal exercise program for reversing frailty still unclear
- Exercise programs that optimize the health of frail older adults seem to be different from those recommended for healthy older adults

Exercise prescription for functionally impaired older adults

- Pre-frail older adults should exercise 3 times/week for 45–60 min/session.
- Frail older adults should exercise 3 times/week but for 30–45 min/session.

Specifics of exercise in frail older adults

- vulnerable population that may require more time to make improvements in physiological factors
- exercise may lead to acute post exercise central or peripheral fatigue, especially when trained at higher intensities
- challenging, yet safe, which seems to be more difficult for frailer groups
- special consideration should be given to learning by frail older adults, such as impaired vision and hearing, orthopedic conditions, multiple comorbidities, and limited financial resources
- to facilitate adherence to regular exercise, program participation by spouse or caregivers may be required
Is there any added benefit combining exercise and nutritional interventions?
Preventing frailty- CSA

Meta-analysis of RCTs, 48-72 years healthy participants

resistance exercise (>6 wk) plus protein supplement or a modified higher protein diet vs exercise

A - type I fibers (WMD: 212 mm²; 95% CI: 109, 315 mm²; P < 0.0001)
B - type II fibers (WMD: 291 mm²; 95% CI: 71.7, 510 mm²; P < 0.01)

1-repetition maximum leg press in both younger and older subjects (weighted mean difference: 13.5 kg; 95% CI: 6.4, 20.7 kg; P < 0.001). 

Preventing frailty - muscle mass

Finger et al. Sports Med 2015;45:245

● Meta-analysis of 9 RCTs, mean 61-79 years
● Mixed functional status
● Resistance exercise (>6 wk) plus protein or amino acid supplementation vs exercise

SMD (95% CI) Weight (%)

Campbell et al (1995)\textsuperscript{[14]} \(-0.19 (-1.32, 0.94)\) 2.64
Verdijk et al (2009)\textsuperscript{[11]} \(-0.40 (-1.18, 0.38)\) 5.64
Kim et al (2012)\textsuperscript{[18]} 0.12 (-0.35, 0.59) 15.46
Iglay et al (2009)\textsuperscript{[17]} 0.40 (-0.26, 1.06) 7.80
Candow et al - Protein before exercise (2006)\textsuperscript{[15]} 0.63 (-0.29, 1.56) 3.97
Candow et al - Protein after exercise (2006)\textsuperscript{[16]} -0.16 (-1.04, 0.72) 4.41
Kukuijan et al (2009)\textsuperscript{[19]} 0.20 (-0.22, 0.63) 19.16
Leenders et al - Women (2013)\textsuperscript{[10]} 0.00 (-0.54, 0.54) 11.73
Leenders et al - Men (2013)\textsuperscript{[10]} 0.00 (-0.54, 0.54) 11.73
Chalé et al (2013)\textsuperscript{[16]} 0.32 (-0.12, 0.76) 17.44
Overall I\textsuperscript{2} = 0.0%, p-value for heterogeneity = 0.780 0.14 (-0.05, 0.32) 100.00

Changes in muscle mass, [SMD (95% CI)]

SMD = 0.14; 95 % CI -0.05 to 0.32
Preventing frailty- knee extension

SMD = 0.13; 95% CI -0.06 to 0.32.

Finger et al. Sports Med 2015;45:245
Lack of transfer

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Muscle size</th>
<th>Muscle strength</th>
<th>Physical performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>protein/amino acids + exercise training</td>
<td>↓ (n=6)</td>
<td>↓ (n=6)</td>
<td>↓ (n=4)</td>
</tr>
<tr>
<td></td>
<td>↑ (n=1)</td>
<td>↑ (n=1)</td>
<td></td>
</tr>
<tr>
<td>multinutrient supplements + exercise training</td>
<td>↓ (n=6)</td>
<td>↓ (n=5)</td>
<td>↓ (n=5)</td>
</tr>
<tr>
<td></td>
<td>↑ (n=1)</td>
<td>↑ (n=1)</td>
<td></td>
</tr>
<tr>
<td>vitamin d + exercise training</td>
<td>↓ (n=1)</td>
<td>↓ (n=2)</td>
<td>↓ (n=2)</td>
</tr>
<tr>
<td>creatine + exercise training</td>
<td>↑ (n=2)</td>
<td>↑ (n=2)</td>
<td>↓ (n=2)</td>
</tr>
</tbody>
</table>

— no interactions were found between exercise training and supplementation

↑ significantly improved outcome in the group with the combined intervention compared to the exercise group

Lack of effect in older samples

- 70+, progressive RET + protein/EAA supplement vs exercise + placebo/non-protein/no supplement
- N=15 studies, including N=6 considered frail
- progressive resistance exercise; 5 studies added functional and/or balance exercises; 7wk-1y (8 (11)); 2-5/wk (3 (1))
- daily protein supplementation, supplementation on 6d/wk, supplements only on day of training; amount of protein supplemented from 6g/d to 45g<7d (19 (11))
- Overall no added effect on any of the specified outcomes; exceptions included measures of muscle strength (3 studies) and body composition (2 studies)
  → these 2 studies had baseline protein levels below recommendations
  → added benefit (?)
Recent RCTs

- N=130 sarcopenic, mean age: 80.3 y; Ex (muticomponent; 12wk, 5/wk, 20min) + nutritional supplementation with whey protein (22 g), EAA (10.9 g, including 4 g leucine), and vitamin D [2.5 mg (100 IU); 1/d at lunch] vs exercise + placebo → increased fat-free mass, relative skeletal muscle mass, android distribution of fat, handgrip strength, ADLs, nutritional status (MNA)

- N=30, 70+, nursing homes/day care; Ex (PRT; 12wk, 3/wk + Bal 1/wk) + leucine (5 g twice a day, 60 minutes after lunch and dinner) vs Ex + placebo → trends for improved leg strength, chair rise, TUG at 12weeks; medium effects

- N=34, mean 66y, longterm care, subjective muscle strength loss; Ex (strength+stretching; 12wk, 2/wk, 30min) + oral nutritional supplement (20 g whey protein, 10 g EAA, 3 g total leucine, 9 g carbohydrates, 3 g fat, 800 IU vitamin D, and a mixture of vitamins, minerals, and fibers; twice/d before breakfast and lunch) vs Ex + placebo → hand grip, muscle mass improved

What is missing so far?
Reserve – capacity - vulnerability

Frail persons reduced/no exercise tolerance → not trainable?
- RCT, long-term care centers, mean age 85,
- Balance or Walking vs None
- 20 wk, follow-up 1y

“The FW and IB exercise programs were effective in reducing fall risk and improving the scores on the POMA and the physical performance score in the subgroup of pre-frail elderly. In the frail subgroup, however, the risk to become a faller was significantly increased by the intervention, without any significant changes in physical performance measures.”

Table 5: Effects of the Interventions on Time to First Fall, After Correction for Confounders

<table>
<thead>
<tr>
<th>Group</th>
<th>Intervention Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>FW</td>
<td>1.59 (1.04–2.44)*</td>
</tr>
<tr>
<td>IB</td>
<td>1.09 (0.72–1.64)</td>
</tr>
<tr>
<td>Exercise†</td>
<td>1.36 (0.94–1.96)</td>
</tr>
<tr>
<td>Frail subgroup</td>
<td></td>
</tr>
<tr>
<td>Total period‡</td>
<td>2.95 (1.64–5.32)§</td>
</tr>
<tr>
<td>Pre-frail subgroup</td>
<td></td>
</tr>
<tr>
<td>Total period (wk)‡</td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>0.62 (0.29–1.33)</td>
</tr>
<tr>
<td>≥12</td>
<td>1.18 (0.55–2.54)</td>
</tr>
<tr>
<td></td>
<td>0.39 (0.18–0.88)*</td>
</tr>
</tbody>
</table>

NOTE. Values are HR (95% CI).
*P<.05.
†FW versus IB (P=.096); frailty effect modification (P=.002).
‡Time-dependent covariate: frail subgroup (P=.350), pre-frail subgroup (P=.052).
§P<.001.
Natural transition

- 5,086 men
- 35% progressed in frailty status or died, 56% had no change in frailty status, and 15% of prefrail or frail participants improved

Take home message
● Prevention by being generally physically active in young and middle-aged years
● In high age exercise should be implemented to prevent frailty

● Exercise is feasible and safe in frail individuals
● Exercise is effective in pre-frail and frail older adults

● There is very limited evidence on the added benefit of nutritional component, suggesting that in frail people with reduced protein intake it may be beneficial

● More research is required
Thank you for your attention!

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