Endocrinology of Sarcopenia

Olga Kotelko  1.5m
Women’s high school  6.9m
Women’s world  7.5m
Publications on Sarcopenia in PubMed (1993 to 2015)

2016 = 1026
Sarcopenia

Kratopenia
Thinamopenia

Dynapenia

Frailty

Disability

- DEXA
- Bioelectrical impedance
- MRI/CT
- MAMC/Calf Circumference
- Ultrasound

- Isometric (Dynamometry)
- Isotonic

- Walking speed (>1 m/sec)
- Walking distance (6 min)
- Stair climbing

- CHS (Fried) Criteria
- IANA Criteria
- SOF Criteria

- ADLs
- Barthel Index
- Functional Index Measure
## Comparison of Sarcopenia Definitions

( EWGSOP = European Working Group of Sarcopenia in Older Persons; SCWD = Sarcopenia Cachexia and Wasting Diseases; IANA = International Association of Nutrition and Aging )

<table>
<thead>
<tr>
<th>Definition</th>
<th>Function</th>
<th>Muscle Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIG: Cachexia-Anorexia in Chronic Wasting Disease [3]</td>
<td>Gait Speed &lt;0.8m/s, OR other physical Performance test</td>
<td>Low muscle mass (2SD)</td>
</tr>
<tr>
<td>EWGSOP [4]</td>
<td>Gait speed &lt;0.8m/s Grip strength 40kg males 30kg females</td>
<td>Low muscle mass (not defined)</td>
</tr>
<tr>
<td>IWGS Sarcopenia Task Force [5]</td>
<td>Gait speed &lt;1.0m/s Grip strength</td>
<td>Low appendicular lean mass (&lt;7.23kg/m2 in men; 5.67 in women)</td>
</tr>
<tr>
<td>Sarcopenia with Limited Mobility (SCWD) [6]</td>
<td>6 min walk &lt;400 m OR gait speed &lt;1.0m/s</td>
<td>Low appendicular lean mass/height²</td>
</tr>
<tr>
<td>Asian Working Group for Sarcopenia [7]</td>
<td>Gait speed &lt;0.8m/s Grip strength 26kg males 18kg females</td>
<td>Low appendicular lean mass/height²</td>
</tr>
<tr>
<td>Foundation National Institute of Health [8]</td>
<td>Gait speed &lt;0.8m/s Grip strength 26kg males 16kg females</td>
<td>Appendicular lean mass/BMI</td>
</tr>
</tbody>
</table>
In the New Mexico Aging Process Study we found obese sarcopenia to be longitudinally the best predictor of future disability and mortality.

Epidos Study
- Odds of climbing stairs: 2.60
- Odds of going down stairs: 2.35

WHO Fracture Risk Assessment (FRAX)

www.shef.ac.uk/FRAX/

- Previous fracture
- Parent fractured hip
- Current smoking
- Glucocorticoids
- Secondary osteoporosis
- Alcohol >3 units/day
- Femoral neck BMD
FRAX Questions vs BMD

Leslie et al, Osteoporosis Int
Participants with a total score higher than 4 were classified as having sarcopenia.
<table>
<thead>
<tr>
<th>6-Year Outcomes</th>
<th>Males and Females</th>
<th>Males and Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI )</td>
<td>P-Value</td>
</tr>
<tr>
<td>Incident ADLs &gt; 1*</td>
<td>4.46 (2.68-7.42)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Incident IADLs &gt; 1*</td>
<td>2.52 (1.56-4.07)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospitalized overnight past year**</td>
<td>2.43 (1.46-4.05)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gait Speed &lt; 0.8 m/s**</td>
<td>2.46 (1.13-5.34)</td>
<td>.023</td>
</tr>
<tr>
<td>Mortality*</td>
<td>1.87 (1.17-2.98)</td>
<td>.009</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Yes (n=93)</th>
<th>No (n=483)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chair stands**</td>
<td>16.00±7.1</td>
<td>11.76±5.1</td>
</tr>
<tr>
<td>Grip strength**</td>
<td>28.11±12.0</td>
<td>31.53±11.2</td>
</tr>
</tbody>
</table>
SARC-F in Baltimore Longitudinal Study 60+ years

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gait Speed &lt;0.8 m/s</td>
<td>9.41(2.51-35.27)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mortality</td>
<td>3.07(1.60-5.73)</td>
<td>0.001</td>
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</tbody>
</table>

Chart Title

<table>
<thead>
<tr>
<th></th>
<th>ADLs</th>
<th>IADLs</th>
<th>Grip Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARC-F &lt;4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SARC-F &gt;4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Odds Ratio for 4 year outcomes associated with different sarcopenia definitions
Woo et al: Hong Kong Data

Males

- Physical limitation
- Chair stand
- Walking Speed

Females

- Physical limitation
- Chair stand
- Walking Speed

Legend:
- FNIH
- FNIH(slow)
- EWGSOP
- IWGS
- AWGS
- SARC-F
**Figure.** Comparisons for physical function among elderly patients with cardiovascular disease with low (<4) vs. high (≥4) SARC-F scores.

Dots represent adjusted mean values with error bars representing 95% CI.

P values represent group differences by ANCOVA models. Adjusted for age, gender, and BMI.


Aging Clin Exp Res. 2016 Nov 10

CONCLUSIONS:

The retest reliability of SARC-F-J was regarded to be good. When EWGSOP was assumed as a reference, the specificity of SARC-F-J was high;
Allelic Variations Associated with Strength and Body Mass

- Myostatin (GDF8, K133R)
- CNTF and its receptor
- Vitamin D receptor (VDR Bsm1)
- Angiotensin Converting Enzyme
- Androgen receptor gene (CAG-repeats)
- Cyclin dependent kinase inhibitor 1A
- MYOD1
HERTFORDSHIRE COHORT STUDY
SARCOPENIA ORIGINATES AT BIRTH
Sayer et al J Gerontol A 59:930,2004

730 men 673 women
Known weight at birth and one year

GRIP STRENGTH CORRELATES WITH BIRTH WEIGHT
NOT INFANT GROWTH
BIOCHEMISTRY OF SARCOPENIA

GH/Testosterone/Creatine

Rejuvenation of aged progenitor cells by exposure to a young systemic environment

Irina M. Conboy*, Michael J. Conboy†, Amy J. Wagers‡, Eric R. Girma§, Irving L. Weissman* & Thomas A. Rando†

ORIGINAL ARTICLE

Antiproteolytic effects of plasma from hibernating bears: A new approach for muscle wasting therapy?*

Gemma Fuster*, Silvia Busquets*, Vanessa Almendro, Francisco J. López-Soriano, Josep M. Argilés

Cancer Research Group, Departament de Bioquímica i Biologia Molecular, Facultat de Biologia, Universitat de Barcelona, Diagonal 645, 08028 Barcelona, Spain

Received 19 January 2007; accepted 2 July 2007

Available at www.sciencedirect.com

ScienceDirect
Parabiosis Rejuvenates Old Mice

Muscle

Heart

Neurogenesis
Old muscle shows fiber size heterogeneity and fiber grouping.

Increase in muscles with MYOSIN HEAVY CHAIN with aging and denervation.
The Motor Unit Number Index (MUNIX) in sarcopenic patients

MOTORNEURONS and AGING

25-30% reduction in motorneurons

Small motorneurons sprout and innervate type II with eventual loss of type II fibers

Elevated levels of a C-terminal agrin fragment identifies a new subset of sarcopenia patients
INCREASED LEPTIN

DECREASED CALORIE AND PROTEIN INTAKE

DECREASED PHYSICAL ACTIVITY

INCREASED FAT INFILTRATION

INCREASED GROWTH HORMONE AND GHRELIN

DECREASED MGF

DECREASED CNTF

DECREASED GROWTH HORMONE AND GHRELIN

VITAMIN D DEFICIENCY

DECREASED IGF-1 Ea

DECREASED ANABOLIC HORMONES

TESTOSTERONE DHEA

DECREASED MOTOR UNITS

ATHEROSCLEROSIS

DECREASED CNTF

HYPOXIA

HYPERTRIGLICYERIDEMIA

INCREASED FAT INFILTRATION

INCREASED LEPTIN

VISCERAL OBESITY

INCREASED INSULIN RESISTANCE

DECREASED ADIPONECTIN

GENETIC

Myostatin ActivinIIR Notch I IGF-2 CNTF

MITOCHONDRIAL ABNORMALITIES

CYTOKINE EXCESS egTNFα IL-6

HYPOXIA
3-Years Mortality in Older Type 2 DM Patients According to Frailty Status and Disease

Data from the Toledo Study of Healthy Aging

Adjusted by age, sex, and comorbidity
Skeletal muscle fiber typing in serial sections of biopsies from the vastus lateralis muscle in a NGT healthy volunteer.

Red / Slow (Type I fibres, 'slow twitch fibres')
Red / Fast (Type Ila fibres, 'fast oxidative fibres')
White / Fast (Type IIb fibres, 'fast glycolytic fibres')

Oberbach A et al. Dia Care 2006;29:895-900
A pilot study of regional perfusion and oxygenation in calf muscles of individuals with diabetes with a noninvasive measure


http://dx.doi.org/10.1016/j.jvs.2013.07.115
Eccentric Exercise Increases Satellite Cell Content in Type II Muscle Fibers

Reduced skeletal muscle quantity and quality in patients with diabetic polyneuropathy assessed by magnetic resonance imaging

Reduced skeletal muscle quantity and quality in patients with diabetic polyneuropathy assessed by magnetic resonance imaging
Patients With Type 2 Diabetes Show a Greater Decline in Muscle Mass, Muscle Strength, and Functional Capacity With Aging

Marika Leenders, Lex B. Verdijk, Letty van der Hoeven, Jos J. Adam, Janneau van Kranenburg, Rachel Nilwik, L...

Journal of the American Medical Directors Association, Volume 14, Issue 8, 2013, 585 - 592
Sarcopenia and Diabetes
African Americans 50 - 65 years
Frailty and Sarcopenia as Predictors of Adverse Health Outcomes in Persons With Diabetes Mellitus

Anthony P. Liccini, Theodore K. Malmstrom,

**Hospital Utilization**
3.80 (1.67–8.6)  p<.001

**New Disability**
4.24 (1.76–10.18)  p<.001

---

**Chart Title**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Normal</th>
<th>Sarcopenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>80</td>
<td>70</td>
</tr>
<tr>
<td>60-69</td>
<td>70</td>
<td>60</td>
</tr>
<tr>
<td>70+</td>
<td>50</td>
<td>40</td>
</tr>
</tbody>
</table>

**SARC-F**

Frail or prefrail n= 77

n = 57 (42.5%)

Sarcopenia n = 1
Treatment for SARCOPENIA is RESISTANCE EXERCISE
Myokine secretion from differentiated hSMC obtained from non-diabetic (ND, open bars) and Type 2 Diabetic (T2D, solid bars) subjects.
- although both younger and older participants benefited from the ILI treatment compared with DSE, there was a greater benefit for older than younger participants.

- Also, there was strong evidence that the rate of decline was steeper for older than younger participants with aging.

- This pattern suggests that a legacy effect may be operative and warrants attention as this cohort is followed into the future.

Figure 3. Plot of the SF-36 physical functioning subscale by treatment group for younger and older participants across 8 years of the Look AHEAD study.
From: Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults: The LIFE Study Randomized Clinical Trial


1635 sedentary men and women aged 70 to 89 years who had physical limitations
## Sarcopenia in Elderly Diabetic Patients: Role of Dipeptidyl Peptidase 4 Inhibitors

Maria Rosaria Rizzo, MD, Michelangela Barbieri, MD, Ilaria Fava, MD, Manuela Desiderio, MD, Carla Coppola, MD, Raffaele Marfella, MD, Giuseppe Paolisso, MD

<table>
<thead>
<tr>
<th></th>
<th>All Patients (N = 80)</th>
<th>Sulfonylureas Group (n = 43)</th>
<th>P Value</th>
<th>DPP4-I Group (n = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFM (kg)</td>
<td>51.8 ± 7.1</td>
<td>49.4 ± 6.5</td>
<td>.001</td>
<td>54.5 ± 6.8</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>19.7 ± 1.6</td>
<td>19.9 ± 1.7</td>
<td>.186</td>
<td>19.4 ± 1.6</td>
</tr>
<tr>
<td>FFM/FM</td>
<td>2.6 ± 0.4</td>
<td>2.5 ± 0.3</td>
<td>.001</td>
<td>2.8 ± 0.4</td>
</tr>
<tr>
<td>FFM index (kg/m²)</td>
<td>19.1 ± 2.2</td>
<td>18.4 ± 2.1</td>
<td>.001</td>
<td>19.9 ± 2.1</td>
</tr>
<tr>
<td>SMM (kg)</td>
<td>22.4 ± 5.3</td>
<td>20.5 ± 4.7</td>
<td>.001</td>
<td>24.7 ± 5.3</td>
</tr>
<tr>
<td>SMM index (kg/m²)</td>
<td>8.2 ± 1.7</td>
<td>7.6 ± 1.5</td>
<td>.001</td>
<td>9.0 ± 1.6</td>
</tr>
<tr>
<td>Handgrip strength (kg)</td>
<td>23.5 ± 4.9</td>
<td>21.4 ± 4.2</td>
<td>.001</td>
<td>26.1 ± 4.4</td>
</tr>
<tr>
<td>Gait speed 4 m (m/s)²</td>
<td>3.5 ± 0.7</td>
<td>3.7 ± 0.7</td>
<td>.001</td>
<td>3.1 ± 0.6</td>
</tr>
</tbody>
</table>

A

B

C

GPL-1 AUC (pmol x h x L)
Comprehensive Geriatric Assessment and 12 months resistance training twice weekly

Mortality OR 0.19 (0.04 – 0.91)
Nursing Home OR 0.16 (0.04 – 0.64)
ADL’s p <0.02
Assistive Device p<0.01
PROVIDE (PROTEIN) STUDY CENTRES ACROSS EUROPE
PROT-AGE recommendations for dietary protein intake in healthy older adults

• To maintain and regain muscle, older people need more dietary protein than do younger people; older people should consume an average daily intake in the range of 1.0 to 1.2 g/kg BW/d.

• The per-meal anabolic threshold of dietary protein/amino acid intake is higher in older individuals (ie, 25 to 30 g protein per meal, containing about 2.5 to 2.8 g leucine) in comparison with young adults.

• Protein source, timing of intake, and amino acid supplementation may be considered when making recommendations for dietary protein intake by older adults.

• More research studies with better methodologies are desired to fine tune protein needs in older adults.
### Longitudinal Changes in Testosterone

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Testosterone (nmol/L)</th>
</tr>
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<tbody>
<tr>
<td>10</td>
<td>(177)</td>
</tr>
<tr>
<td>12</td>
<td>(144)</td>
</tr>
<tr>
<td>14</td>
<td>(151)</td>
</tr>
<tr>
<td>16</td>
<td>(158)</td>
</tr>
<tr>
<td>18</td>
<td>(109)</td>
</tr>
<tr>
<td>20</td>
<td>(43)</td>
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<tr>
<td>30</td>
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<tr>
<td>40</td>
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<tr>
<td>50</td>
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<td>60</td>
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<td>80</td>
<td></td>
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<tr>
<td>90</td>
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**Factor Analysis**

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<tr>
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<th>Muscle Mass</th>
<th>Muscle Strength</th>
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<tbody>
<tr>
<td>Age</td>
<td>0.30</td>
<td>0.45</td>
</tr>
<tr>
<td>Energy Intake</td>
<td>0.25</td>
<td>0.06</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>0.34</td>
<td>0.35</td>
</tr>
<tr>
<td>IGF-1</td>
<td>0.27</td>
<td>0.23</td>
</tr>
<tr>
<td>FTI</td>
<td>0.45</td>
<td>0.27</td>
</tr>
</tbody>
</table>

**Australia Andriol Study**

12 Months  
$n=76$

60+ Years  
Borderline Hypogonadal  
Andriol 80mg BID

Lean Body Mass  
P<0.0001
Androgens

May be of particular benefit for the treatment of “sarcopenic obesity”

% Change in Lean Body Mass

% Change in Fat Mass

* P < 0.0001

* P < 0.002
**Testosterone Dose Response**

Bhasin et al JCEM 90:678-688

2005

- **Change in Fat Free Mass (kg)**
  - Dose effects p<0.0001
  - Age effect p=0.54

- **Changes in Skeletal Muscle Mass (kg)**
  - Dose effects p<0.0001
  - Age effect p=NS

- **Change in Fat Mass (kg)**
  - Dose effects p=0.17
  - Age effect p=0.02

- **Change in Leg Press strength 1RM (kg)**
  - Dose effects p=0.008
  - Age effect p=0.84

**Testosterone Dose (mg wk)**

- **Young**
- **Old**
Pluripotent Stem Cells

Mesenchymal Stem Cells

Fat cell lineage

Pre-adipocyte Progenitor cell

Pre-adipocyte

Mature adipocyte

LPL
PPARy
C/EBPα

Muscle cell lineage

Increased Notch
No change in Numb
Inc.PCNA

TESTOSTERONE

Muscle protein synthesis

Muscle protein turnover

ubiquitin-proteasome pathway

Satellite cell

Myoblast

Myotube

MyoD
Desmi
MHC
THE MECHANISM BY WHICH TESTOSTERONE INCREASES SATELLITE CELLS AND DECREASES ADIPOGENESIS

- **PPARγ c1a** decreases adipogenesis
- **GSK3b**, **β Catenin**, **Smad4**, and **MYOSTATIN** increase myogenesis
- **Wnt**, **Frizzled homolog 4**, and **Ubiquitin-proteasome** decrease adipogenesis
- **Cyclin 1**, **Cyclin 6**, and **Cyclin cr kinase** decrease cell cycling

↑ MYOGENESIS
↑ CELL CYCLING
# Physical Function Trial Outcomes

## Table 2. Physical Function Trial Outcomes

<table>
<thead>
<tr>
<th>Cohort and Outcome</th>
<th>No. of Men</th>
<th>Baseline Value</th>
<th>No. of Participants or Change from Baseline Value</th>
<th>Treatment Effect (95% CI)</th>
<th>Effect Size (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Month</td>
<td>Month 6</td>
<td>Month 9</td>
<td>Month 12</td>
<td></td>
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<tr>
<td>Men enrolled in Physical Function Trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Primary outcome: increase of ≥50 m in 6 min walk test — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>191</td>
<td>0/191</td>
<td>20/179 (11.2)</td>
<td>24/174 (13.8)</td>
<td>28/172 (16.3)</td>
<td>35/172 (20.3)</td>
</tr>
<tr>
<td>Placebo</td>
<td>196</td>
<td>0/196</td>
<td>14/179 (7.6)</td>
<td>23/171 (13.5)</td>
<td>22/159 (12.3)</td>
<td>20/165 (12.3)</td>
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<tr>
<td>Secondary outcomes</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>6 Min walking distance — m</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>191</td>
<td>347.7±69.1</td>
<td>10.2±35.8</td>
<td>8.2±41.5</td>
<td>5.3±50.3</td>
<td>14.3±45.9</td>
</tr>
<tr>
<td>Placebo</td>
<td>196</td>
<td>349.9±68.3</td>
<td>4.6±35.2</td>
<td>7.8±41.4</td>
<td>3.2±52.4</td>
<td>5.5±46.4</td>
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<tr>
<td>Increase of ≥50 in PF-10 score — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Testosterone</td>
<td>184</td>
<td>77/176 (43.8)</td>
<td>77/171 (42.3)</td>
<td>77/172 (44.8)</td>
<td>66/173 (38.2)</td>
<td>1.34 (0.90 to 2.00)</td>
</tr>
<tr>
<td>Placebo</td>
<td>181</td>
<td>59/171 (34.5)</td>
<td>59/159 (36.7)</td>
<td>59/159 (36.7)</td>
<td>58/167 (34.9)</td>
<td>1.34 (0.90 to 2.00)</td>
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<tr>
<td>PF-10 score</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>184</td>
<td>65.4±20.0</td>
<td>5.6±15.2</td>
<td>6.5±16.7</td>
<td>5.9±19.4</td>
<td>5.8±17.5</td>
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<tr>
<td>Placebo</td>
<td>181</td>
<td>64.8±21.3</td>
<td>4.2±13.7</td>
<td>4.8±17.0</td>
<td>3.3±18.9</td>
<td>2.4±17.3</td>
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<tr>
<td>All Testosterone Trials participants</td>
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<tr>
<td>Increase of ≥50 m in 6 min walk test — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>192</td>
<td>40/192</td>
<td>52/192</td>
<td>54/198</td>
<td>71/196</td>
<td>71/196</td>
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<tr>
<td>Placebo</td>
<td>195</td>
<td>39/195</td>
<td>27/195</td>
<td>33/195</td>
<td>37/195</td>
<td>37/195</td>
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<tr>
<td>6 Min walking distance — m</td>
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</tr>
<tr>
<td>Testosterone</td>
<td>192</td>
<td>387.0±83.7</td>
<td>10.9±45.1</td>
<td>11.0±40.2</td>
<td>6.7±45.1</td>
<td>13.6±43.4</td>
</tr>
<tr>
<td>Placebo</td>
<td>195</td>
<td>387.0±83.7</td>
<td>1.6±41.9</td>
<td>5.7±45.1</td>
<td>3.2±47.4</td>
<td>6.4±45.8</td>
</tr>
<tr>
<td>Increase of ≥50 in PF-10 score — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>109</td>
<td>111/283 (38.9)</td>
<td>113/281 (40.2)</td>
<td>115/276 (41.7)</td>
<td>103/281 (36.7)</td>
<td>1.50 (1.00 to 2.09)</td>
</tr>
<tr>
<td>Placebo</td>
<td>105</td>
<td>87/273 (31.6)</td>
<td>101/283 (35.9)</td>
<td>89/260 (32.9)</td>
<td>82/272 (30.3)</td>
<td>1.50 (1.00 to 2.09)</td>
</tr>
<tr>
<td>PF-10 score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>109</td>
<td>71.2±20.2</td>
<td>5.0±14.7</td>
<td>6.1±16.7</td>
<td>5.3±18.5</td>
<td>4.3±16.9</td>
</tr>
<tr>
<td>Placebo</td>
<td>105</td>
<td>69.7±21.2</td>
<td>3.9±12.8</td>
<td>3.4±16.2</td>
<td>2.3±17.9</td>
<td>1.3±16.9</td>
</tr>
</tbody>
</table>

* Plus-minus values are means ±SD.
† The treatment effect for dichotomous outcomes is the odds ratio for achieving the outcome versus not achieving the outcome among men assigned to testosterone versus those assigned to placebo. For continuous outcomes, the treatment effect is the mean difference in the outcome among men assigned to testosterone versus those assigned to placebo. All analyses are adjusted for balancing factors: baseline total testosterone level (≤200 or >200 ng per decile), age (<75 or ≥75 years), trial site, participation in the main trials, use or non-use of antidepressants, and use or non-use of phosphodiesterase type 5 inhibitors.
‡ For continuous outcomes, the effect size is the treatment effect divided by the baseline standard deviation.
§ The P value for the treatment effect was determined with the use of a logistic mixed model with a random effect for participant for dichotomous outcomes and a linear mixed model with a random effect for participant for continuous outcomes.
¶ Scores on the physical-function scale (PF-10) of the Medical Outcomes Study 36-item Short-Form Health Survey range from 0 to 100, with higher scores indicating better function.
|"The results for all Testosterone Trials participants are exploratory outcomes."

Increase 6 min walk distance >50m
Testosterone and Heart Failure
Caminiti et al, JACC 54:919;2009
STEROIDS ENHANCE PERFORMANCE
GTx SARM (Ostarine)
n=120, Mean age 64.8 yrs

Fat Free Mass (Dexa)

Stair Climb Power
(Watts)

Placebo 3 mg
All
Men
Women

Placebo 3 mg
All Subjects
VITAMIN D AND FRAILTY

Longitudinal Fall in Vitamin D with Age

Beta-hydroxyvitamin D concentrations correlated with handgrip force ($r = 0.16$; $P = 0.02$)

Body mass index and absolute fat mass correlated with the DBP-concentrations

Effect of Vitamin D on Upper and Lower Body Strength

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>Experimental SD</th>
<th>Control Mean</th>
<th>Control SD</th>
<th>Std. Mean Difference IV, Fixed, 95% CI</th>
<th>Std. Mean Difference IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caillé 2012 - CP GM</td>
<td>58.2 ± 20</td>
<td>10</td>
<td>55.1 ± 20</td>
<td>7.1</td>
<td>0.15 [0.08, 0.22]</td>
<td>-0.05 [-0.22, 0.12]</td>
</tr>
<tr>
<td>Close et al 2013 - EP FW</td>
<td>94 ± 18</td>
<td>5</td>
<td>93 ± 20</td>
<td>5</td>
<td>0.00 [-0.16, 0.16]</td>
<td>0.00 [-0.16, 0.16]</td>
</tr>
<tr>
<td>Close et al 2013 - EP IK 20,000</td>
<td>92 ± 15</td>
<td>10</td>
<td>79 ± 18</td>
<td>10</td>
<td>0.08 [-0.18, 0.34]</td>
<td>0.08 [-0.18, 0.34]</td>
</tr>
<tr>
<td>Close et al 2013 - EP IK 40,000</td>
<td>90 ± 20</td>
<td>10</td>
<td>79 ± 19</td>
<td>10</td>
<td>0.00 [-0.18, 0.18]</td>
<td>0.00 [-0.18, 0.18]</td>
</tr>
<tr>
<td>Gowrani et al 2013 - Handgrip</td>
<td>20.6 ± 3.2</td>
<td>40</td>
<td>16.4 ± 3.92</td>
<td>43</td>
<td>0.26 [-0.12, 0.66]</td>
<td>0.26 [-0.12, 0.66]</td>
</tr>
<tr>
<td>Gowrani et al 2013 - Pinchgrip</td>
<td>5.5 ± 0.8</td>
<td>43</td>
<td>5.3 ± 0.9</td>
<td>43</td>
<td>0.39 [0.10, 0.78]</td>
<td>0.39 [0.10, 0.78]</td>
</tr>
<tr>
<td>Gupta 2010 - Handgrip</td>
<td>34 ± 10.3</td>
<td>20</td>
<td>30 ± 7.5</td>
<td>20</td>
<td>0.12 [0.01, 0.23]</td>
<td>0.12 [0.01, 0.23]</td>
</tr>
<tr>
<td>Gupta 2010 - Pinchgrip</td>
<td>6.5 ± 1.5</td>
<td>20</td>
<td>5.9 ± 1.4</td>
<td>20</td>
<td>0.12 [0.01, 0.23]</td>
<td>0.12 [0.01, 0.23]</td>
</tr>
</tbody>
</table>

Total (95% CI): 164 100.0%

Heterogeneity: $Chi^2 = 5.45, df = 7 (P = 0.84); I^2 = 0$

Test for overall effect $Z = 2.81 (P = 0.005)$
LESSONS FROM GH STUDIES

- GH increases nitrogen retention
- GH causes weight gain
- GH increases muscle mass
- GH possibly increases type II muscle fibers
- GH does not increase strength
- GH long term produces side effects
Anamorelin for patients with cancer cachexia: an integrated analysis of two phase 2, randomised, placebo-controlled, double-blind trials.

Garcia JM¹, Boccia RV², Graham CD³, Yan Y⁴, Duus EM⁴, Allen S⁴, Friend J⁴.

- Over 12 weeks, lean body mass increased in 38 patients in the anamorelin group by a least-squares mean of 1.89 kg (95% CI 0.84 to 2.95) compared with a decrease of a least-squares mean of -0.20 kg (-1.23 to 0.83) for 36 patients in the placebo group (difference 2.09 kg [0.94-3.25]; p=0.0006)
MYOSTATIN DELETIONS
**Muscle Mass, Volume (DXA, MRI)**

- Total body lean mass (DXA) and thigh muscle volume (MRI) increased in higher dose groups and was sustained post-dosing.

**Bone Markers, Density**

- BSAP (a marker of bone formation) increased, sCTX (a marker of bone resorption) decreased, and lumbar spine BMD (DXA) increased.

**Fat Markers, Mass**

- Adiponectin increased, leptin decreased, and total body fat mass (DXA) decreased.
Treatment of sporadic inclusion body myositis with bimagrumab.
Amato, Anthony; Sivakumar, Kumaraswamy; Goyal, Namita; David, William; MD, PhD; Salajegheh, Mohammad; Praestgaard, Jens; Lach-Trifilieff, Estelle; Trendelenburg, Anne-Ulrike; Laurent, Didier; Glass, David; Roubenoff, Ronenn; MD, MHS; Tseng, Brian; MD, PhD; Greenberg, Steven

DOI: 10.1212/WNL.0000000000001070

[Diagrams and images related to the study results]

Inclusion-Body Myositis (IBM) is characterized by muscle fibers that contain empty, bubble-like spaces (vacuoles) and clumps of cellular material (inclusion bodies). Inflammatory cells can be seen between the fibers.