Epidemiology: Life trajectories of lean, fat and bone mass

Cyrus Cooper  OBE, DL, FMedSci

Professor of Rheumatology and Director,  MRC Lifecourse Epidemiology Unit, University of Southampton; and
Professor of Epidemiology, University of Oxford, UK

President, International Osteoporosis Foundation

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Body composition trajectories throughout the lifecourse

• Bone mass trajectory through lifecourse
• Implications for prevention from conception to old age
• Linkage in trajectories of bone, muscle and fat

MRC Lifecourse Epidemiology Unit, University of Southampton

Institute of Musculoskeletal Science, University of Oxford
Bone mass across the lifecourse: gain and loss

Determinants of peak bone mass
- Gene
- Nutrition
- Physical activity
- Hormonal status

Determinants of bone loss and fracture risk
- Menopause
- Body mass
- Smoking
- Alcohol
- Dietary Ca/D
- Physical activity
- Diseases
- Drugs (GC)

Peak 50%
Loss rate 50%
Preventive strategies: High-risk and population approaches

Bone mass

Target those with a low bone density

Bone mass

Move entire distribution by intervening in everyone

Mean

-1SD

+1SD

Screening based on clinical risk factors and FRAX leads to reduced risk of hip fracture

HR = 0.72; 95% CI 0.59-0.89

Shepstone L et al. Lancet 2018; 391: 741-7
Lifecourse determinants of health and disease: A conceptual framework

Vitamin D supplementation increases offspring BMC in winter births by eliminating steep winter decline in maternal vitamin D status: MAVIDOS Trial

Cooper C et al  Lancet Diabetes Endocrinol 2016; 4: 393-402
Gestational vitamin D supplementation leads to reduced perinatal RXRA methylation (MAVIDOS)

1000 IU/d vs. Placebo

DNA methylation

Curtis E et al J Bone Miner Res 2019; 34: 231-40
Prevention of fragility fracture throughout the lifecourse

Conclusions

• Population/individual mortality and morbidity burden attributable to osteoporotic fracture established

• Risk assessment well validated through FRAX, and widely incorporated in international treatment guidelines

• Effectiveness of FRAX-based programmes for treatment targeting demonstrable and cost-effective (MRC SCOOP)

• Secondary preventive strategies well designed, widely available and cost-effective

• Novel approaches point at prevention throughout the lifecourse
Sarcopenia

Components:
- Muscle mass
- Muscle strength
- Physical performance

“A syndrome characterised by progressive, generalised loss of skeletal muscle mass and strength with the risk of adverse outcomes such as physical disability, poor quality of life and death.”

Novel approaches to definition:
- EWGSOP-2
- SDOC (FNIH-2)

ICD-10 Registration 2016

Cruz-Jentoft A et al Age Ageing 2019; 48: 16-31
Muscle strength across the lifecourse

12 population studies in Great Britain; 60,803 observations from 49,964 participants (26,687 female)

Cross-cohort centile curves for grip strength.

Peak 45%
Loss rate 55%

Annual percentage change in muscle function and body composition: HealthABC

Boxes show median, lower quartile and upper quartile

<table>
<thead>
<tr>
<th>Measure</th>
<th>Median (LQ, UQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking speed</td>
<td>-2.0 (-3.7, -0.6)</td>
</tr>
<tr>
<td>Grip strength</td>
<td>-1.5 (-2.9, 0.0)</td>
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<tr>
<td>Lean mass</td>
<td>-0.4 (-1.0, 0.1)</td>
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<tr>
<td>ALM</td>
<td>-0.7 (-1.4, -0.1)</td>
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<tr>
<td>Fat mass</td>
<td>-0.4 (-1.9, 1.1)</td>
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<tr>
<td>Hip BMD</td>
<td>-0.5 (-1.1, 0.0)</td>
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</table>

Westbury L et al  ICFSR (2019)
## Relationships between conditional change measures

<table>
<thead>
<tr>
<th>Measures</th>
<th>Grip strength</th>
<th>Walking speed</th>
<th>Lean mass</th>
<th>ALM</th>
<th>Fat mass</th>
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<tr>
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<tr>
<td>Lean mass</td>
<td>0.24</td>
<td>0.08</td>
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<td>P-value</td>
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<td>Fat mass</td>
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<td>Hip BMD</td>
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ALM: Appendicular lean mass; Correlations where r>0.3 are in red

*Westbury L et al. ICFSR (2019)*
Proportion of variance at Year 10 explained by baseline level and change since baseline

Conditional change measures were derived for each characteristic

Westbury L et al. ICFSR (2019)
Conclusions

• All indices of body composition and muscle function show significant age-related declines

• Among muscle indices, proportionate declines over 10 years greatest for gait speed, then grip strength and lean mass

• Latent trajectory models identify subgroups with more pronounced differences in levels of characteristics, as compared with rates of loss

• Trajectories of change in indices of body composition (lean mass, ALM, fat mass and hip BMD), more strongly correlated with each other, than between these and gait speed or grip strength

• Extension to studying trajectories in multiple cohorts

• Findings support a lifecourse approach to preventive strategies, rather than purely a focus on environmental influences in later life
Linked Pathophysiologic Entity: Osteosarcopenic Obesity?
With thanks to all at Southampton, Oxford and Health ABC