



Positive, Negatives and Unknowns in Obesity Treatment in Older Adults

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Obesity in Older Adults: Technical Review and Position Statement of ASN and TOS, 2005

“The appropriate clinical approach to obesity in older persons is controversial because of the reduction in relative health risks associated with increasing BMI in older adults, the uncertain effectiveness of obesity treatment in this group, and the potential harmful effects of weight loss on muscle and bone mass.”

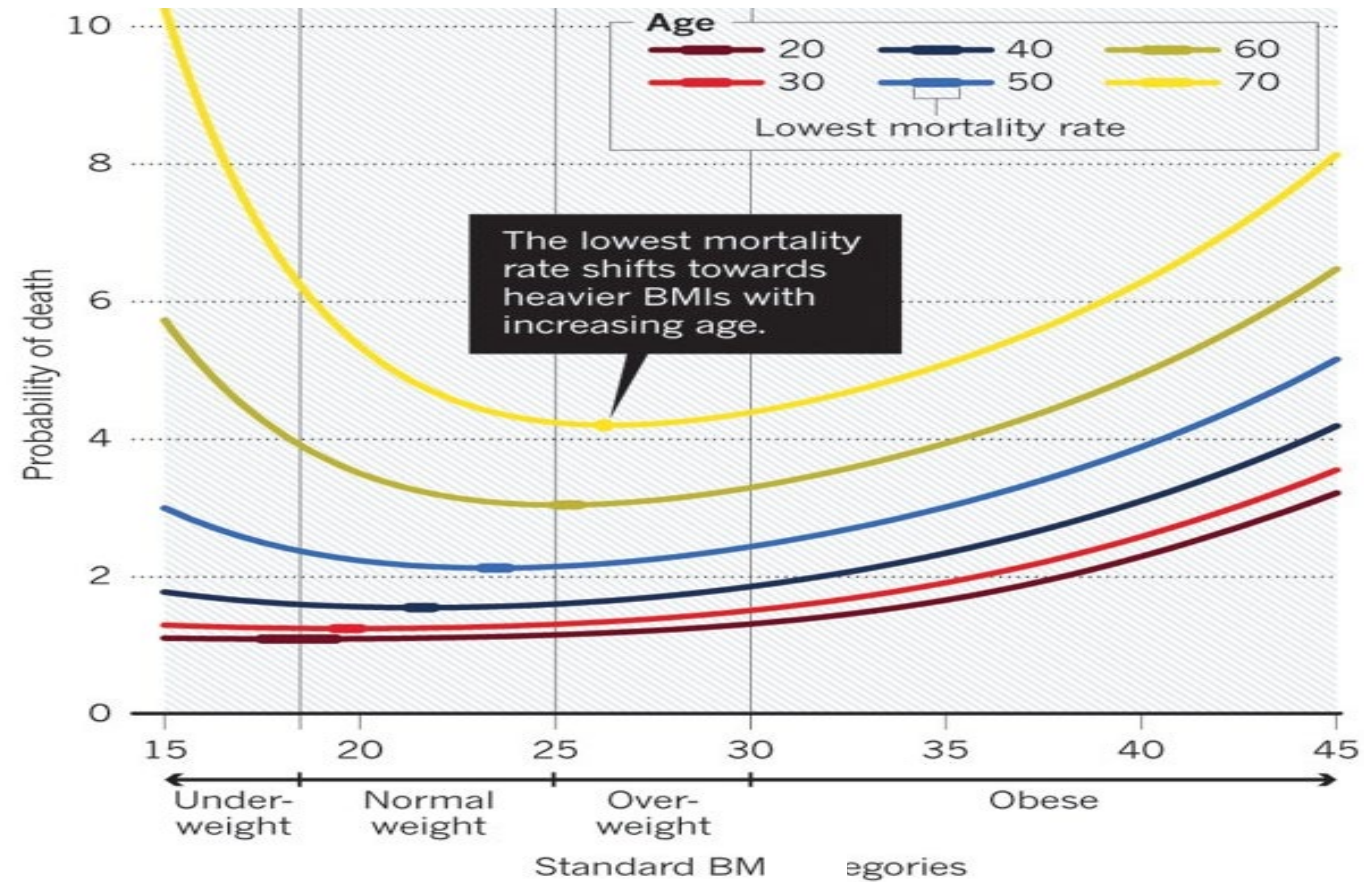
2013 AHA/ACC/TOS Guidelines for the Management of Overweight and Obesity in Adults

“The overall safety of weight loss interventions for patients aged 65 and older remains controversial.

Although older participants tend to respond well to comprehensive behavioral weight loss treatments and they experience the same improvements in CVD risk factors as do middle-age participants, the effect of weight loss treatment on risk for CVD, longevity, and osteoporosis has not been extensively studied.”

Associations between BMI, Weight Loss and Mortality: Observational Studies

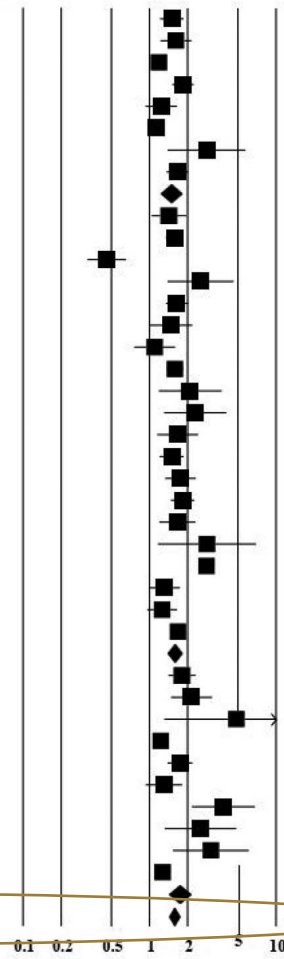
BMI and Mortality by Age



Hughes, *Nature* 2013 (adapted from Childers & Allison, *Int J Obesity* 2010).

Weight Loss and Mortality: a Meta-analysis

Group by Gender	Study name	Country	Sample size	Exposure: follow up (y)	Weight/BMI	Statistics for each study				Hazard ratio and 95% CI	
						Hazard Ratio	Lower limit	Upper limit	p-Value		
M	Cornoni-Huntley,1991	USA	438	3;10	weight	1.50	1.20	1.88	0.00		
M	Dey, 2001	Sweden	343	5;10	weight	1.62	1.21	2.16	0.00		
M	Kundoston, 2005	USA	1029	2;10	weight	1.19	1.06	1.33	0.00		
M	Lee, 2011	USA	971	5;9	weight	1.84	1.50	2.26	0.00		
M	Murphy, 2014	USA	306	5;8	weight	1.24	0.92	1.67	0.16		
M	Santanasto, 2016	USA	934	5;12	weight	1.12	1.02	1.23	0.02		
M	Wallace, 1995	USA	247	4;2	weight	2.83	1.38	5.81	0.00		
M	Wanamethee, 2005	UK	527	4;7	weight	1.66	1.35	2.04	0.00		
Overall men						1.47	1.22	1.76	0.00		
M&W	Amador, 2005	USA	161	2;5	weight	1.41	1.03	1.93	0.03		
M&W	Arnold,2010	USA	1057	NR;7	weight	1.58	1.33	1.88	0.00		
M&W	Atlantis, 2010	Australia	127	10;12	weight	0.46	0.32	0.66	0.00		
M&W	Crotty, 2002	Australia	1,396	2;4	weight	2.53	1.37	4.67	0.00		
M&W	Dahl, 2013	Sweden	211	2;18	BMI	1.65	1.34	2.04	0.00		
M&W	DeHlander, 2013	Europe	1053	4;7	weight	1.48	0.99	2.21	0.05		
M&W	Graf, 2015	Switzerland	46	21;2	BMI	1.10	0.75	1.61	0.62		
M&W	Haugsgjerd, 2016	Norway	460	5;14	weight	1.59	1.34	1.88	0.00		
M&W	Keller,2005	Canada	539	2;6	BMI	2.10	1.17	3.77	0.01		
M&W	Lee, 2018	Taiwan	NR	2;18	weight	2.30	1.30	4.08	0.00		
M&W	Locher, 2007	USA	188	NR;3	weight	1.67	1.14	2.45	0.01		
M&W	Lunchsinger,2008	USA	441	2;18	weight	1.50	1.19	1.89	0.00		
M&W	Maralani, 2013	Australia	109	5;14	BMI	1.76	1.32	2.35	0.00		
M&W	Mulligan, 2017	UK	577	3;15	weight	1.83	1.46	2.29	0.00		
M&W	Newman, 2001	USA	1645	3;4	weight	1.66	1.18	2.33	0.00		
M&W	Nishida, 2019	Japan	160	2;3	weight	2.85	1.15	7.04	0.02		
M&W	Park, 2018	USA	749	3;10	weight	2.83	2.52	3.17	0.00		
M&W	Schaap, 2018 <26 BMI	Netherlands	108	3;20	BMI	1.32	0.99	1.76	0.06		
M&W	Schaap, 2018 >26 BMI	Netherlands	153	3;20	BMI	1.26	0.95	1.67	0.11		
M&W	Son, 2020	Korea	609	4;12	weight	1.68	1.64	1.72	0.00		
Overall men & women						1.58	1.40	1.79	0.00		
W	Cornoni-Huntley ,1991	USA	1034	3;10	weight	1.80	1.40	2.31	0.00		
W	Dey, 2001	Sweden	343	5;10	weight	2.15	1.46	3.16	0.00		
W	Ho,1994	Hong Kong	34	2;3	weight	4.88	1.30	18.36	0.02		
W	Kundoston, 2005	USA	1459	2;10	weight	1.23	1.13	1.34	0.00		
W	LeBlanc, 2018	USA	183	20;5	weight	1.74	1.37	2.20	0.00		
W	Murphy, 2014	USA	356	5;8	weight	1.30	0.92	1.83	0.13		
W	Reynolds 1999 normal BMI	USA	93	2;6	weight	3.84	2.14	6.89	0.00		
W	Reynolds 1999 high BMI	USA	63	2;6	weight	2.53	1.30	4.91	0.01		
W	Reynolds 1999 low BMI	USA	49	2;6	weight	3.06	1.52	6.16	0.00		
W	Santanasto, 2016	USA	934	5;12	weight	1.27	1.16	1.40	0.00		
Overall women						1.74	1.45	2.11	0.00		
Overall						1.59	1.45	1.74	0.00		



Among adults aged 65+ yrs, weight loss was associated with a 59% increased risk of mortality over follow-up ranging from 2 to 18 yrs

Only 2 of the studies included results for “intentional” weight loss (HR [95% CI]: 0.92 [0.54, 1.54])

Perceived Weight Change and Mortality: British Regional Heart Study

Among men aged 56-75 yrs, unintentional weight loss predicted mortality over 7 yrs of follow-up

	No change (53%)	Weight gain (29%)	Unintentional weight loss (11%)	Intentional Weight Loss		
				All (7%)	Personal reason	Physician's advice/ ill health
Total mortality, all	1.00	0.86 (0.69, 1.08)	1.71 (1.33, 2.19)	1.00 (0.91, 1.10)	0.59 (0.34, 1.00)	1.37 (0.96, 1.94)
Total mortality, ≥ 65 y	1.00	0.92 (0.75, 1.13)	1.66 (1.35, 2.04)		0.73 (0.41, 1.30)	1.38 (0.90, 2.10)
CVD mortality	1.00	0.94 (0.68, 1.30)	1.63 (1.16, 2.43)	0.98 (0.85, 1.14)	0.90 (0.46, 1.78)	0.98 (0.55, 1.72)

Wannamethee et al., *Arch Intern Med* 2005; Adjusted for age, social class, smoking, PA, alcohol, BMI in 1996, obesity in 1992, perceived health status, Hx of HTN, CHD, stroke, DM, other CVD conditions, and cancer



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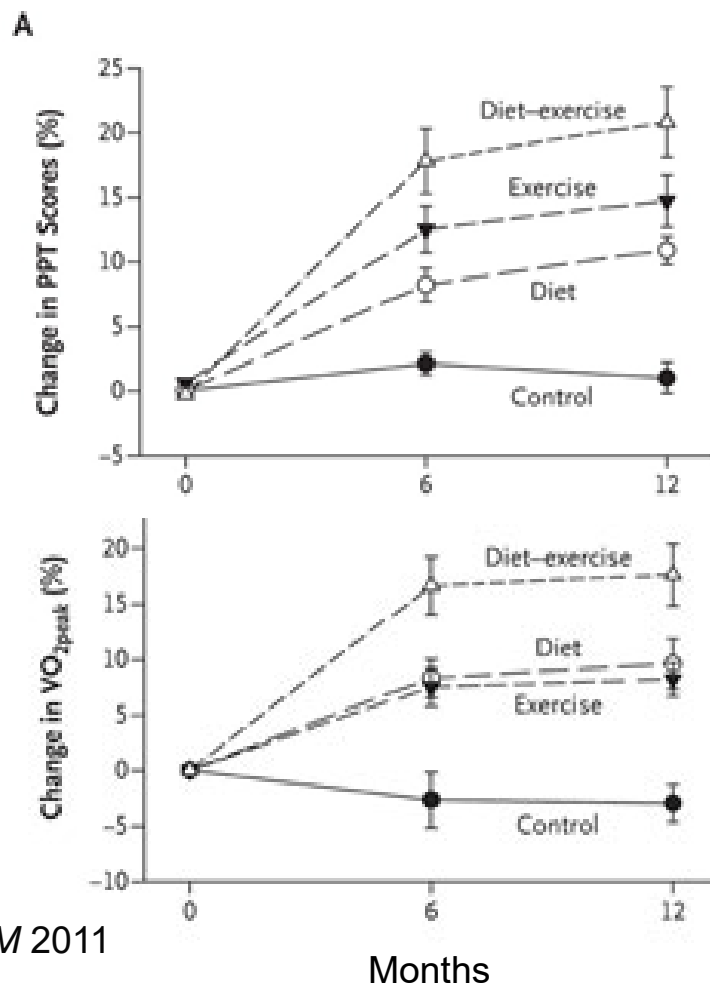
Evidence in Support of Obesity Treatment in Older Adults with Overweight/Obesity from Randomized Controlled Trials

RCTs show benefits of caloric restriction on metabolic risk factors and disease

- A lifestyle intervention involving caloric restriction and increasing physical activity reduced blood pressure in older adults with hypertension in TONE (Whelton et al., *JAMA* 1998; ~2.5 yrs of follow-up)
- A lifestyle intervention involving caloric restriction and increasing physical activity in the Diabetes Prevention Program was most effective for prevention of diabetes in 60-85 yr olds compared to younger adults (Crandall et al., *J Geron Med Sci* 2006; ~3.2 yrs of follow-up)
- An intensive lifestyle intervention involving caloric restriction and increasing physical activity was at least, if not more, effective in producing weight loss and improving fitness and CVD risk factors among those aged 65+ vs. 45-64 yrs of age in Look AHEAD (Espeland et al., *J Am Geriatr Soc* 2013; ~4 yrs of follow-up)



RCTs suggests caloric restriction improves physical function over the short term



Caloric restriction, particularly when combined with exercise, results in significant improvements in physical performance and cardiorespiratory fitness (VO₂ peak, 6 minute walk distance, 400-m walk time, stair climb time)

Villareal et al., *NEJM* 2011

Despite this evidence, there is reluctance to recommend obesity treatment in older adults

- **Risk of nutritional inadequacy**
 - Caloric restriction during weight loss may exacerbate already low nutrient intakes
- **Exacerbate age-related losses in lean mass**
 - Sarcopenic obesity
 - Initiate/worsen functional decline

Adults lose muscle mass and strength with increasing age

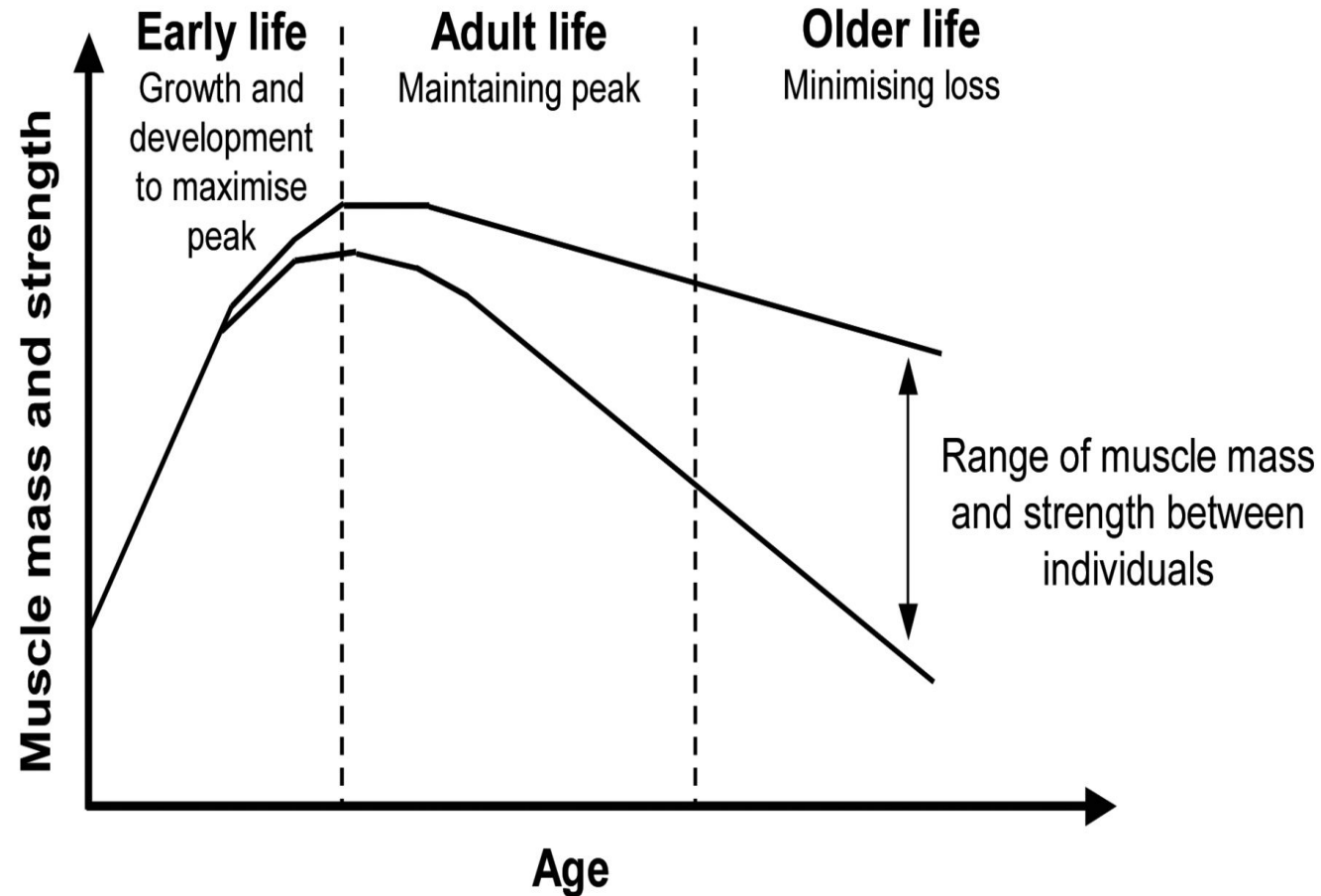
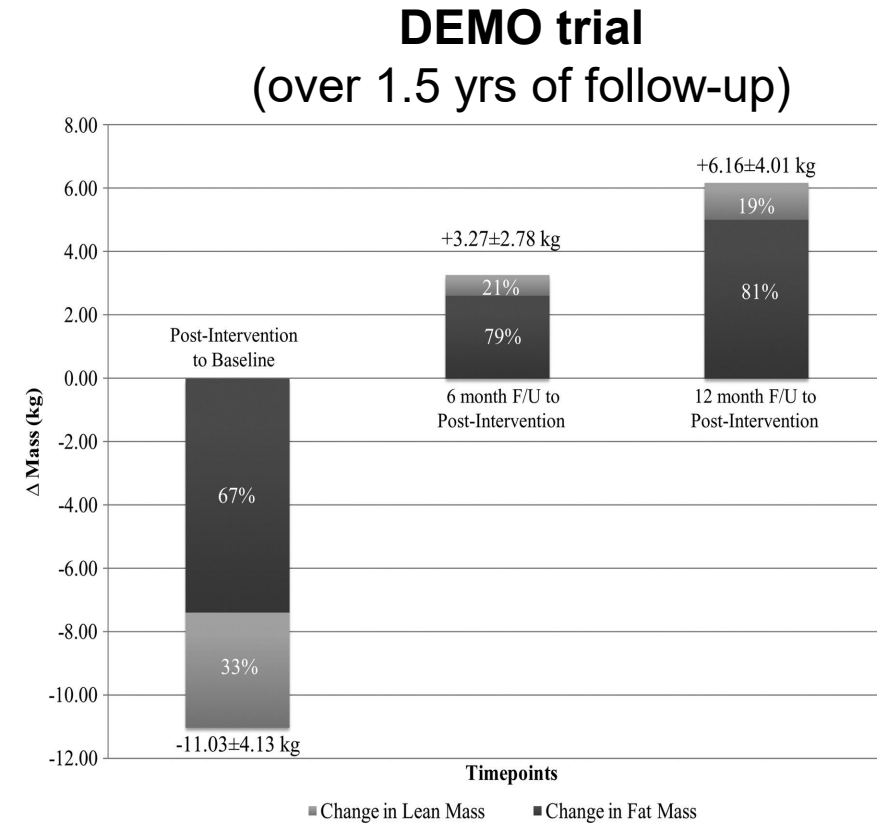
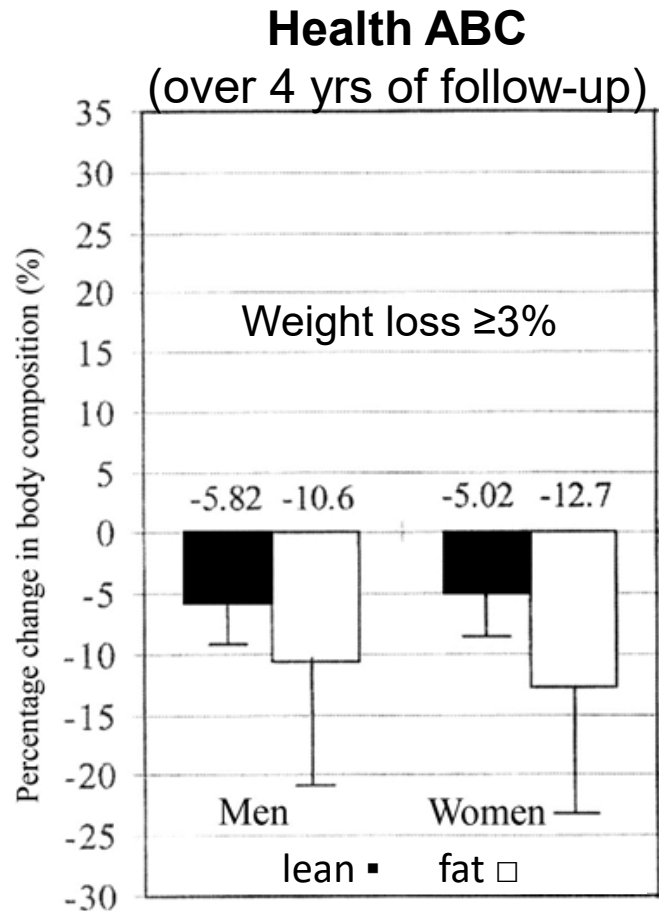


Figure adapted from Sayer et al., *Age Ageing* 2013

Effect of weight loss on lean mass

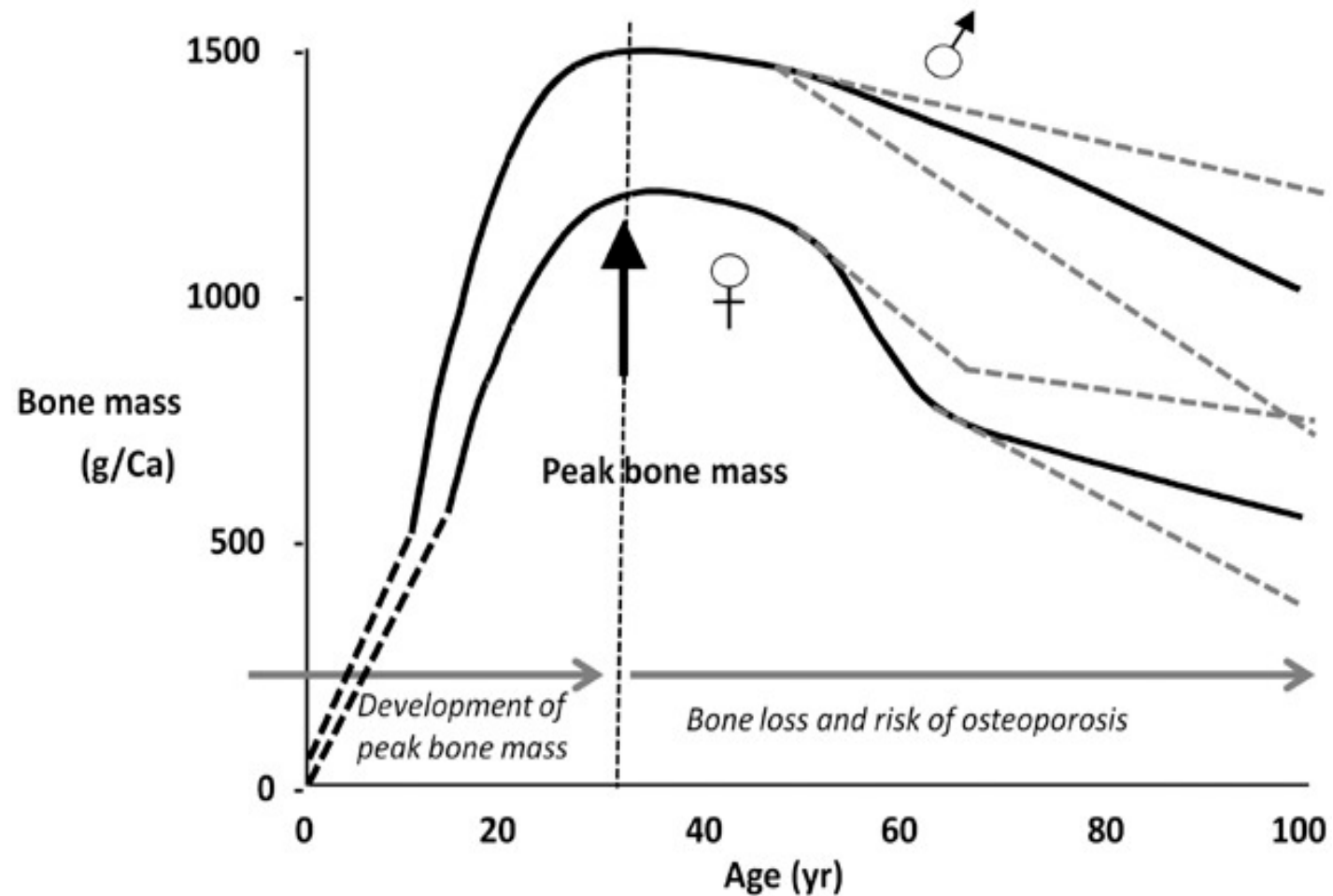


More lean mass is lost during weight loss than is gained during weight regain

Despite this evidence, there is reluctance to recommend obesity treatment in older adults

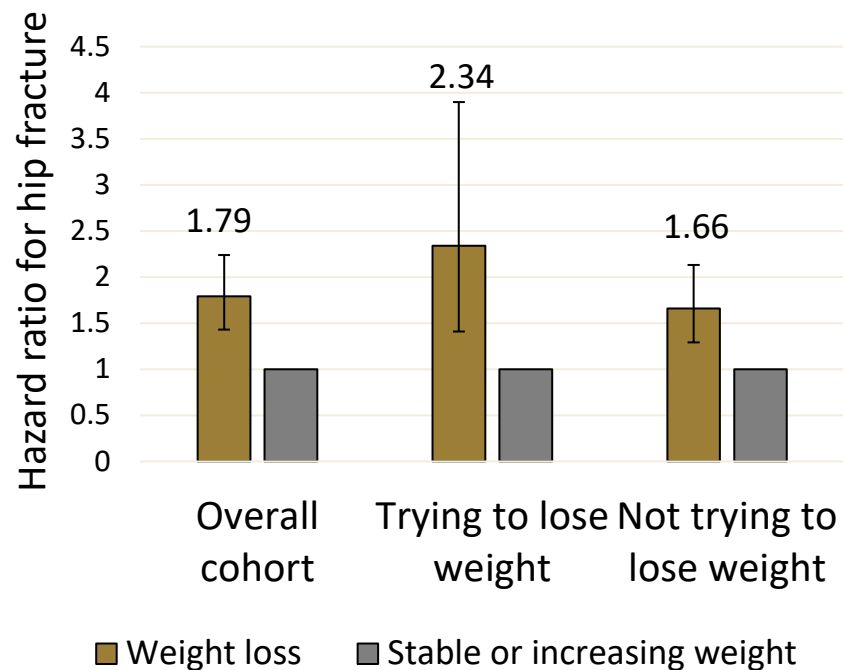
- **Risk of nutritional inadequacy**
 - Caloric restriction during weight loss may exacerbate already low nutrient intakes
- **Exacerbate age-related losses in lean mass**
 - Sarcopenic obesity
 - Initiate/worsen functional decline
- **Exacerbate age-related losses in bone mineral density**
 - Increase risk of fractures

Adults lose bone mass with increasing age



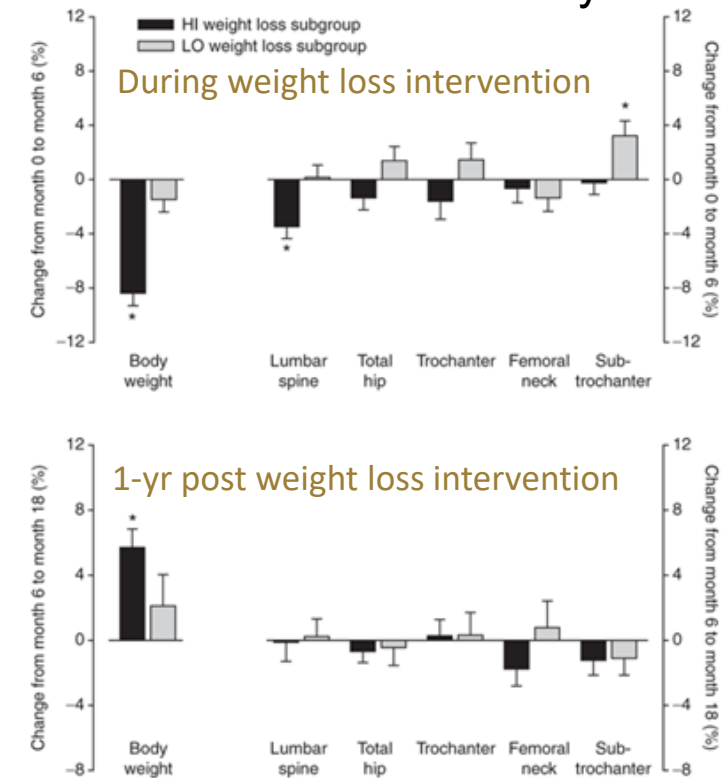
Effect of weight loss on bone mineral density and risk of fractures

Study of Osteoporotic Fractures (over ~6.6 yrs of follow-up)



* ≥5% weight change

Bone Mineral Density



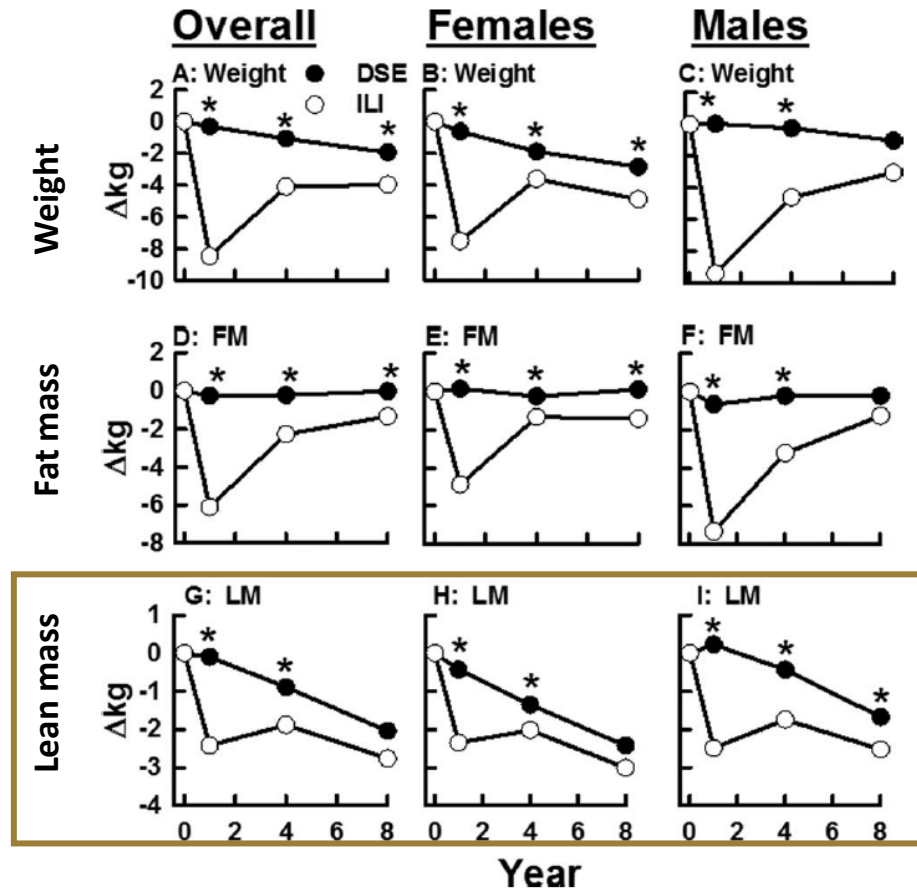
Weight regain does not restore weight loss-induced bone loss

Weight loss may result in worse functional / metabolic health in the long-term IF (when...) weight regain occurs

Since the accretion of muscle and bone are impaired
– and fat accretion is accelerated – with aging,
does weight loss and subsequent regain result in persistent
muscle and bone loss, and more relative fat, in older adults?

Limited evidence suggests improvements in physical function and other health outcomes can be maintained and mortality risk reduced over the long-term despite weight regain and lean mass and bone loss

Effect of an intensive lifestyle intervention on total body, fat and lean mass over 8 years: Look AHEAD

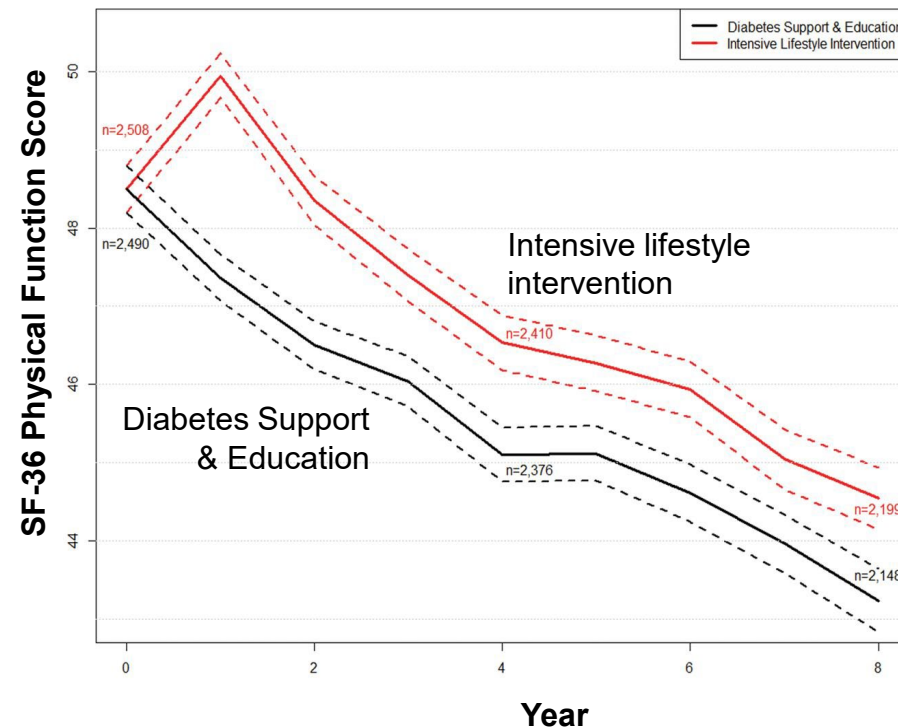
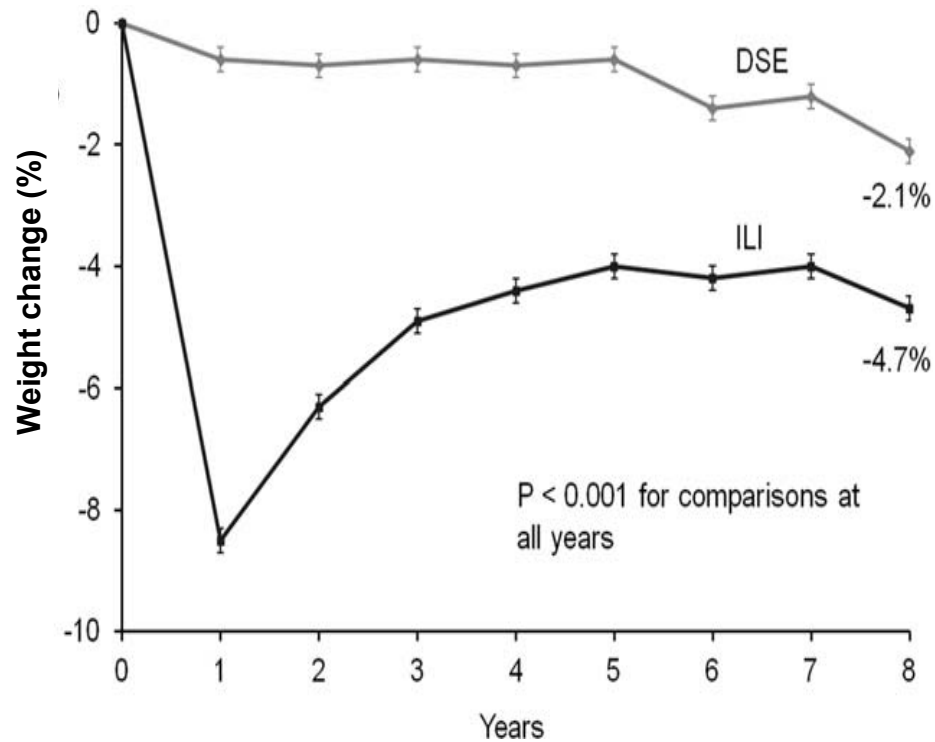


● DSE (control) ○ Intensive lifestyle intervention

Participants randomized to the intensive lifestyle intervention arm regained body weight and fat mass to a greater extent than lean mass.

Participants randomized to the diabetes support and education (control) arm also lost lean mass...

Effect of an intensive lifestyle intervention on self-reported physical function over 8-years: Look AHEAD

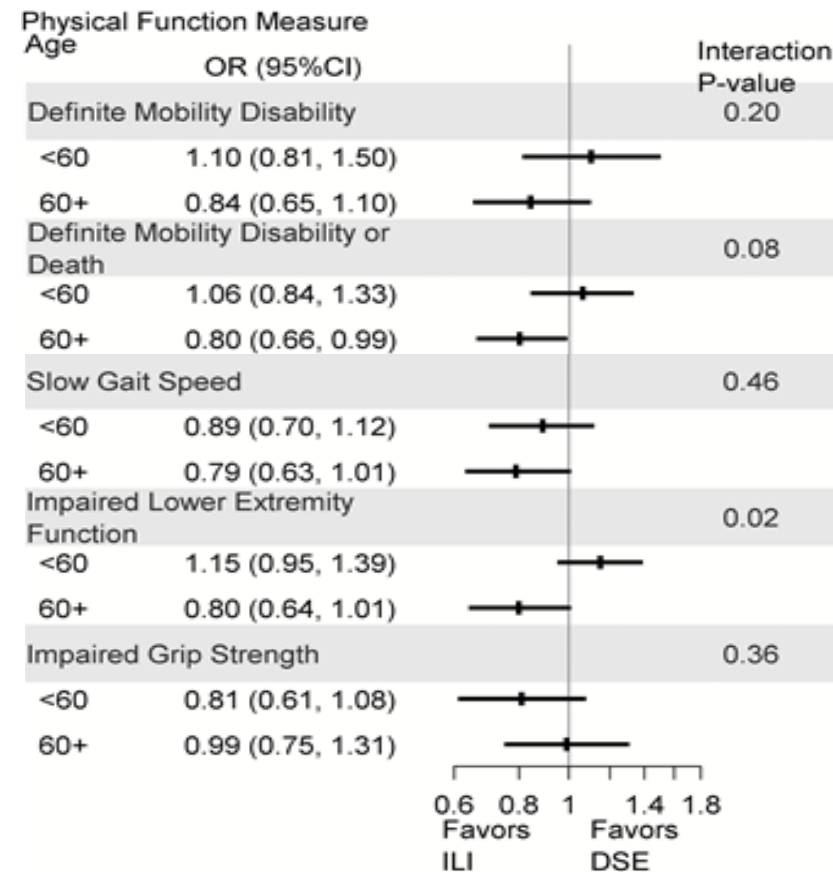


Participants randomized to the intensive lifestyle intervention arm had improved self-reported physical function that was maintained despite weight regain

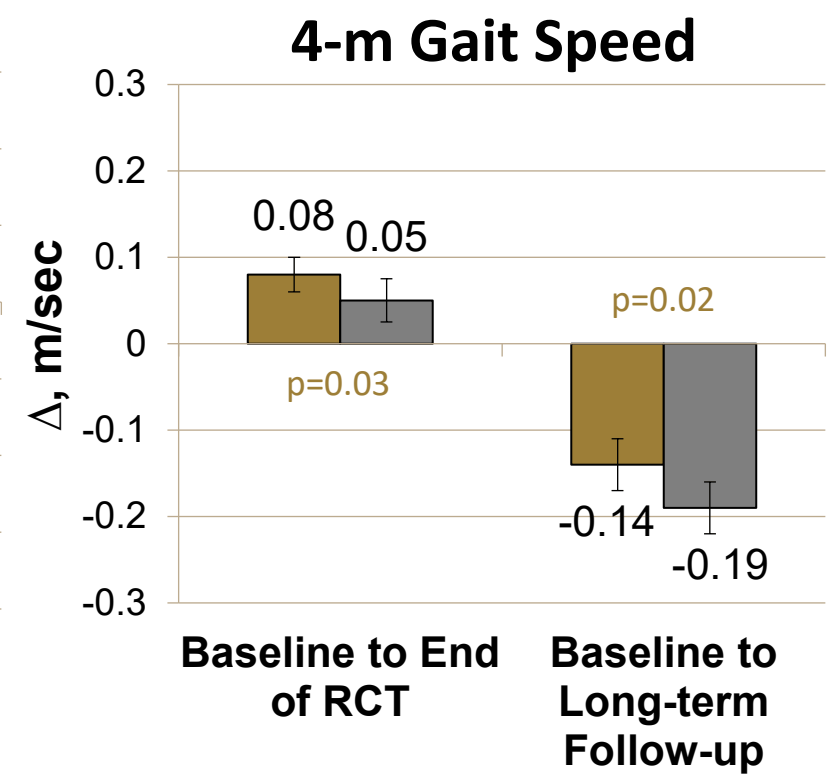
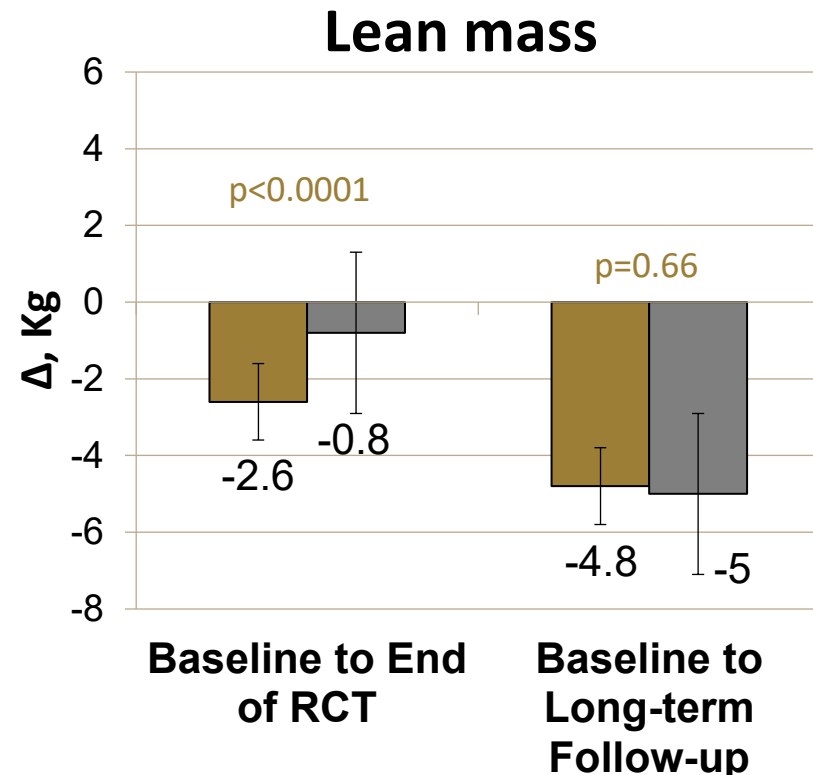
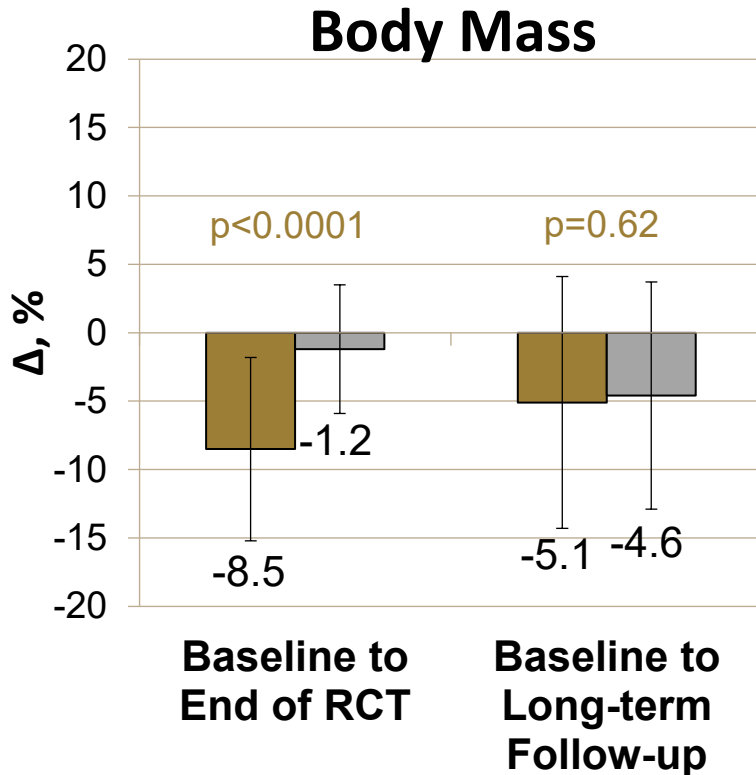
Effect of an intensive lifestyle intervention* on physical performance ~11 years post-randomization: Look AHEAD

Participants randomized to the intensive lifestyle intervention (ILI) arm had faster gait speed and better physical performance and were less likely to have slow gait speed (<0.8 m/s; OR [95% CI]: 0.84 [0.71-0.99]).

Intervention effect tended to be stronger in older than in younger participants.



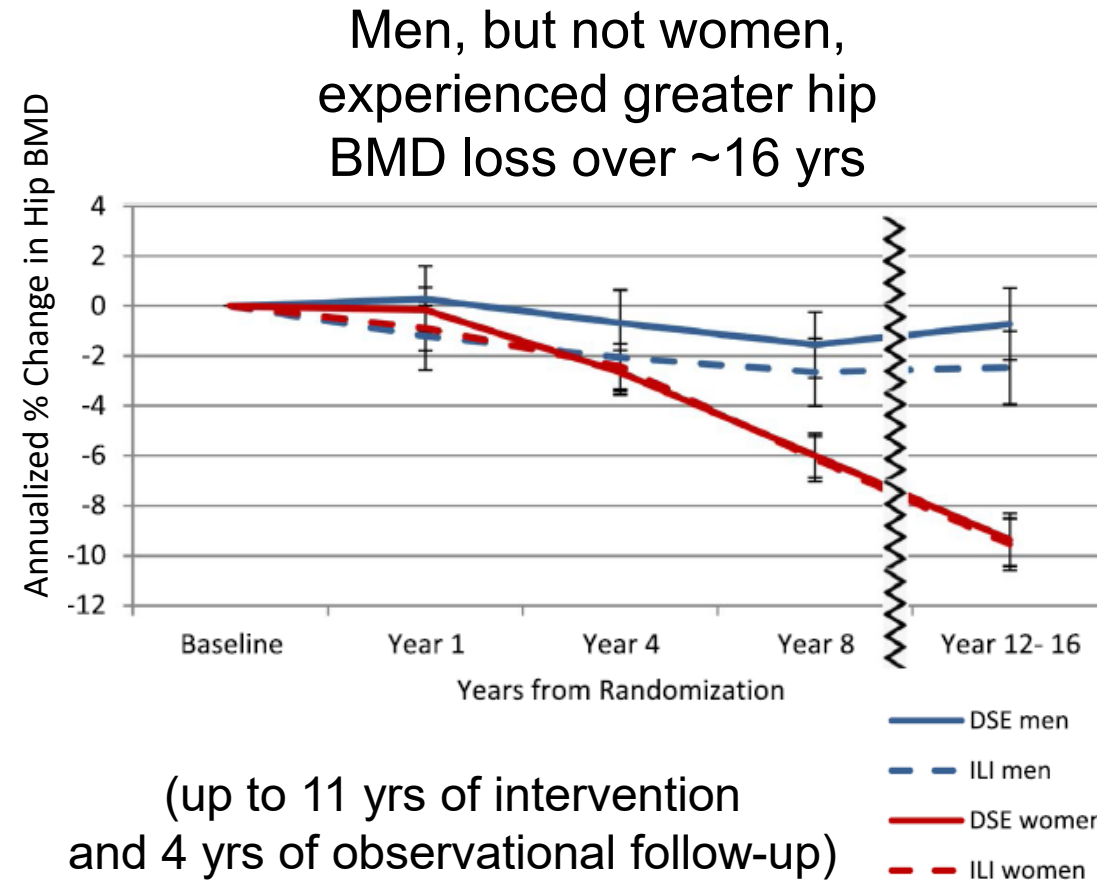
Effect of caloric restriction on weight, lean mass and gait speed at end of RCT and ~9 years post-RCT: HOPE



■ CR ■ No CR

Houston et al., *Obesity Week* 2022. Pooled analysis of participants from 5 prior RCTs of caloric restriction ~9 years post-intervention (n=426). LS means (95% CI) adjusted for sex, race, baseline value, exercise assignment, time and study

Effect of an intensive lifestyle intervention* on bone mineral density over ~16 years: Look AHEAD

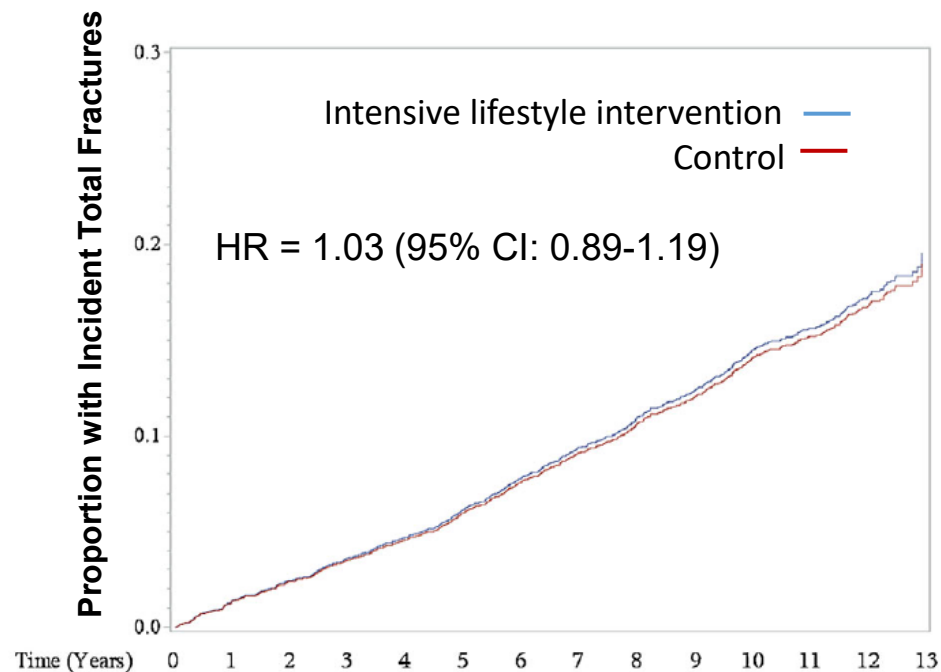


Johnson et al., *Arch Osteoporos* 2023.

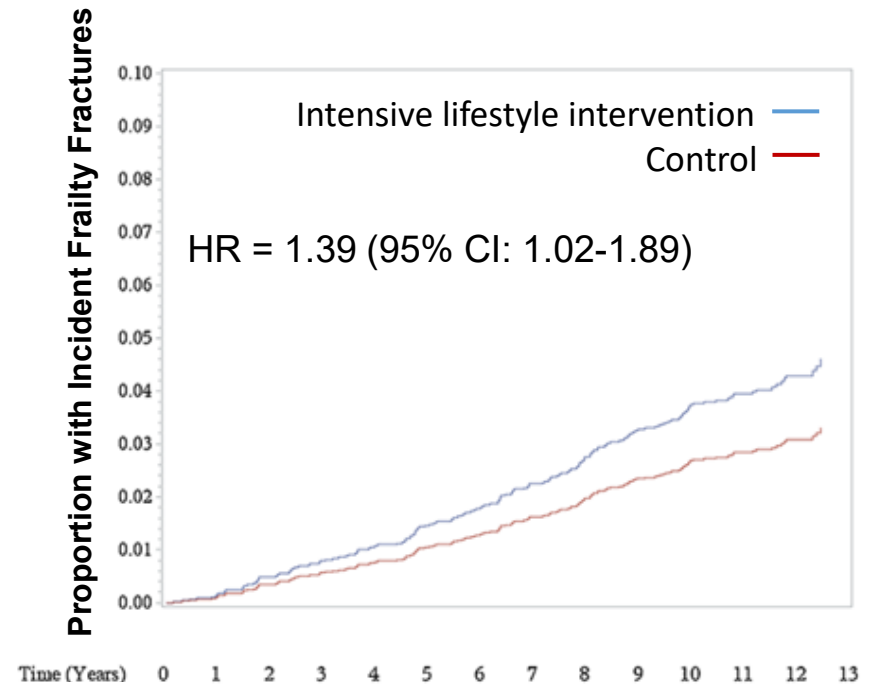
* intervention ended ~10 years post-randomization

Effect of an intensive lifestyle intervention* on risk of fractures over ~11 years: Look AHEAD

No difference in total (or hip) fractures but increased risk of frailty fractures



Hip fracture HR = 1.69 (95% CI: 0.93–3.07)

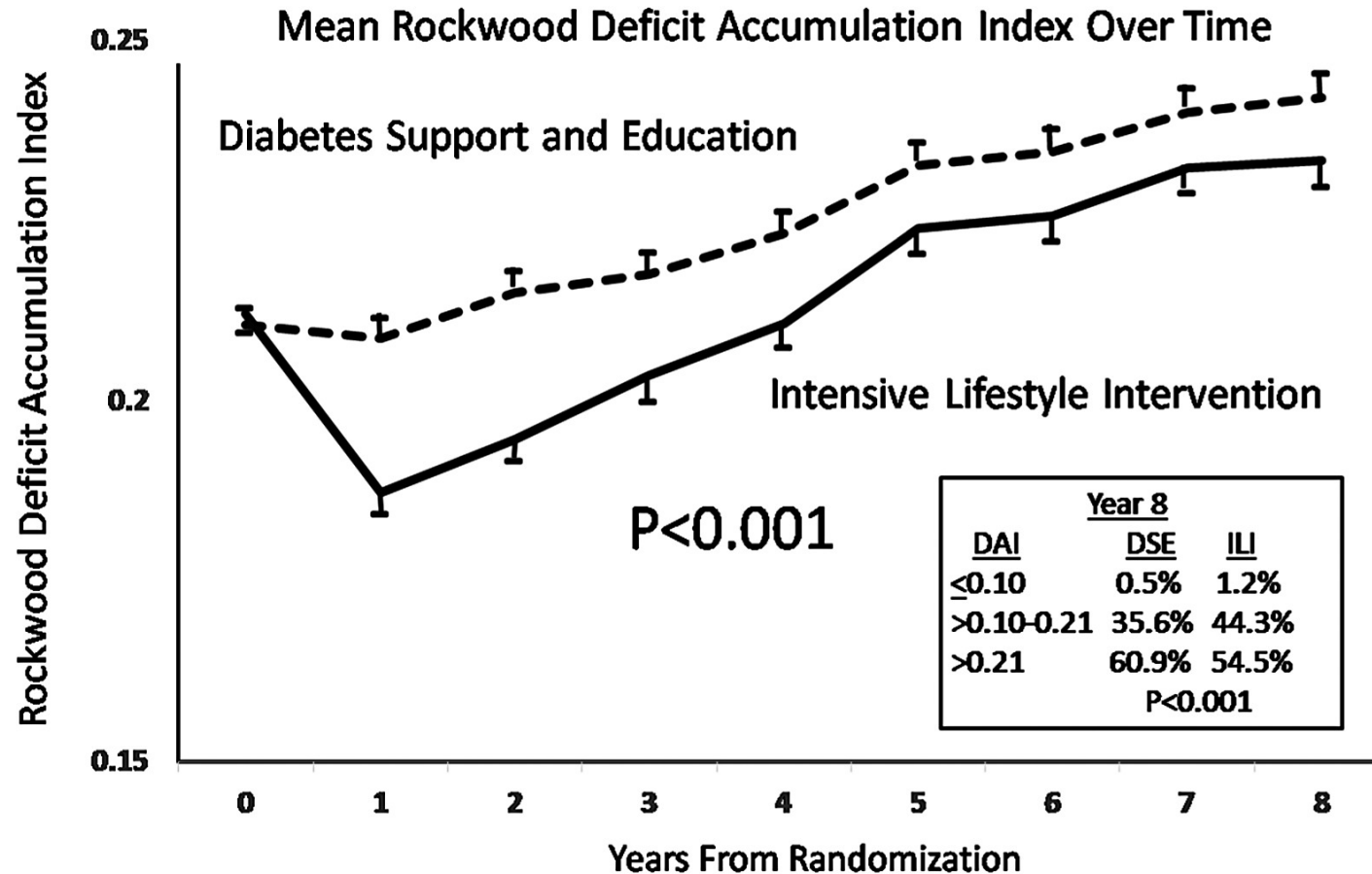


Frailty fracture = hip, pelvis, upper arm or shoulder fracture

Johnson et al., *J Bone Miner Res* 2017

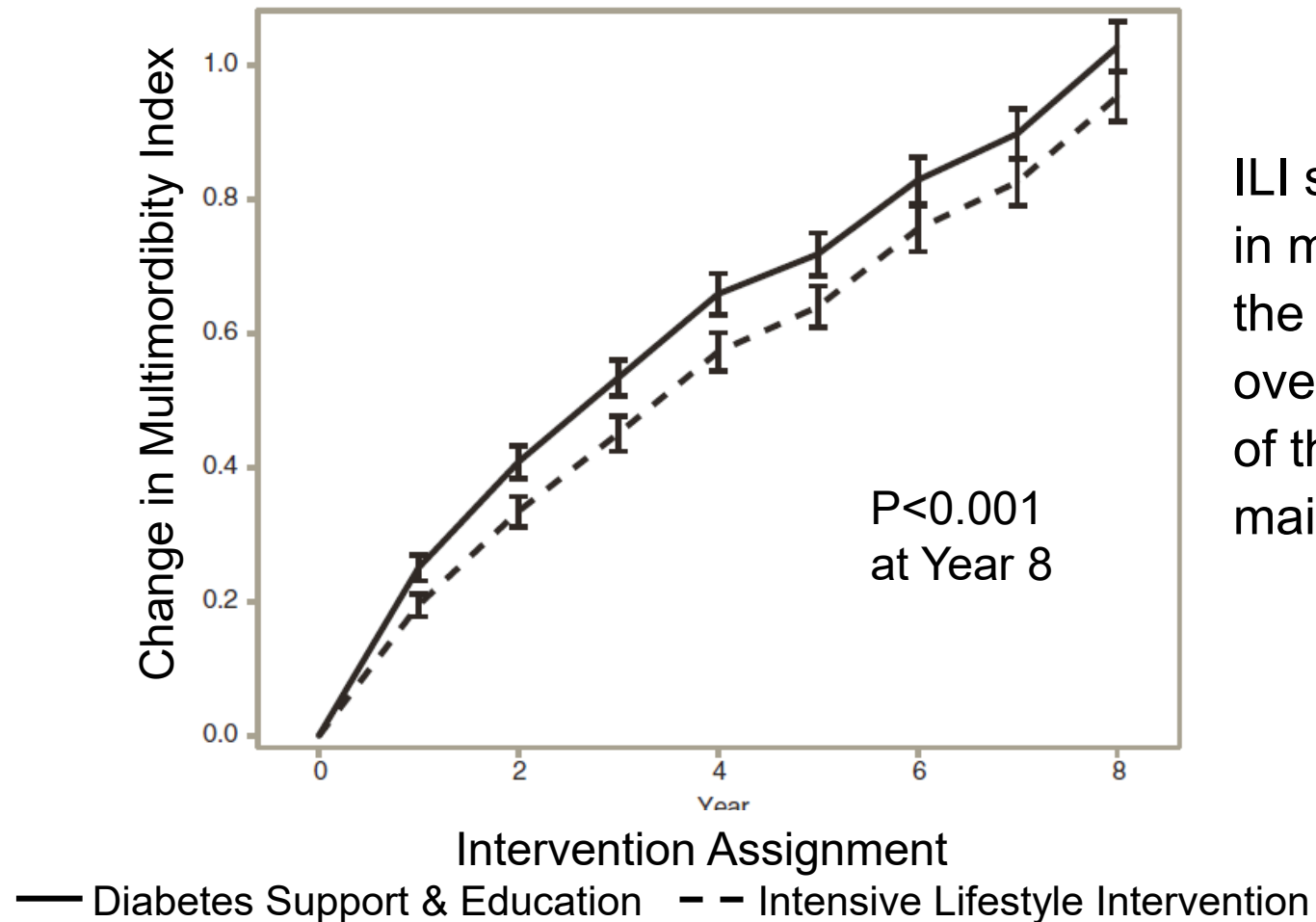
* intervention ended ~10 years post-randomization

Effect of an intensive lifestyle intervention on frailty over 8 years: Look AHEAD



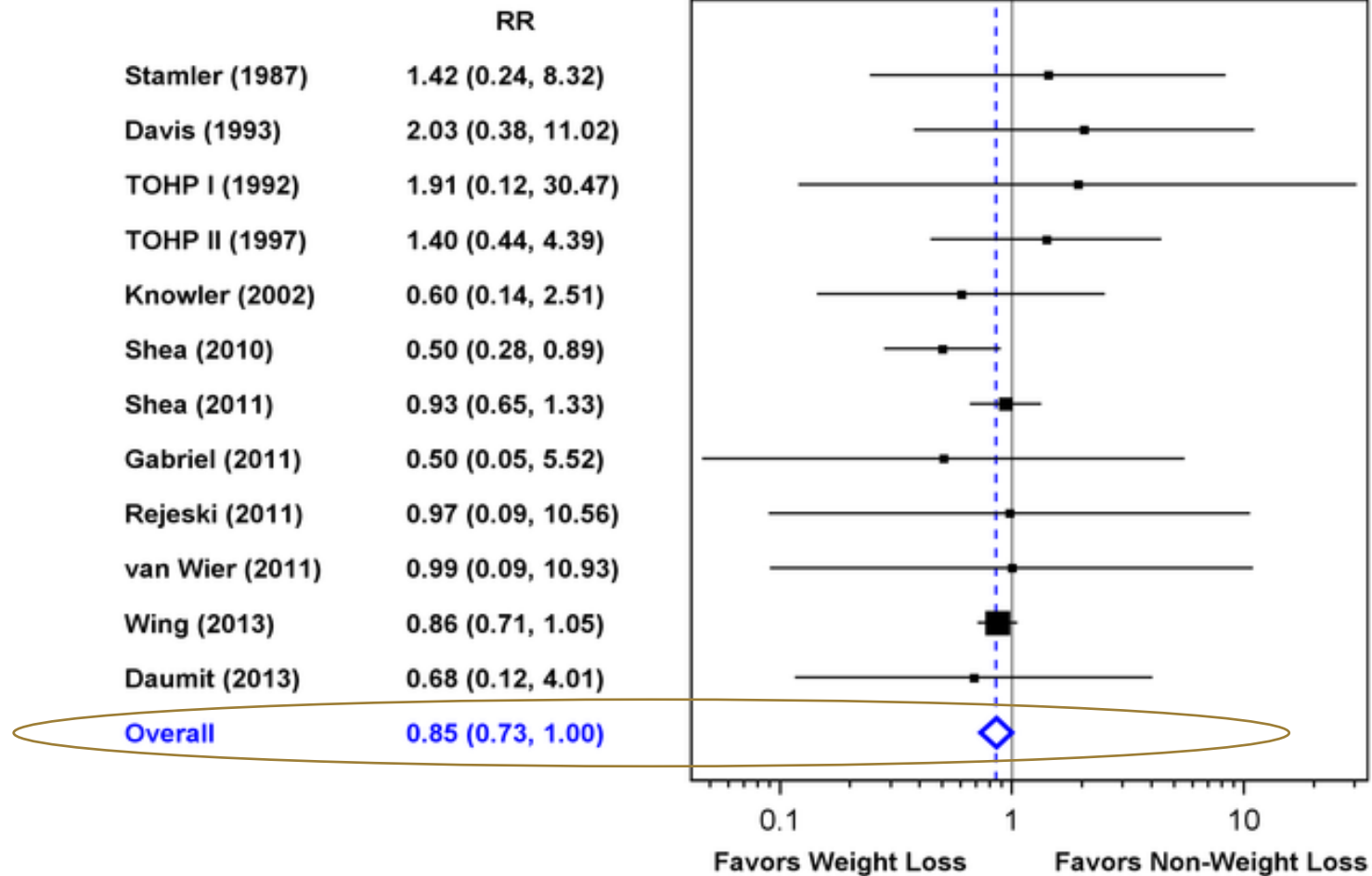
Benefits of ILI* were maintained over 18 years of follow-up, even after the intervention was terminated

Effect of an intensive lifestyle intervention on multimorbidity over 8 years: Look AHEAD



ILI slowed the increase in multimorbidity, with the benefits accruing over the first four years of the intervention and maintained over 8 years

Randomization to Caloric Restriction and Mortality: a Meta-Analysis



Risk of mortality was lower in individuals randomized to caloric restriction compared to no caloric restriction over follow-up ranging from 18 months to 13 yrs

Is obesity treatment recommended in older adults with overweight or obesity?

- Evidence shows weight loss improves metabolic risk factors, chronic conditions, and physical function in older adults with obesity... at least over the short term
- However... weight loss recommendations may require adaptation for older adults
 - Many weight-related disease risk factors lose predictive power in older age
 - The clinical context is markedly different (frailty, multimorbidity, and polypharmacy)
 - Physical, cognitive and emotional functioning are as important outcomes for older adults as disease and mortality
 - The weight trajectory is markedly different in older adults
 - Losing weight might be good, but gaining weight back may be worse

Additional research needed to answer...

- Are there weight loss interventions (nutrition, physical activity, or medications) that preferentially target fat while preserving lean and bone mass?
- Does weight regain after weight loss interventions result in gain of fat, lean and bone mass — or mainly fat?
 - Increase risk of sarcopenic and/or osteopenic obesity?
- Does the age-related loss of lean and bone mass in individuals not randomized to a weight loss intervention catch up with the weight-loss accelerated losses observed in individuals who underwent a weight loss intervention?
- If weight is regained, do health benefits of the past weight loss persist?

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