Clinical Treatment of Obesity in Older Women

Barbara Nicklas
J. Paul Sticht Center on Aging
“In my day, people died.”
Trajectory of physical ability

Functional Independence → Impairment → Disability

Time

- Independence
- Aging, Disease
- Successful compensation
- Difficulty in task perform.
- Compensation partly successful
- IADL dependence
- 1-2 ADLs dependence
- ≥3 ADLs institutionalization
Causal model of disability

- Genes
  - Biological factors
    - Inflammation, hormones, oxidative damage, anemia, angiotensin
  - Co-morbid factors
    - CVD, COPD, cognitive disorders, diabetes, osteoporosis
  - Behavioral factors
    - Exercise - diet

- Social, economic & environmental factors

- Sarcopenia
  - Adiposity

- Impairment
  - Functional limitation

- Disability
Outline

• Adverse consequences of excess adipose tissue in older women

• Reasons for reluctance to recommend weight loss in older women

• Treatment of excess adipose tissue in older persons
  – What we know
  – What we don’t know

• Unanswered questions
Adverse consequences of excess adipose tissue in older women

• ↑ prevalence of frailty, ↓ physical function, and self-reported disability with ↑ fat mass

• greater ↓ in function and earlier onset of disability in more obese elders

• prior weight gain/obesity status also associated with risk for disability

• TG more likely to be redistributed to ectopic (abnormal) locations (eg., in muscle) with age
Reluctance to recommend weight loss in older women because:

1) Unintentional weight loss:
   – Associated with more severe disease
   – Predicts ↑ hospitalization, disability, & mortality

![Graph showing adjusted HR for mobility limitation with different weight categories: intentional loss, unintentional loss, unintentional gain, stable weight.](Lee et al, J Gerontol 2005)
Reluctance to recommend weight loss in older women because it may:

2) Exacerbate age-related losses in bone mineral content and skeletal muscle

“Intentional and unintentional weight loss increase bone loss and hip fracture risk in older women”

Ensrund, 2003
Reluctance to recommend weight loss in older women because:

3) Relative risk of ↑ BMI on all-cause mortality, CVD ↓ with age

Association of BMI and 12-yr mortality risk by age

Stevens et al, NEJM 1998
Reluctance to recommend weight loss in older women because:

“It may initiate or worsen functional decline”

“In older persons, weight loss, whether intentional or unintentional, represents one of the best indicators of an underlying disease process”  (Rolland Y, 2006)

“….dietary restriction may prolong life, but weight loss in older men and women shortens life.”  (Wilson M, 2003)

“Outcomes of weight loss in older persons, even when the body mass index is initially elevated, tend to be poor.”  (Rolland Y, 2006)

“There are few studies on the effects of intentional weight loss in the elderly……. There have been no large clinical trials of the effects of weight loss on health outcomes in old age.”  (Zamboni, 2005)
“Weight loss reduces risk factors and improves functional status in older persons in the same manner as in younger adults.”
Limited data (in >65 yrs) show benefits of diet-induced weight loss on metabolic risk factors and disease

- Weight loss ↓ prevalence of hypertension in older adults with hypertension  
  (TONE study, Whelton, JAMA, 1998)

- Weight loss ↓ chronic inflammation in older adults  
  (Nicklas, AJCN, 2004; Villareal, AJCN, 2006)

Diet-induced weight loss improves lipid profile, pulmonary function and glucose metabolism in older adults  
(Colman, 1995; Katzel, JAMA, 1995; Dengel, JAP, 1996; Purnell, JCEM, 2000; Womack, J Geron, 2000; Nicklas, J Geron, 2003; Villareal, AJCN, 2006)
Weight loss & exercise in DPP most effective for prevention of diabetes in 60-85 yr olds

"ILS became significantly more effective than Metformin with increasing age (p=.005)"

J Geron, 2006
Design: single-blind, randomized controlled 18 mo trial
N=316 persons with knee osteoarthritis

4 groups: Control, Weight loss, Exercise, WL+EX
- behavioral weight loss classes with RD, 1x/wk
- low-intensity aerobic/resistance exercise, 3x/wk

Subjects: 68±6 yrs; BMI=34±5 kg/m²;
72% women; 22% African-American

Messier et al, Arthritis & Rheumatism, 2004
ADAPT: weight loss results

% change in body weight

-6
-5
-4
-3
-2
-1
0

Control
Diet
Exercise
Diet+Exercise

-5.7
-2.2
-4.2

***
ADAPT: physical performance results

<table>
<thead>
<tr>
<th></th>
<th>6-min walk distance (m)</th>
<th>Stair-climb time (secs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline mean (SEM)</td>
<td>Δ from baseline (95% CI)</td>
</tr>
<tr>
<td>Healthy lifestyle</td>
<td>434.6 (10.9)</td>
<td>-4.7 (-29.8,20.3)</td>
</tr>
<tr>
<td>Diet only</td>
<td>425.9 (10.9)</td>
<td>9.6 (-15.8,35.1)</td>
</tr>
<tr>
<td>Exercise only</td>
<td>424.2 (11.4)</td>
<td>48.6 (22.9,74.3)</td>
</tr>
<tr>
<td>Diet + exercise</td>
<td>416.2 (11.3)</td>
<td>61.6 (35.9,87.3)</td>
</tr>
</tbody>
</table>
Physical Activity, Diet, Inflammation, & Body Composition Trial (PACT):

Participants:

- Age ≥ 60 yrs; Mean age = 70 ± 6 yrs
- BMI ≥ 30 kg/m²; Mean BMI = 35.3 ± 7.3 kg/m²
- Knee pain & radiographic evidence of knee OA
- Sedentary (< 20 min/wk) for the past 6 mo
- 62% female; 83% Caucasian
- N = 87 randomized;
- N = 69 completed interventions and follow-up

Miller et al, *Obesity*, 2006
PACT: Body composition results

Weight lost was 62 ± 42% fat mass; 20 ± 25% lean mass

All group X time interaction P values < 0.001
PACT: Changes in knee strength

**Concentric/lean mass**
- Baseline: 3
- Post-intervention: 5
  - p=0.030 (WL group)
  - p>0.05 (WS group)

**Eccentric/lean mass**
- Baseline: 7
- Post-intervention: 5.5
  - p=0.044 (WL group)
  - p>0.05 (WS group)

Interaction p=0.013

Interaction p=0.023

PACT: Changes in concentric extension knee strength inversely related to changes in fat mass

$r = -0.307, p=0.015$
Effects of weight loss and exercise on frailty in obese older adults
(Villareal et al, Arch Int Med, 2006)

• Healthy >65 yr old men and women
• BMI >30 kg/m²
• Mild-moderate frailty
• 26 wks of WL (n=17) or CONTROL (n=10):
  – Weight loss by CR (750 kcal/d dietary energy deficit) and EX (3 d/wk, 30 mins aerobic + 30 mins strength training)
**Effects of weight loss and exercise on frailty in obese older adults**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group</th>
<th>Treatment Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight, kg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>103.2 ± 19.8</td>
<td>99.7 ± 13.6</td>
<td></td>
</tr>
<tr>
<td>Final</td>
<td>103.9 ± 21.3</td>
<td>91.5 ± 15.4†</td>
<td></td>
</tr>
<tr>
<td>Absolute change</td>
<td>0.7 ± 2.7</td>
<td>−8.2 ± 5.7†</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>% Change</td>
<td>0.5 ± 2.8</td>
<td>−8.4 ± 5.6†</td>
<td></td>
</tr>
<tr>
<td><strong>Fat mass, kg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>47.5 ± 8.9</td>
<td>42.6 ± 7.9</td>
<td></td>
</tr>
<tr>
<td>Final</td>
<td>49.1 ± 13.4</td>
<td>35.9 ± 10.1†</td>
<td></td>
</tr>
<tr>
<td>Absolute change</td>
<td>1.7 ± 4.1</td>
<td>−6.6 ± 3.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>% Change</td>
<td>2.6 ± 6.9</td>
<td>−17.1 ± 11.3</td>
<td></td>
</tr>
<tr>
<td><strong>Fat-free mass, kg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>55.7 ± 13.1</td>
<td>57.1 ± 10.9</td>
<td></td>
</tr>
<tr>
<td>Final</td>
<td>54.7 ± 12.8</td>
<td>55.9 ± 10.9‡</td>
<td></td>
</tr>
<tr>
<td>Absolute change</td>
<td>−1.0 ± 3.5</td>
<td>−1.2 ± 2.1</td>
<td>.75</td>
</tr>
<tr>
<td>% Change</td>
<td>−1.5 ± 5.3</td>
<td>−2.1 ± 3.7</td>
<td></td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD. Obese older adults in the control group received no lifestyle changes; those in the treatment group received 6 months of weekly behavioral therapy for weight loss in conjunction with exercise training 3 times per week.*

†Final value significantly different from baseline, P <.001.

‡Final value significantly different from baseline, P = .04.
**Effects of weight loss and exercise on frailty in obese older adults**

Table 4. Effect of Diet and Exercise Therapy on Strength, Gait, and Balance*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group</th>
<th>Treatment Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee extension, ft/lb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>71.5 ± 23.5</td>
<td>80.2 ± 17.1</td>
<td></td>
</tr>
<tr>
<td>Final</td>
<td>73.7 ± 22.2</td>
<td>89.3 ± 15.3†</td>
<td></td>
</tr>
<tr>
<td>Absolute change</td>
<td>2.2 ± 7.3</td>
<td>9.1 ± 8.0</td>
<td>.04</td>
</tr>
<tr>
<td>% Change</td>
<td>4.3 ± 13.0</td>
<td>12.9 ± 12.5</td>
<td></td>
</tr>
<tr>
<td>Knee flexion, ft/lb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>44.9 ± 16.41</td>
<td>50.3 ± 16.1</td>
<td></td>
</tr>
<tr>
<td>Final</td>
<td>50.3 ± 16.1</td>
<td>61.0 ± 15.1†</td>
<td></td>
</tr>
<tr>
<td>Absolute change</td>
<td>5.4 ± 5.6</td>
<td>10.3 ± 11.3</td>
<td>.008</td>
</tr>
<tr>
<td>% Change</td>
<td>1.1 ± 17.9</td>
<td>25.5 ± 26.6</td>
<td></td>
</tr>
<tr>
<td>Walking speed, m/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>71.6 ± 8.4</td>
<td>71.5 ± 12.9</td>
<td></td>
</tr>
<tr>
<td>Final</td>
<td>70.4 ± 12.7</td>
<td>76.4 ± 11.8‡</td>
<td></td>
</tr>
<tr>
<td>Absolute change</td>
<td>1.3 ± 8.6</td>
<td>4.9 ± 6.5</td>
<td>.04</td>
</tr>
<tr>
<td>% Change</td>
<td>-1.9 ± 12.5</td>
<td>7.6 ± 10.2</td>
<td></td>
</tr>
<tr>
<td>One leg limb stand, s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>5.5 ± 5.9</td>
<td>6.8 ± 8.0</td>
<td></td>
</tr>
<tr>
<td>Final</td>
<td>5.2 ± 5.21</td>
<td>2.2 ± 9.8§</td>
<td></td>
</tr>
<tr>
<td>Absolute change</td>
<td>-0.3 ± 3.9</td>
<td>5.4 ± 9.3</td>
<td>.04</td>
</tr>
<tr>
<td>% Change</td>
<td>-5.5 ± 61.0</td>
<td>79.5 ± 120.0</td>
<td></td>
</tr>
<tr>
<td>Obstacle course, s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>11.8 ± 2.1</td>
<td>11.9 ± 1.9</td>
<td></td>
</tr>
<tr>
<td>Final</td>
<td>11.6 ± 1.7</td>
<td>10.5 ± 1.7‖</td>
<td></td>
</tr>
<tr>
<td>Absolute change</td>
<td>-0.2 ± 0.8</td>
<td>-1.4 ± 1.4</td>
<td>.03</td>
</tr>
<tr>
<td>% Change</td>
<td>-0.8 ± 6.9</td>
<td>-11.3 ± 9.6</td>
<td></td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD. Obese older adults in the control group received no lifestyle changes; those in the treatment group received 6 months of weekly behavioral therapy for weight loss in conjunction with exercise training 3 times per week.

†Final value significantly different from baseline, P = .001.
‡Final value significantly different from baseline, P = .04.
§Final value significantly different from baseline, P = .03.
‖Final value significantly different from baseline, P = .08.
What about dietary-induced weight loss without exercise?
# ADAPT: physical performance results

<table>
<thead>
<tr>
<th></th>
<th>6-min walk distance (m)</th>
<th>Stair-climb time (secs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline mean (SEM)</td>
<td>Baseline mean (SEM)</td>
</tr>
<tr>
<td></td>
<td>Δ from baseline (95% CI)</td>
<td>Δ from baseline (95% CI)</td>
</tr>
<tr>
<td>Healthy lifestyle</td>
<td>434.6 (10.9)</td>
<td>9.59 (0.64)</td>
</tr>
<tr>
<td></td>
<td>-4.7 (-29.8,20.3)</td>
<td>-0.22 (-1.71,1.27)</td>
</tr>
<tr>
<td>Diet only</td>
<td>425.9 (10.9)</td>
<td>9.74 (0.65)</td>
</tr>
<tr>
<td></td>
<td>9.6 (-15.8,35.1)</td>
<td>-1.31 (-2.84,0.22)</td>
</tr>
<tr>
<td>Exercise only</td>
<td>424.2 (11.4)</td>
<td>10.52 (0.66)</td>
</tr>
<tr>
<td></td>
<td>48.6 (22.9,74.3)</td>
<td>-1.63 (-3.16,-0.10)</td>
</tr>
<tr>
<td>Diet + exercise</td>
<td>416.2 (11.3)</td>
<td>10.99 (0.67)</td>
</tr>
<tr>
<td></td>
<td>61.6 (35.9,87.3)</td>
<td>-2.54 (-4.13,-0.95)</td>
</tr>
</tbody>
</table>
Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction, but not with exercise-induced weight loss (Weiss et al, JAP, 2006)

- Healthy 50-60 yr old men and women
- BMI 23.5-29.9 kg/m²
- RCT (12 mo interventions):
  - Weight loss by CR (n=18; 12% intake reduction)
    • WL = -10.7±1.4%
  - Weight loss by aerobic EX (n=16; equal caloric deficit--6 d/wk, ~60 mins/session, ~70% HRmax)
    • WL = -9.5±1.5%
Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction but not with exercise-induced weight loss

Weiss et al, JAP, 2006
Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction but not with exercise-induced weight loss
Further questions

• Are there treatments that target adipose tissue but preserve skeletal muscle, and do these treatments improve physical function?

  – Combination of hypocaloric diet and protein supplement?
  – Combination of hypocaloric diet and resistance training?
Dietary Protein and Body Composition in Older Women

**Hypothesis**: Obese, postmenopausal women consuming a high protein (~1.5 times RDA or 1.3 g/kg/d) hypocaloric diet will lose less lean body mass than women consuming a standard protein hypocaloric diet (0.6 g/kg/d)
### Nutrient Content of Prescribed Diets: Means (SD)

<table>
<thead>
<tr>
<th></th>
<th>High Protein</th>
<th>Low Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=9)</td>
<td>(n=15)</td>
</tr>
<tr>
<td>Energy (kcal/d)</td>
<td>1489 (117)</td>
<td>1267 (150)*</td>
</tr>
<tr>
<td>Protein (gm/d)</td>
<td>112.0 (8.8)</td>
<td>53.9 (3.8)*</td>
</tr>
<tr>
<td>Protein (gm/kg/d)</td>
<td>1.32 (0.19)</td>
<td>0.58 (0.07)*</td>
</tr>
<tr>
<td>Protein (% of energy)</td>
<td>30.1 (0.0)</td>
<td>17.1 (0.1)*</td>
</tr>
<tr>
<td>Carbohydrate (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(% of energy)</td>
<td>45.2 (0.0)</td>
<td>52.3 (0.1)*</td>
</tr>
<tr>
<td>Fat (gm/d)</td>
<td>42.7 (4.3)</td>
<td>38.3 (6.0)</td>
</tr>
</tbody>
</table>

* p<0.05
Body Composition Changes

Percent of total mass lost as lean mass: 15.7±27.1% (high protein) versus 37.5±14.6%, (low protein),  p=0.02
Further questions

• Does weight regain after weight loss result in gain of fat and lean tissue—or mainly fat?
  – Long-term follow up weight loss studies needed
  – Identification of interventions designed to optimize weight loss and fat loss maintenance
DEMO: Body composition after weight regain

52% of weight loss was regained
Changes in body fat with weight loss and weight regain

54% of fat lost was regained
Changes in lean tissue with weight loss and weight regain

33% of lean lost was regained
Further questions

• Does long-term sustained weight loss result in:
  – Delayed onset of physical/cognitive disability?
  – Slower progression of chronic disease?
  – Improved quality of life?
  – Increased mortality and/or fracture risk?
“See, the problem with doing things to prolong your life is that all the extra years come at the end, when you’re old.”
Acknowledgements

Claude Pepper Older Americans Independence Center (1P30 AG21332)

NIH/NIA 1R01 AG/DK20583
SlimFast Institute®
WFU General Clinical Research Center

Melanie Bopp
Charlotte Crotts
Michelle Gordon
Linda Easter
Denise Houston
Steve Kritchevsky
Mary Lyles
Marco Pahor
Xuewen Wang
Steve Messier
Gary Miller
Justin Johnson