Body composition

What is the impact of obesity management medications on body composition?

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Disclosures: Professor John B Dixon

I-Nova	Advisory board
Nestle Health Science	Consultant – Advisory board
Reshape Lifesciences	Consultant
Novo Nordisk	Advisory board and speaker fees
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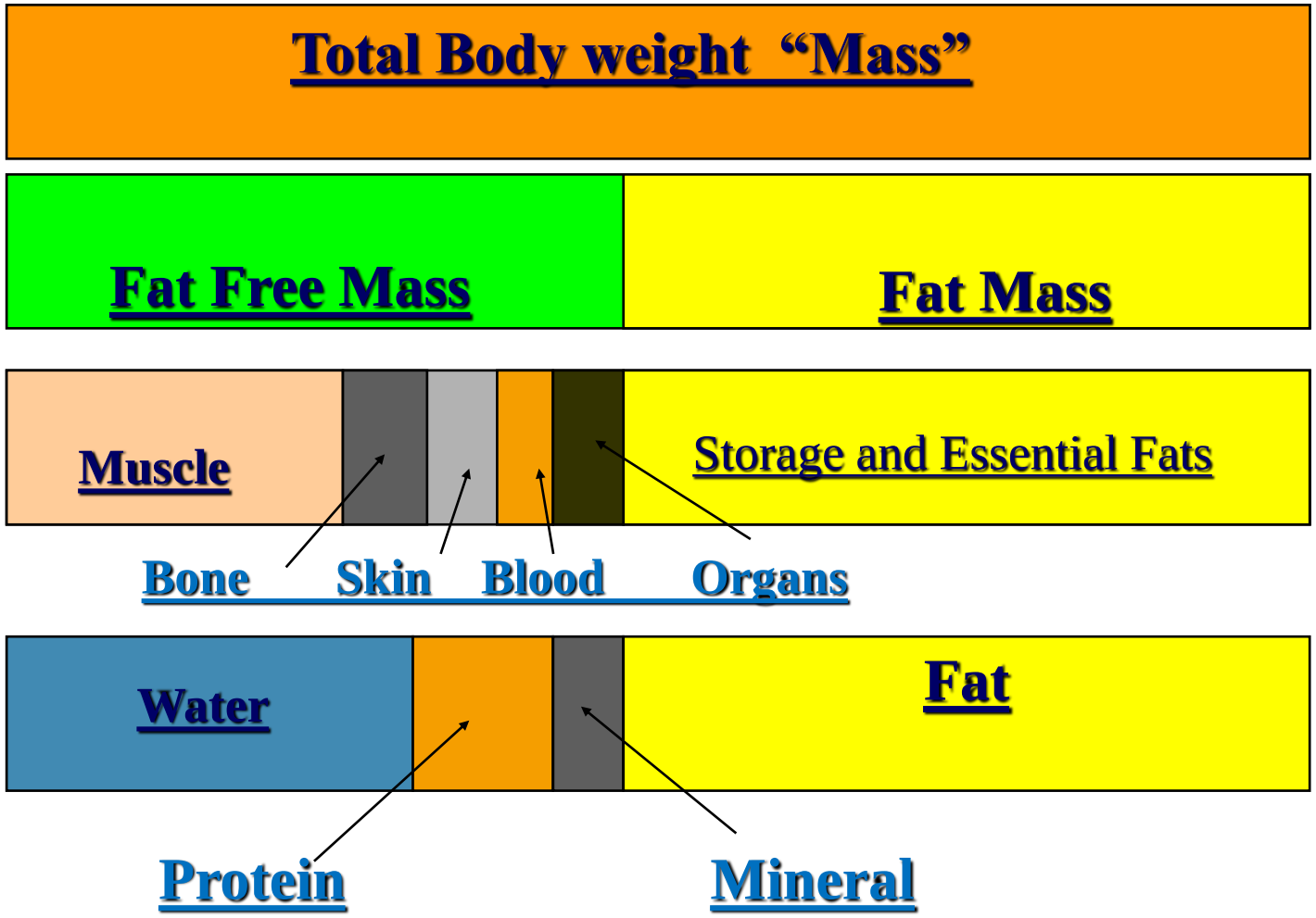
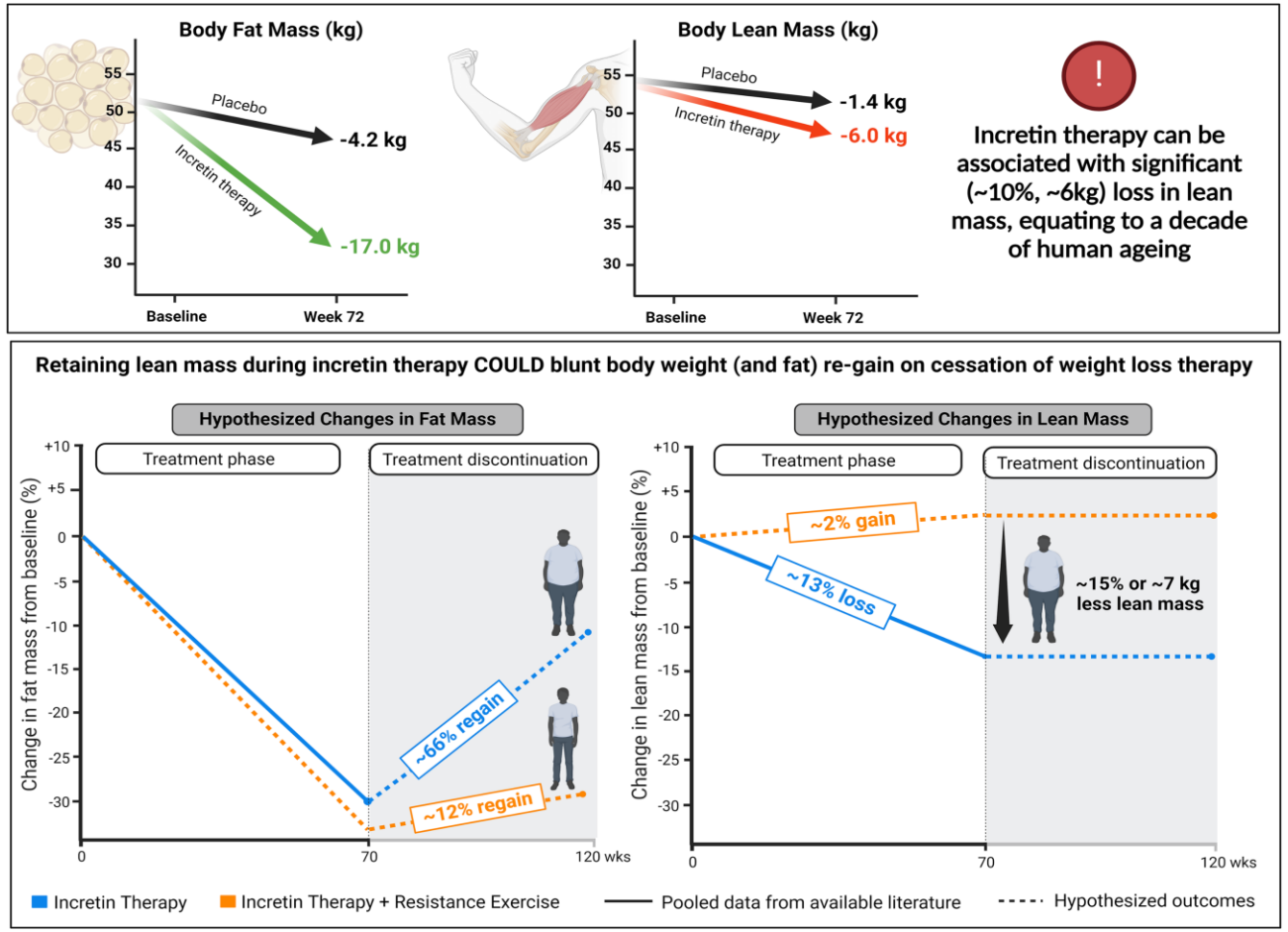
Body Composition Compartments



From: **Incretin-Based Weight Loss Pharmacotherapy: Can Resistance Exercise Optimize Changes in Body Composition?**

Diabetes Care. Published online April 30, 2024. doi:10.2337/dci23-0100



What is the flaw in this hypothesis?

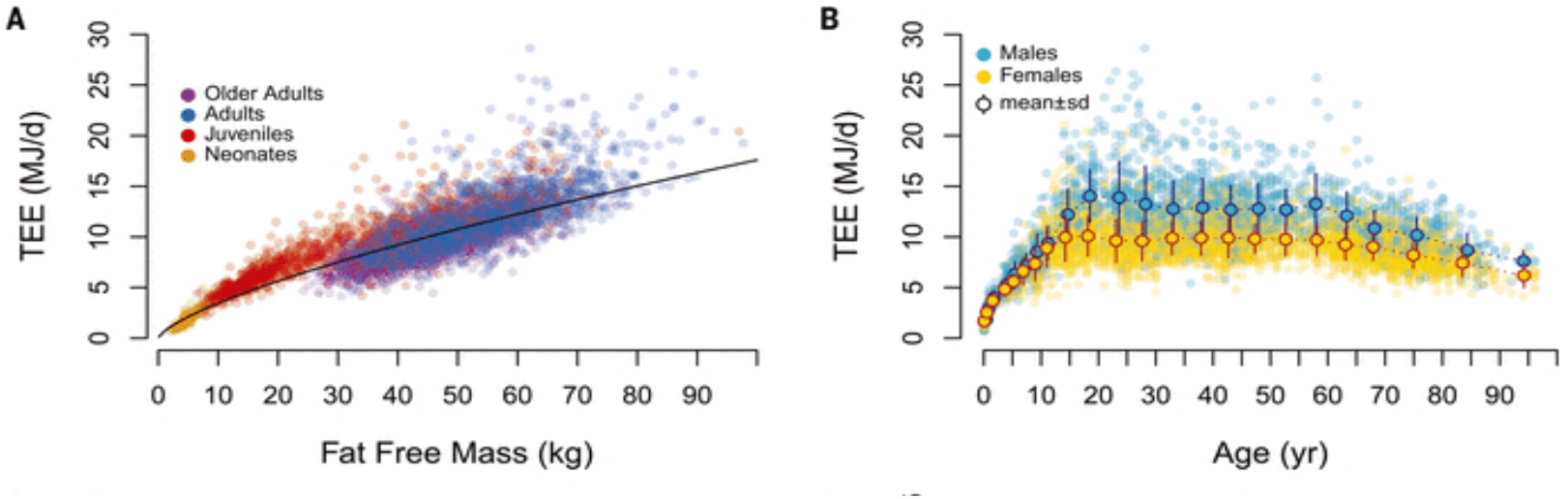
That fat mass and lean body mass act independently with weight loss and weight gain

How much LBM is lost in a year of aging ?

We propose that tailored resistance exercise training be recommended as an adjunct to incretin therapy to optimize changes in body composition by preserving lean mass while achieving fat loss.

Total energy expenditure: Fat free mass and age

Daily energy expenditure through the human life course, Volume: 373, Issue: 6556, Pages: 808-812, DOI: (10.1126/science.abe5017)



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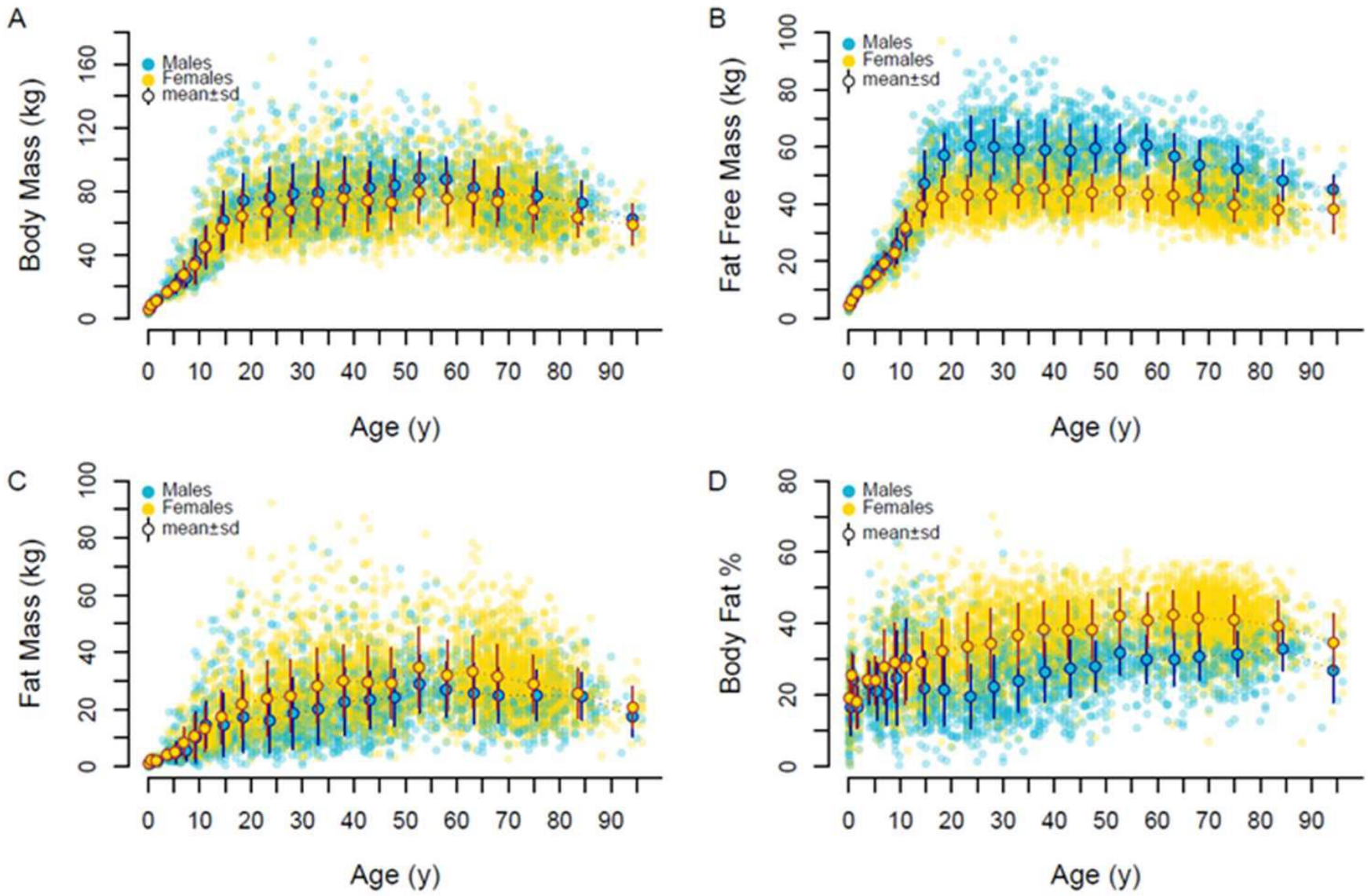
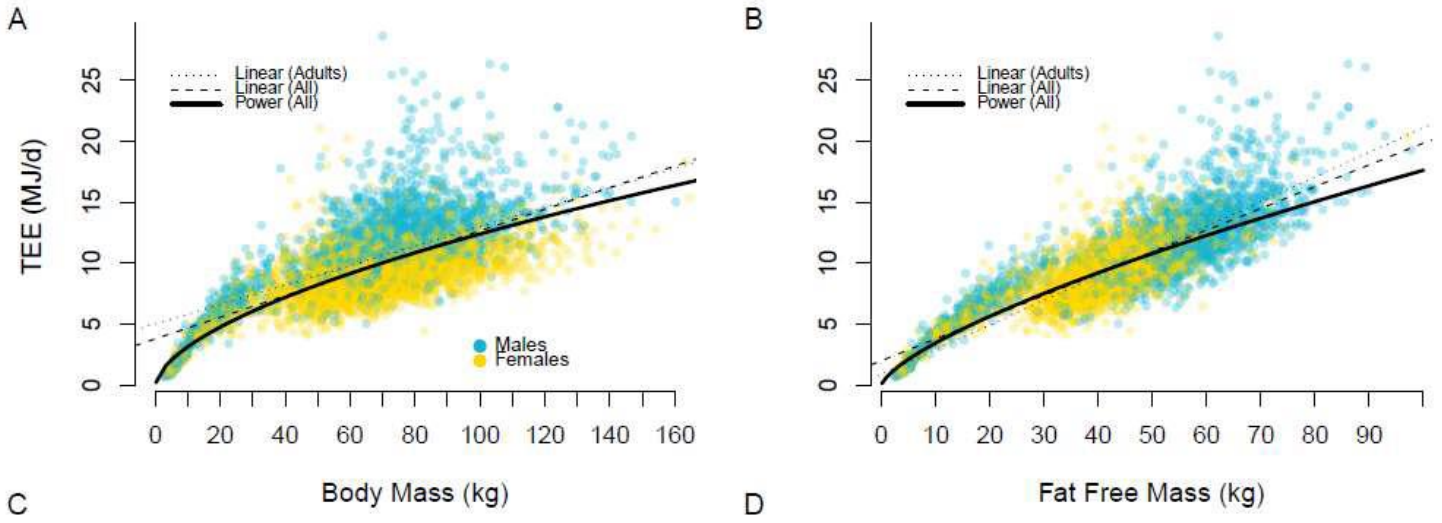


Total energy expenditure and weight and Fat free mass



Daily energy expenditure through the human life course, Volume: 373, Issue: 6556, Pages: 808-812, DOI: (10.1126/science.abe5017)

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What do we know?

- There is always loss of lean body mass with intentional weight loss – Well almost always
- As an approximation, 25% ΔFFM/Δweight was recommended and often used[1]
- The percentage change in FFM to change in weight (ΔFFM/Δweight %) forms an appropriate 2 compartment metric
- With the use of more sophisticated methods have been made using dynamic approaches and results vary with age, gender, BMI, speed of weight reduction and nature of exercise[2].
- In our systematic review we found great variance in outcome and this was influenced by gender, with males losing a greater proportion of FFM; limited effects of exercise; and rapid weight loss with very low energy diets and bariatric surgery generating a greater proportional loss of FFM[3].

[1]**Webster JD, Hesp R, Garrow JS. The composition of excess weight in obese women estimated by body density, total body water and total body potassium.** ***Hum Nutr Clin Nutr*** **1984;** 38**(4): 299-306.**

[2]**Heymsfield SB, Gonzalez MC, Shen W, Redman L, Thomas D. Weight loss composition is one-fourth fat-free mass: a critical review and critique of this widely cited rule.** ***Obesity reviews : an official journal of the International Association for the Study of Obesity*** **2014;** 15**(4): 310-21.**

[3]**Chaston TB, Dixon JB, O'Brien PE. Changes in fat-free mass during significant weight loss: a systematic review.** ***International journal of obesity*** **2007;** 31**(5): 743-50.**

The baseline characteristic of the participants (n=275)

BASELINE MEASURES	Women	Men
	138 (50%)	137 (50%)
Age (years)	47.2 (10.2) Range 18-65	43.8 (13.0 Range 18 - 65
Weight (kg)	98.8 (17.3) Range 63 -151	111.8 (22.8) Range 70 - 172
Height (m)	1.64 (0.07)	1.78 (0.07)
BMI (kg m^{-2})	36.9 (6.2) Range 26 - 55	35.7 (7.0) Range 25-55
Total Body Fat (kg)	49.2 (10.6) Range 28 - 82	41.2 (13.1) Range 16 - 81
Total body Fat Free Mass (kg)	49.5 (7.3) Range 34 - 76	70.7 (11.4) Range 44 - 106
Percent Fat Mass	49.4 (4.5) Range 21 - 61	36.0 (6.0) 19.4 - 50

Dixon JB, Lambert EA, Grima M, Rice T, Lambert GW, Straznicky NE. Fat-free mass loss generated with weight loss in overweight and obese adults: what may we expect? *Diabetes, obesity & metabolism*. 2015;17:91-93. doi: 10.1111/dom.12389

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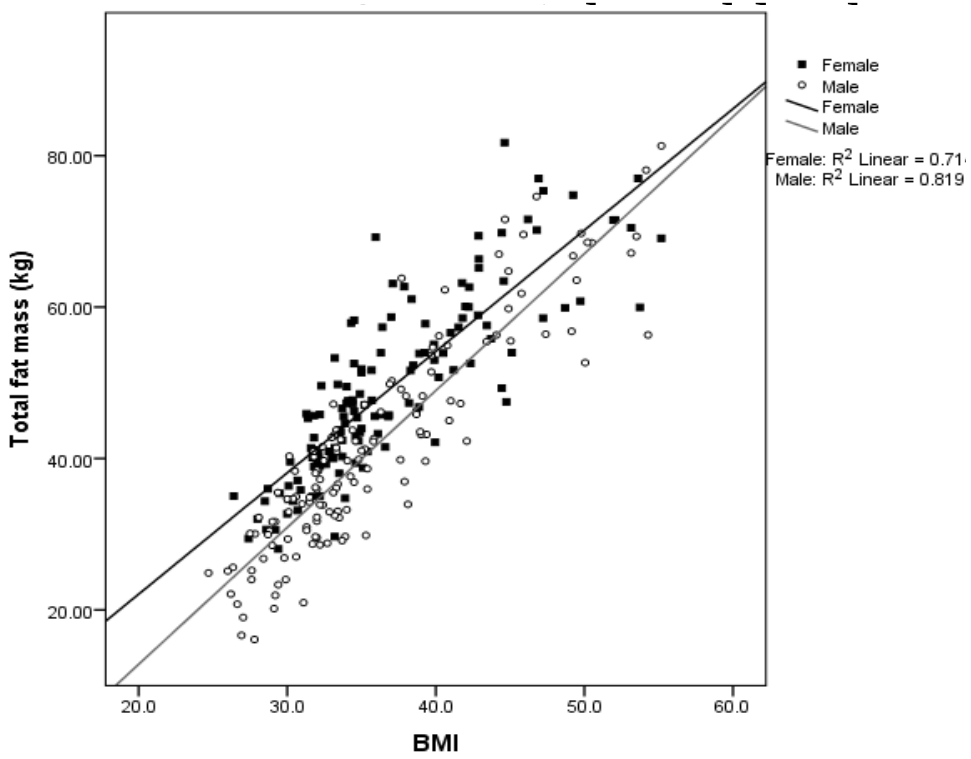
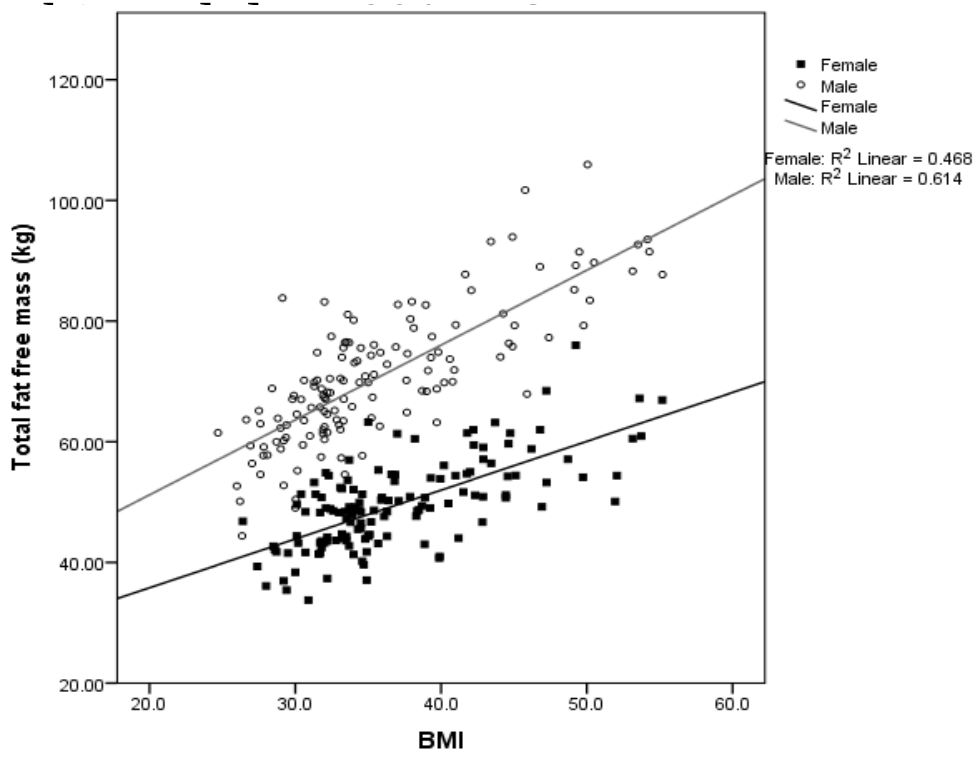
Body composition and body mass index (whole body DEXA)



Fat Mass



Fat Free Mass

These data support a linear relationship

Dixon JB, Lambert EA, Grima M, Rice T, Lambert GW, Straznicky NE. Fat-free mass loss generated with weight loss in overweight and obese adults: what may we expect? *Diabetes, obesity & metabolism*. 2015;17:91-93. doi: 10.1111/dom.12389

Models of the change FFM% with change 10% of weight loss

	BMI 50	BMI 45	BMI 40	BMI 35	BMI 30	R^2	Mean
Males							
Actual	38.7	38.7	45.3	38.1	42.2	-	40.6
Linear	30.6	35.9	41.3	46.6	51.9	0.43	41.3
Inverse	37.1	37.1	37.1	37.1	37.1	0.45	37.1
Quadratic	44.8	40.7	38.9	39.3	42.4	0.46	41.2
FM linear	40.9	40.9	40.9	40.9	40.9	-	40.9
Female							
Actual	37.7	39.4	38.7	28.4	35.7	-	36.0
Linear	27.7	31.4	35.5	38.9	42.6	0.30	35.2
Inverse	29.5	29.5	29.5	29.5	29.5	0.33	29.5
Quadratic	42.7	35.2	30.1	28.1	30	0.36	33.2
FM linear	33.9	33.9	33.9	33.9	33.9	-	33.9

Dixon JB, Lambert EA, Grima M, Rice T, Lambert GW, Straznicky NE. Fat-free mass loss generated with weight loss in overweight and obese adults: what may we expect? *Diabetes, obesity & metabolism*. 2015;17:91-93. doi: 10.1111/dom.12389

The Effects of Overfeeding on Body Composition: The Role of Macronutrient Composition

Author	n - Men / Women Age	Body Fat %	Physical Activity	Dur-ation	Kcal Sur-plus	Protein (g/kg)	BW (kg)	FM (kg)	FFM (kg)	Fat gain (% wt gain)
Salans et al. 1971	5 / 0 26	19%	"Reduced"	3 months			+ 16.2	+ 10.4	+ 5.8	64%
Norgan & Durnin 1980	6 / 0 22	15%	Sedentary	9 weeks	+ 50%	2.2	+ 6.0	+ 3.7	+ 2.3	62%
Webb & Annis 1983	4 / 5 46	15% (M) / 37% (W)	Sedentary	30 days	+ 1000 kcal	2.4 1.7 1.2	+ 1.8 a + 2.7 b + 2.7 b	+ 1.1 a + 2.0 b + 2.1 b	+ 0.7 + 0.7 + 0.6	61% 74% 78%
Ravussin et al. 1985	5 / 0 24	15%	6000-7000 steps/d	9 days	+ 60%	2.1	+ 3.2	+ 1.8	+ 1.4	56%
Poehlman et al. 1986	12 / 0 19	12%	Sedentary	22 days	+ 1000 kcal	2.4	**+ 2.2**	**+ 1.1**	+1.1	50%
Bouchard et al.1990	24 / 0 21	11%	< 30 min walk daily	100 days	+ 1000 kcal		**+ 8.1**	**+ 5.4**	**+ 2.7**	67%
Roberts et al. 1990	7 / 0 24	14%	Sedentary	20 days	+ 1000 kcal	1.5	+ 2.5	+ 1.7	+ 0.8	68%
Horton et al. 1995	16 / 0 33	28%	Inactive	2 weeks	+ 50%	1.2 1.2	**+ 2.9** **+ 2.6**	**+ 1.5** **+ 1.5**	**+ 1.4** **+ 1.1**	52% 58%
Lammert et al. 2000	20 / 0 22	15%	Inactive	3 weeks	+ 1200 kcal	1.7 1.7	**+ 1.4** **+ 1.6**	**+ 0.8** **+ 1.1**	**+ 0.6** + 0.5	57% 69%
Siervo et al. 2008	6 / 0 43	21%	Inactive	3 weeks 3 weeks 3 weeks	+ 20% + 40% + 60%	1.4 1.5 1.7	+ 0.7 **+ 2.9** **+ 5.7**	+ 0.4 + 1.5 **+ 3.6**	+ 0.3 + 1.4 **+ 2.7**	57% 52% 63%
Claesson et al. 2009	11 / 14 23	24%	7800 step avg	14 days	+ 46%	2.0 1.2	+ 0.3 **+ 0.8**	+ 0.0 + 0.3	+ 0.3 + 0.5	0% 38%
Stanhope et al. 2009	16 / 16 54	29% (M) / 41% (W)	Sedentary	8 weeks	+ 8%		**+ 1.6** **+ 1.3**	**+ 0.9** **+ 0.7**	+ 0.7 + 0.6	56% 54%
Ernersson et al. 2010	12 / 6 26	15% (M) / 31% (W)	< 5000 steps/d	4 weeks	+ 70%	2.4	**+ 6.4**	**+ 3.7**	**+ 1.8**	58%

In sedentary subjects FM increase is commonly 60 to 70% of weight gained

FFM =30-40%

Leaf A, Antonio J. The Effects of Overfeeding on Body Composition: The Role of Macronutrient Composition - A Narrative Review. *Int J Exerc Sci*. 2017;10:1275-1296.

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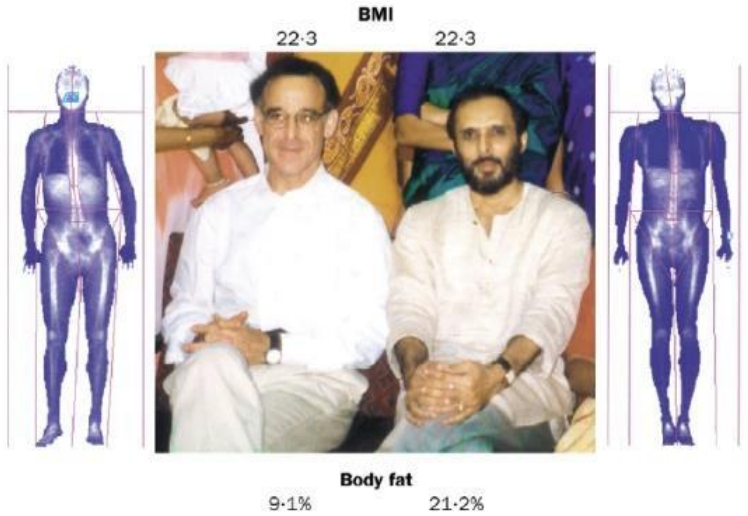
Expected loss of FFM with weight loss

- 41% for men
- 34% for women

- This is greater than the 25% threshold previously used and suggests that intentional weight loss selectively preserves muscle and therefore yo-yo dieting is not a major issue

- Limitations – age (young and old) - ethnicity



Percentage of FFM loss with various methods of weight loss

Method	Number of Study groups	Mean of study groups
LCD	15	17%
LCD & EX	6	19%
LCD & Drugs	3	28%
VLCD	4	29%
VLCD & Ex	5	16%
BPD	15	30%
RYGB	4	30%
LAGB	15	17%

Chaston TB, & Dixon JB. et al, *Int J Obes (Lond).* 2007;31:743-50.

FFM/TWL Liraglutide 3 mg, Naltrexone Bupropion 32mg/360mg

- Liraglutide: TWL6.3 kg FFM/TWL 14%

Elkind-Hirsch KE, Chappell N, Shaler D, Storment J, Bellanger D. 2022;118:371-381. doi: 10.1016/j.fertnstert.2022.04.027

- Naltrexone – Bupropion TWL 8.2 kg FFM/ TWL 22%

Smith SR, Fujioka K, Gupta AK, Billes SK, Burns C, Kim D, Dunayevich E, Greenway FL.*Diabetes, obesity & metabolism*. 2013;15:863-866. doi: 10.1111/dom.12095

- Chaston review – Orlistat and Sibutramine

• Gotfredsen et al. 2001	LCD+Orlistat	11.2kg FFM/TWL 11.6%	52 weeks	n=16
• Kamel et al. 2000	LCD+Sibutramine	10.6kg FFM/TWL 31.1%	26 weeks	n=19
• Berube-Parent et al. 2001	LCD+Sibutramine	10.7kg FFM/TWL 38.3%	13 weeks	n=8

Chaston TB, & Dixon JB. et al, *Int J Obes (Lond).* 2007;31:743-50.

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JAMA Network™

From: **Is Weight Loss–Induced Muscle Mass Loss Clinically Relevant?**

JAMA. Published online June 03, 2024. doi:10.1001/jama.2024.6586

Figure Legend:

Body Composition Before and After Weight LossRepresentation of body composition before and after 25% intentional weight loss induced by energy restriction showing the attenuation of weight loss–induced reduction in fat-free mass (FFM) and skeletal muscle mass (SMM) through dietary protein and exercise (A) and the effect of marked weight loss induced by GLP-1–based antiobesity medications on the proportion of total weight lost derived from fat mass and lean body mass (LBM) or FFM (B). Data are from C Harris et al, J Rosenstock et al, JPH Wilding et al, and AM Jastreboff et al.

Conclusions

- There is a linear association between FM and FFM with weight loss and weight gain
- Most intentional weight loss generates less FFM (50% muscle) loss than expected for the weight loss.
- How would resistance exercise and increasing quality protein assist this situation?
- Three drugs
  - ~~Sibutramine,~~ 31 and 38%
  - Semaglutide 2.4 mg 39%
  - Retatrutide 31%
- We need more information GLP-1 agonists especially those associated with greater weight loss
- We need information about the young, elderly, those at risk of sarcopenia and data from different ethnic groups
- We have very little to no information about drug effects regional Bone density and Bone mineral content

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