

# Impacts of Obesity Treatment on Muscle Quantity and Quality: Are there added benefits of physical activity and exercise?

Bret Goodpaster, Ph.D.

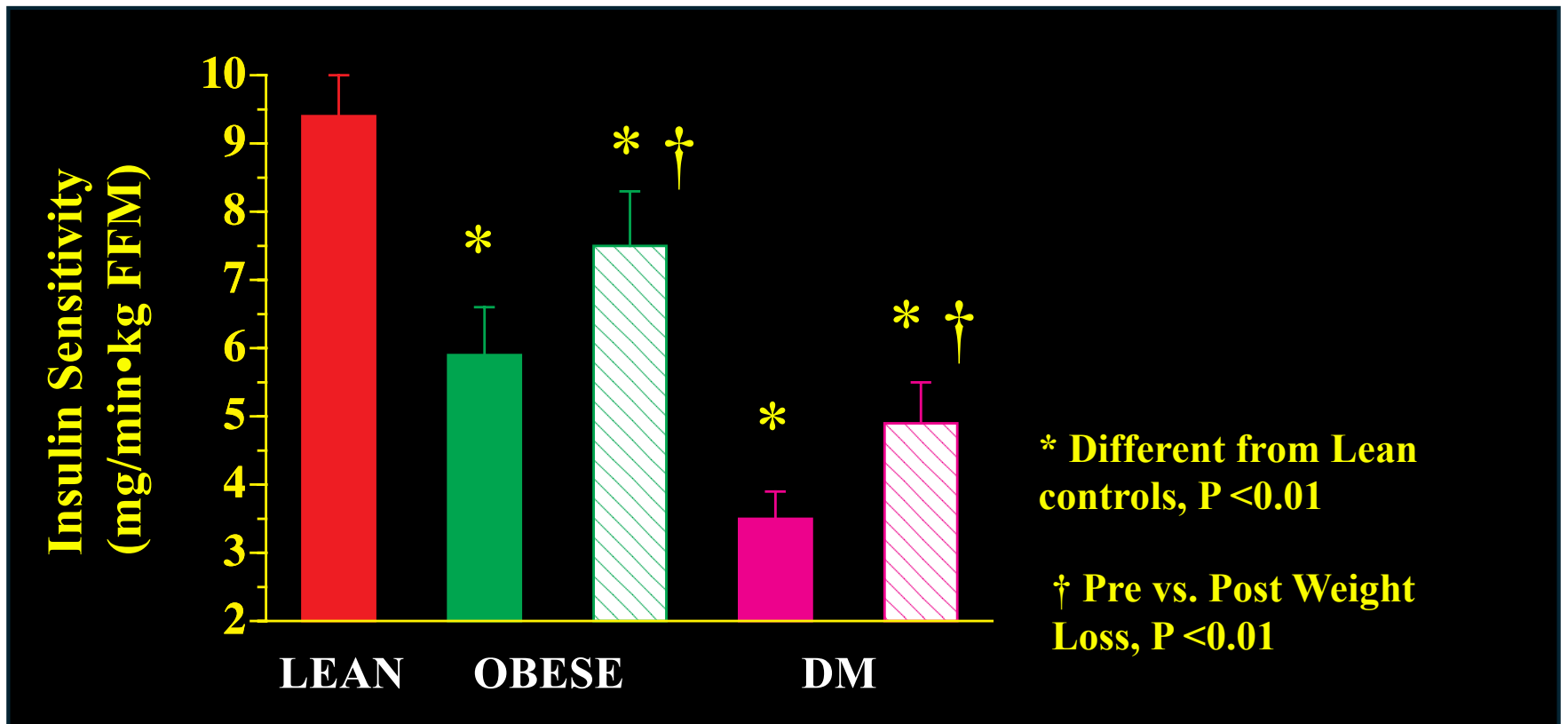
  
**Advent Health**  
Translational Research Institute



# Disclosures

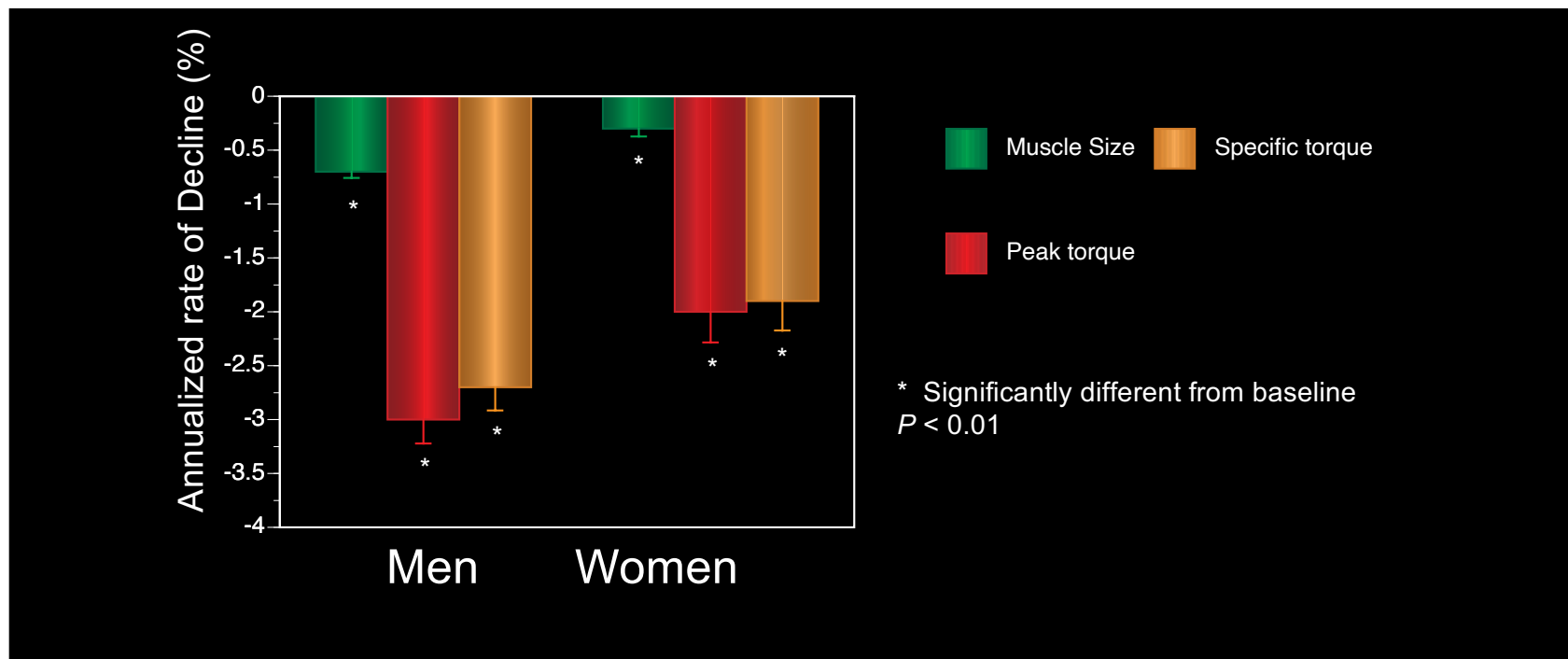
- Received honoraria for serving on advisory boards for:  
Novo Nordisk, Ely Lilly, Merck, Hanmi, Lexicon, Cambrian Bio

## Weight loss improves many metabolic defects in obesity and type 2 diabetes

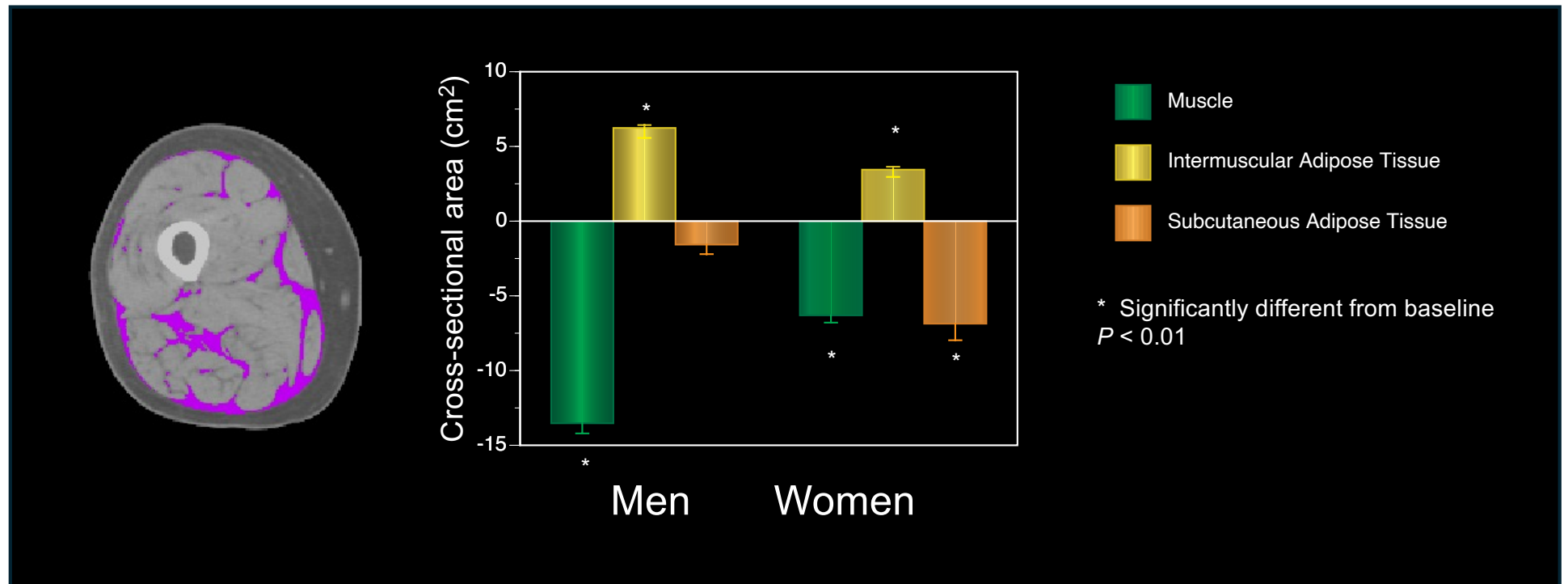


Goodpaster et al. *Diabetes*, 1997.

# Changes in Muscle Size, Strength and Quality with Aging



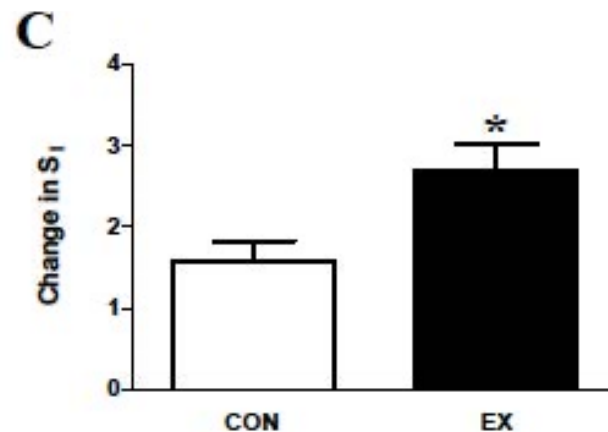
# Changes in Muscle Size and Adipose Tissue Content with Aging



# Clinical trial demonstrates exercise following bariatric surgery improves insulin sensitivity

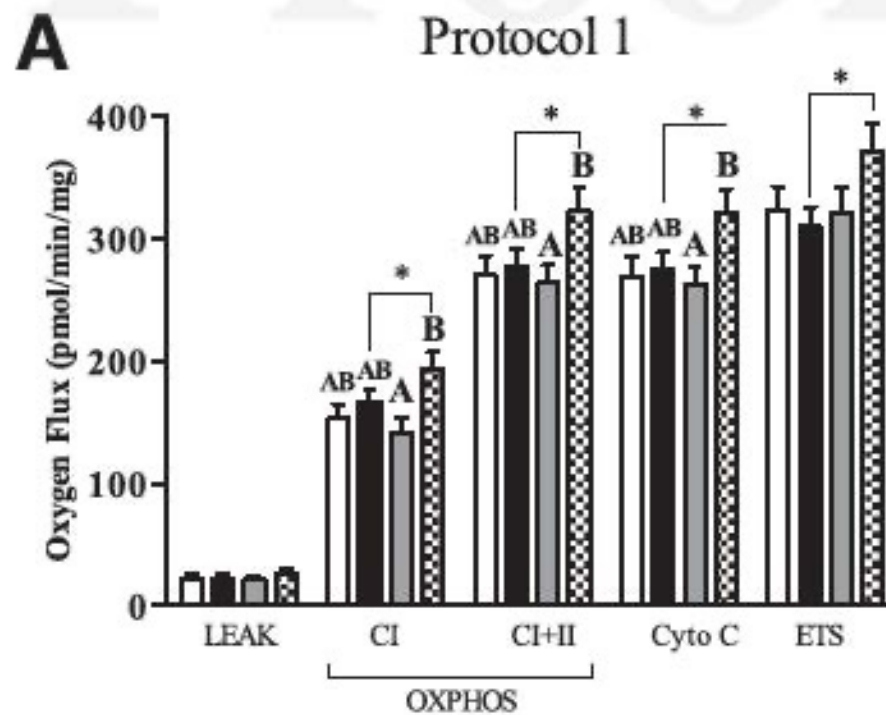
Paul M. Coen,<sup>1,2</sup> Charles J. Tanner,<sup>3</sup> Nicole L. Helbling,<sup>1</sup> Gabriel S. Dubis,<sup>3</sup> Kazanna C. Hames,<sup>1</sup> Hui Xie,<sup>4</sup> George M. Eid,<sup>5</sup> Maja Stefanovic-Racic,<sup>1</sup> Frederico G.S. Toledo,<sup>1</sup> John M. Jakicic,<sup>2</sup> Joseph A. Houmard,<sup>3</sup> and Bret H. Goodpaster<sup>1</sup>

<sup>1</sup>Division of Endocrinology and Metabolism, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA. <sup>2</sup>Department of Health and Physical Activity, University of Pittsburgh, Pittsburgh, Pennsylvania, USA. <sup>3</sup>Department of Kinesiology, East Carolina University, Greenville, North Carolina, USA. <sup>4</sup>Translational Research Institute for Metabolism and Diabetes, Florida Hospital, Orlando, Florida, USA. <sup>5</sup>Department of Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

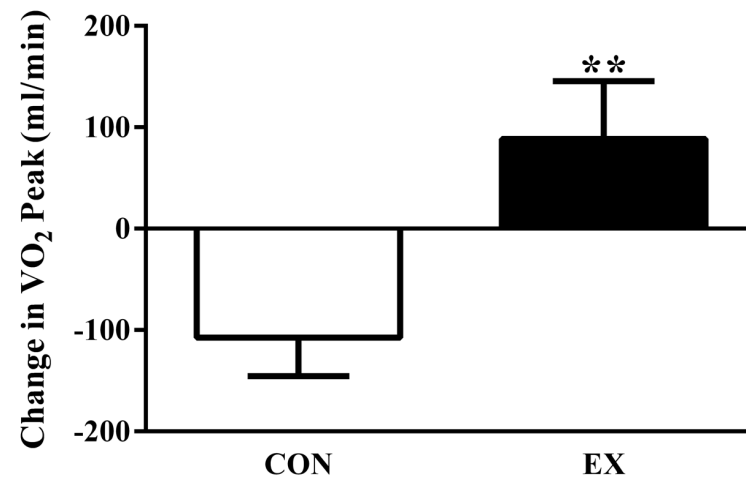


Coen et al. JCI 2015

Effects of profound bariatric surgery-induced weight loss on skeletal muscle mitochondria either with or without post-surgery exercise



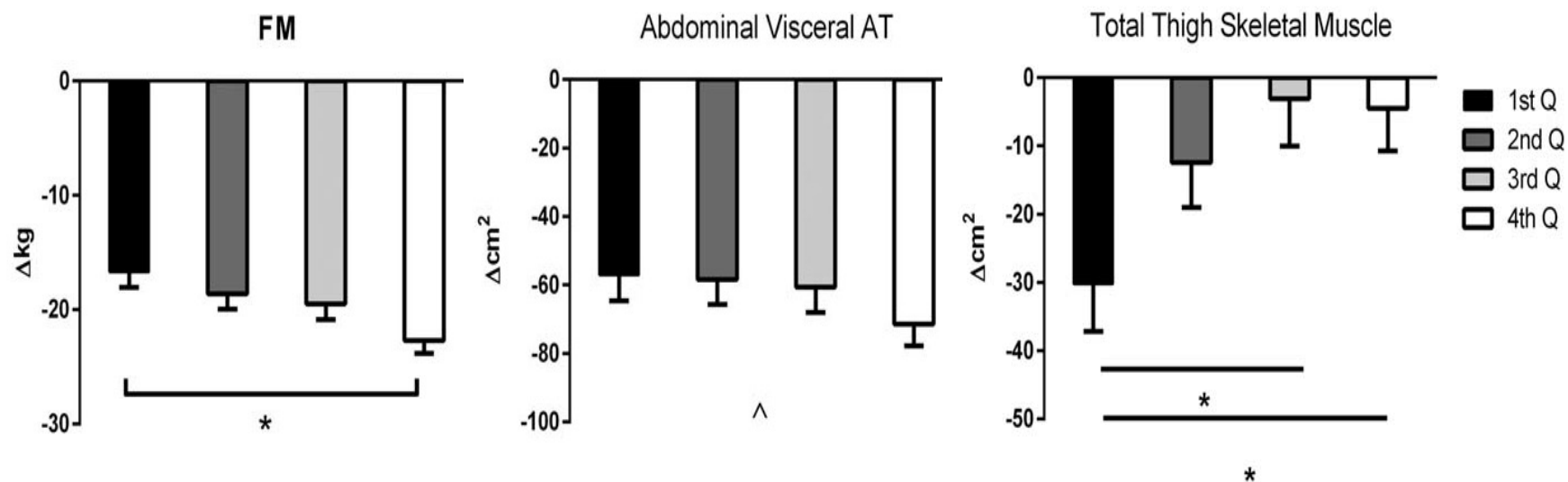
## Exercise increases cardiorespiratory fitness following bariatric surgery





## Randomized Trial Reveals that Physical Activity and Energy Expenditure are Associated with Weight and Body Composition after RYGB

Elvis Alvarez Carnero<sup>1</sup>, Gabriel S. Dubis<sup>2</sup>, Kazanna C. Hames<sup>3</sup>, John M. Jakicic<sup>4</sup>, Joseph A. Houmard<sup>2</sup>, Paul M. Coen<sup>3,4</sup>, and Bret H. Goodpaster<sup>3</sup>



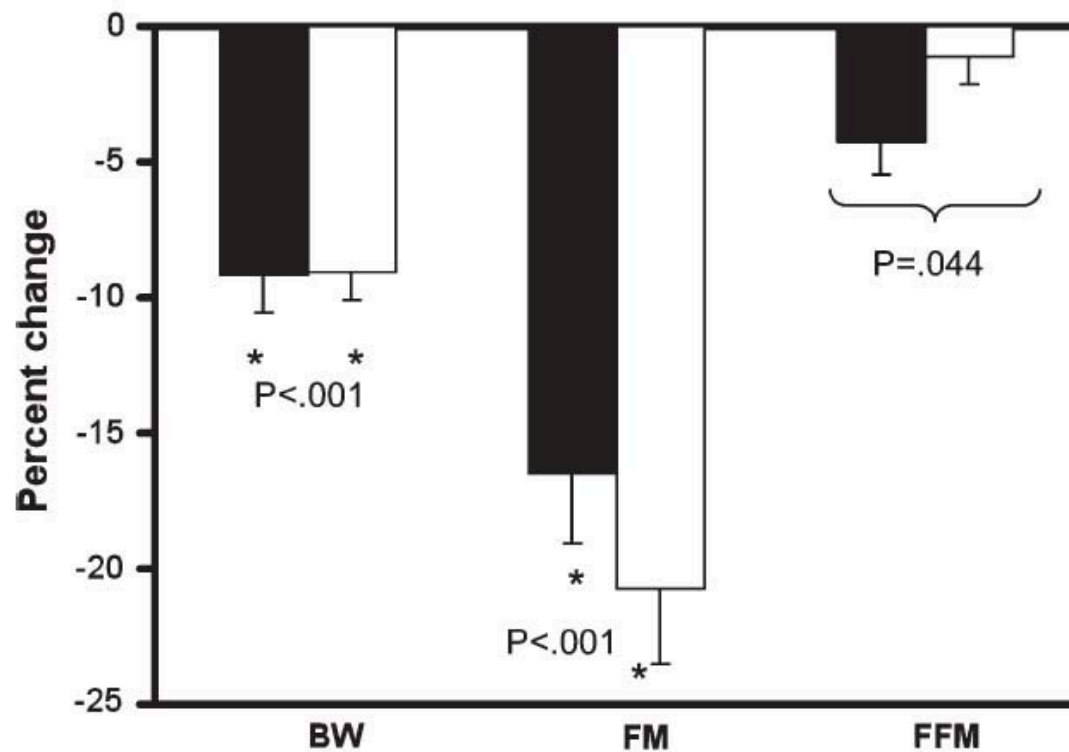
# Is weight loss good for older people who are overweight or obese?



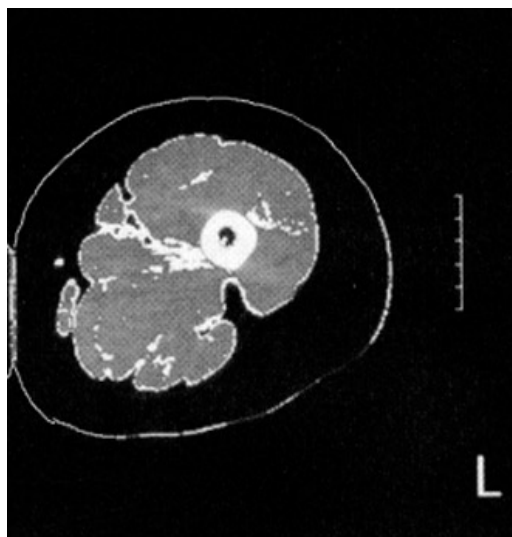
## **A conundrum...**

- Older individuals need to reduce or maintain healthy body fat while maintaining muscle mass.

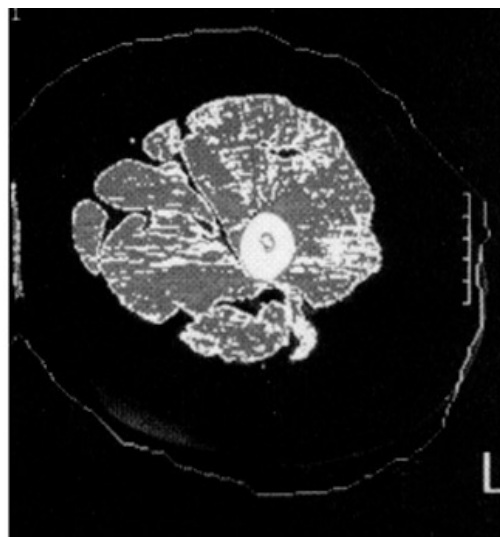
## Moderate Exercise Attenuates the Loss of Skeletal Muscle Mass That Occurs With Intentional Caloric Restriction–Induced Weight Loss in Older Adults with Obesity



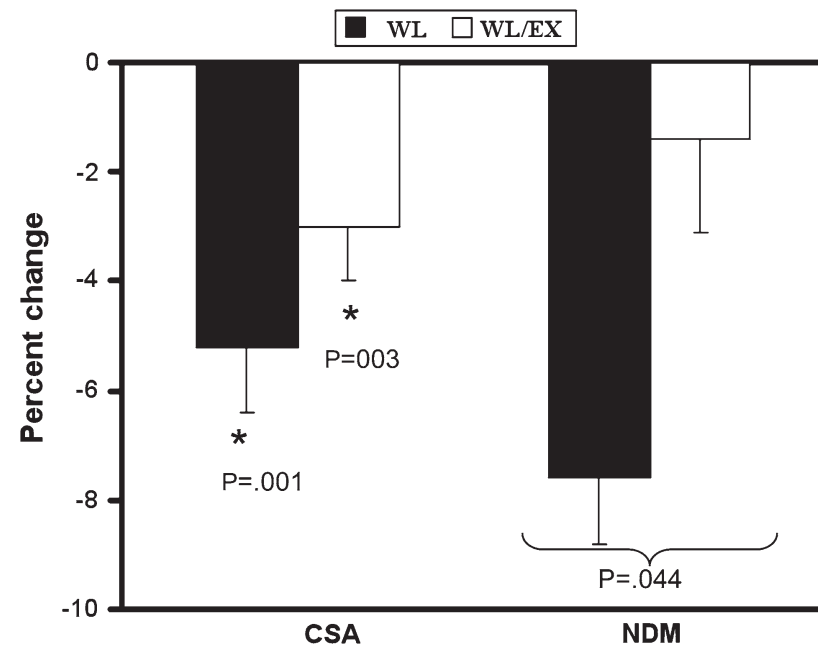
Chomentowski et al. J Gerontol A Biol Sci Med Sci 2009

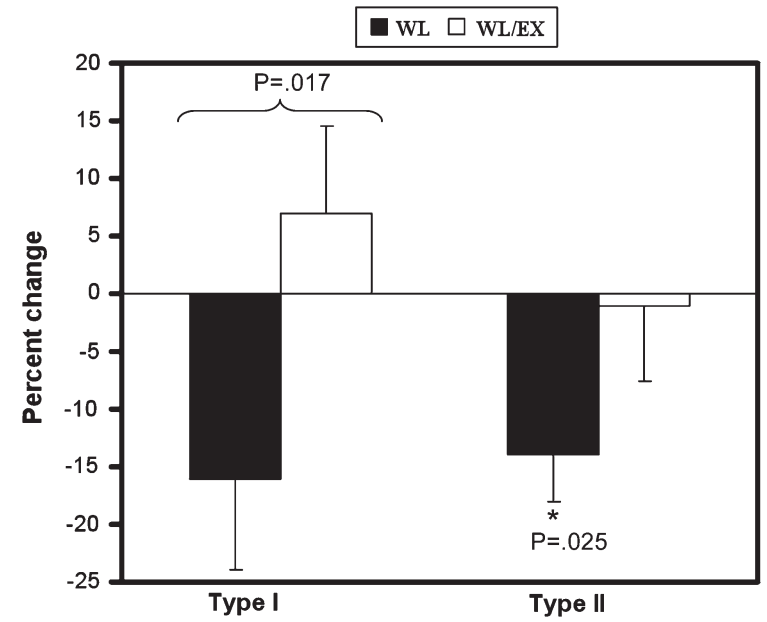
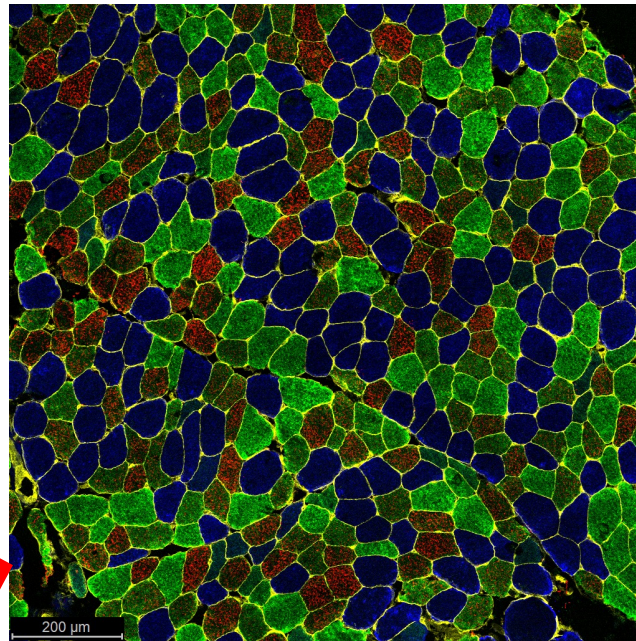
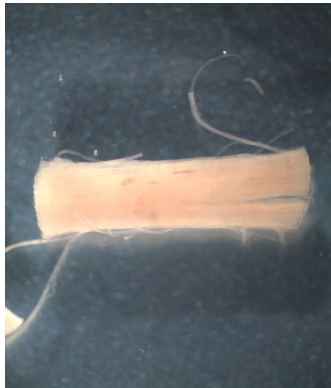


Normal weight



w/Obesity



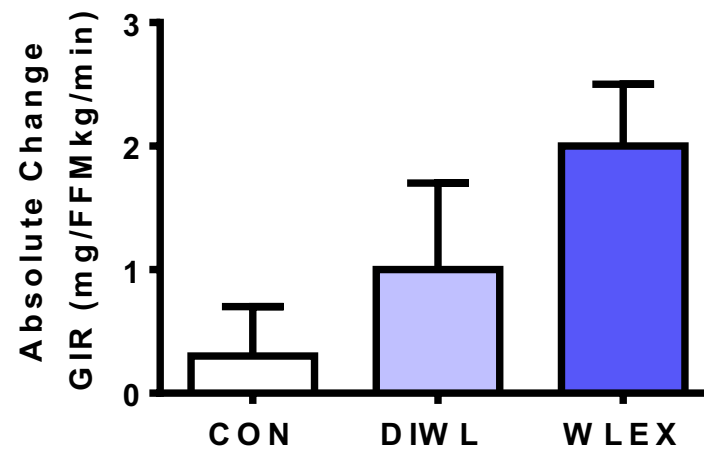
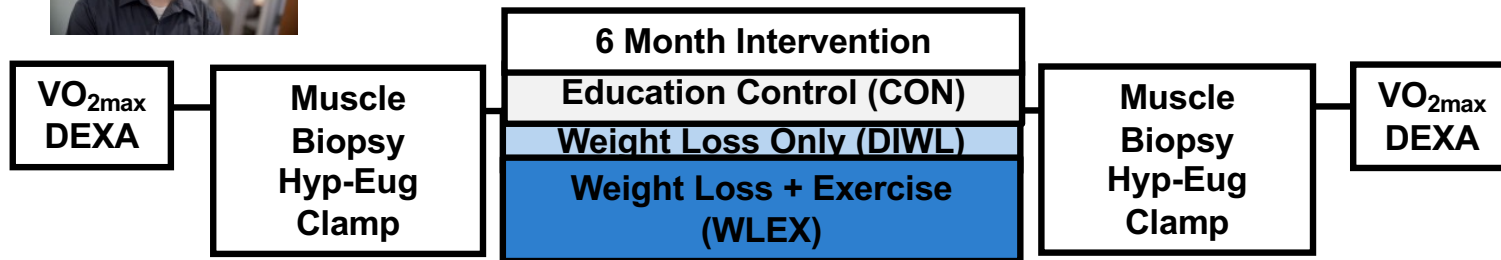




Robert Standley, PhD



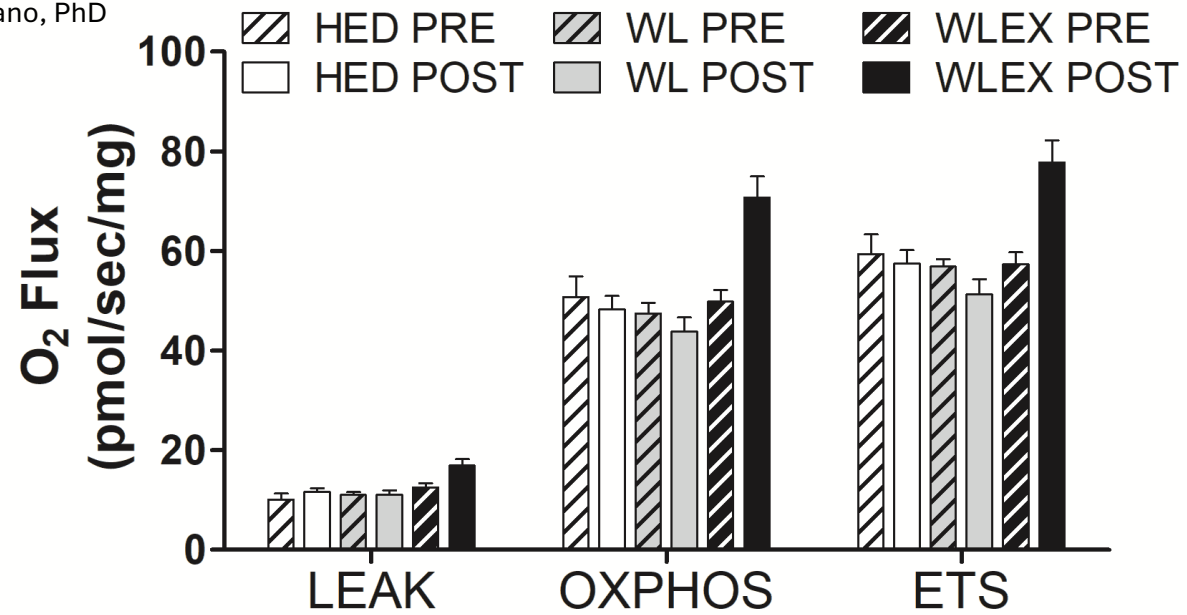
Andrea Brennan, PhD



A. M. Brennan, R. A. Standley,... Goodpaster, BH. J Gerontol A Biol Sci Med Sci 2022

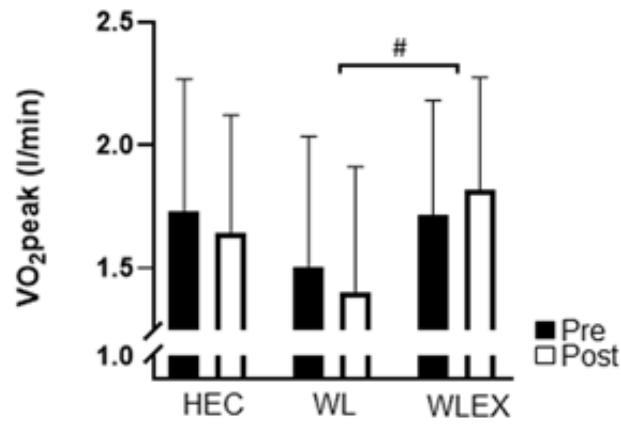


Giovanna Distefano, PhD

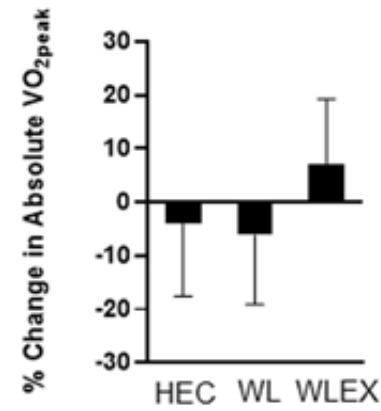




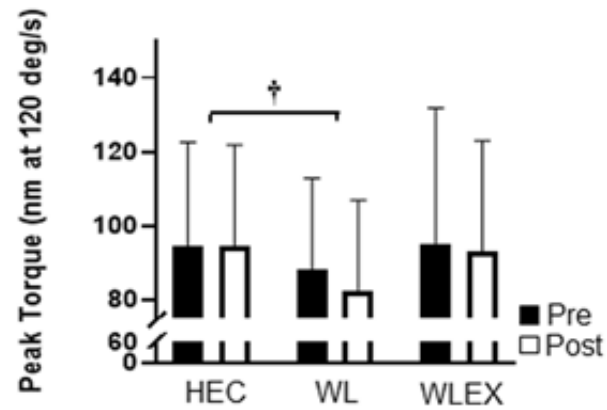
A.



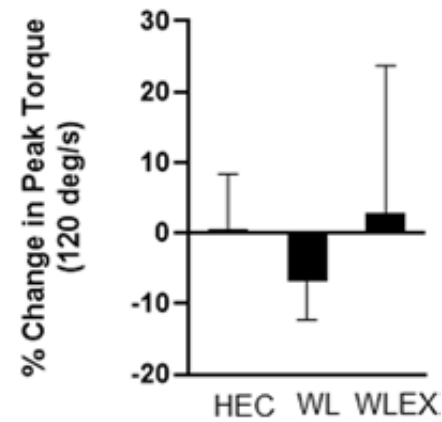
B.



C.



D.



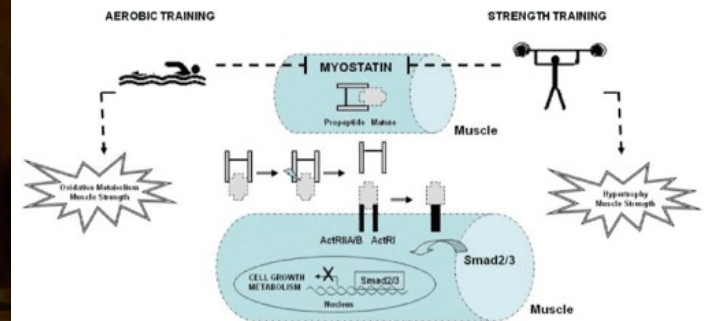
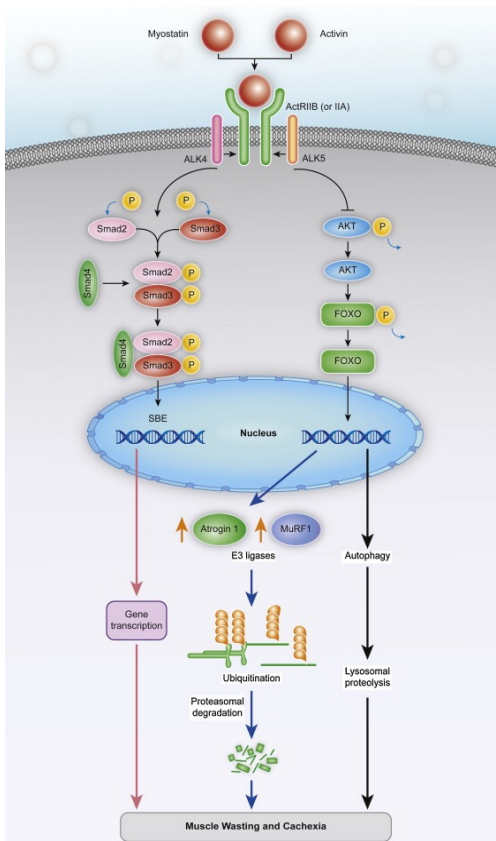
# Most people don't like to exercise!

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www.glasbergen.com








**“Instead of jogging, can you just set my pacemaker to beat faster for 30 minutes a day while I watch TV?”**

# Myostatin



H.Q. Han, et al., Myostatin/activin pathway antagonism: Biochemistry & Cell Biology, 2013,

Fernandes, T., Soci, Ú.P., Melo, S.F., Alves, C.R., & Oliveira, E.M. (2012). Signaling Pathways that Mediate Skeletal Muscle Hypertrophy: Effects of Exercise Training.

Trevogrumab, Garetosmab		mAb	Ph 2	COMBO w/ semaglutide for 26 weeks (26 weeks extension)
Bimagrumab		mAb	Ph 2	COMBO w/ semaglutide for 48 weeks (26 weeks extension)
		mAb	Ph 2	COMBO w/ tirzepatide for 24 weeks
Apitegromab		mAb	Ph 2	COMBO w/ Sema or TZP for 24 weeks
SRK-439		mAb	Preclinical	Should be COMBO w/ Sema or TZP
Taldefgrobep Alfa		Fc-fusion	Ph 2	COMBO w/ open-label GLP-1 for 24 weeks (24 weeks extension)
RG6237		mAb	Ph 1b	Should be COMBO w/ their own incretin (CT-388) or GLP-1



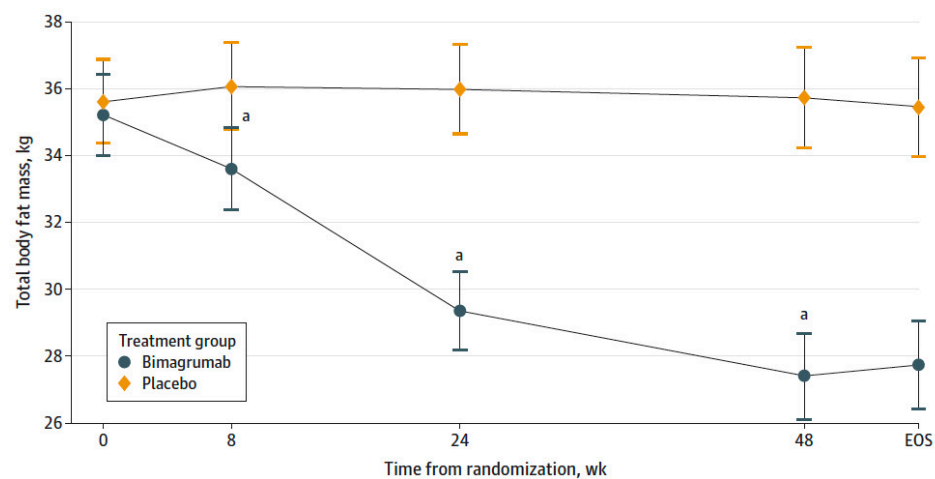
Original Investigation | Nutrition, Obesity, and Exercise

## Effect of Bimagrumab vs Placebo on Body Fat Mass Among Adults With Type 2 Diabetes and Obesity

### A Phase 2 Randomized Clinical Trial

Steven B. Heymsfield, MD; Laura A. Coleman, PhD, RD; Ram Miller, MD; Daniel S. Rooks, PhD; Didier Laurent, PhD; Olivier Petricoul, PhD; Jens Praestgaard, PhD; Therese Swan, PharmD; Thomas Wade, MD; Robert G. Perry, MD; Bret H. Goodpaster, PhD; Ronenn Roubenoff, MD, MHS

Figure 2. Effect of Bimagrumab on Total Body Fat Mass



1 participant in the bimagrumab group did not have a week 48 or end of study (EOS) dual-energy x-ray absorptiometry scan performed.

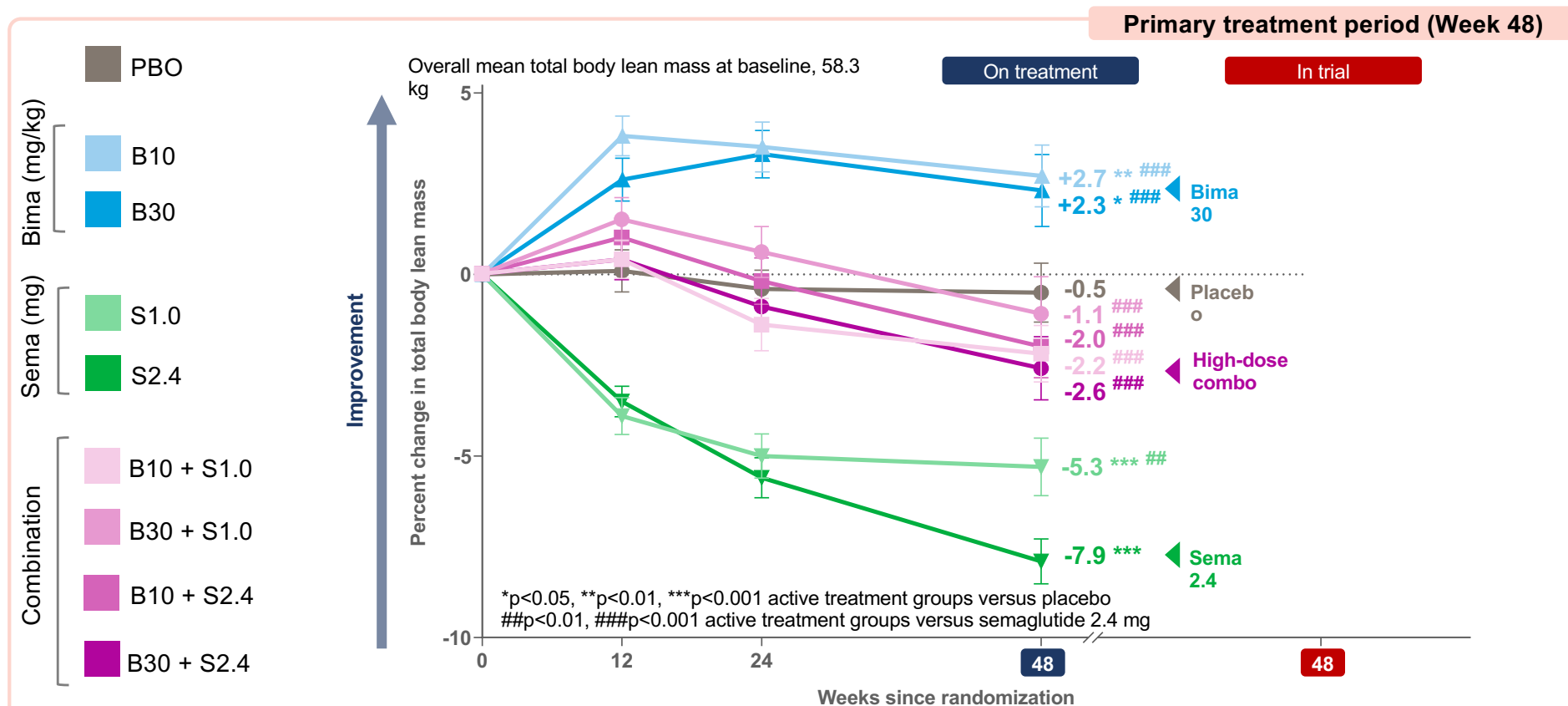
<sup>a</sup>  $P < .001$ .

# Total Body Lean Mass: % Change from Baseline (DXA, Week 48)

*Lean mass largely preserved with bimagrumab-containing groups versus semaglutide*



85<sup>TH</sup> SCIENTIFIC SESSIONS  
CHICAGO, IL | JUNE 20-23, 2025



**Appendicular lean mass (W48; on treatment):** The LSM percent changes were +2.1% to +3.0% (bima), -5.7% to -9.4% (sema), and -1.8% to -2.5% (combination), versus -1.0% (placebo)

Data are presented as LSM ± SE. Percent changes are based on a mixed model for repeated measures model for the efficacy estimand, and an analysis of covariance model with multiple imputation for the treatment-regimen estimand.. Abbreviations: Bima, bimagrumab; combo, combination; DXA, dual-energy X-ray absorptiometry; LSM, least-squares mean; PBO, placebo; SE, standard error; sema, semaglutide.

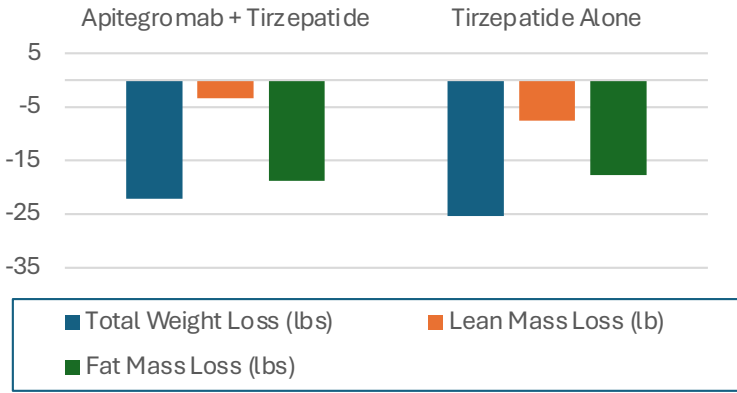
Regeneron COURAGE Trial - Interim Results (June 2025)



Veru Phase 2b QUALITY Trial - Topline Results (May 2025)



Scholar Rock Phase 2 EMBRAZE Trial Results (June 2025)



# Summary

- Weight loss can improve many metabolic defects and reduce risk for Type 2 diabetes and CVD.
- Weight loss decreases muscle mass (*the functional consequences of reduced muscle mass are not known*)
- Exercise can correct both dual defects in obesity - insulin resistance and impaired capacity for (mitochondrial) fatty acid oxidation.
- Exercise can attenuate the loss of muscle with weight loss.
- *Exercise and other non-exercise therapies are needed adjunct to weight loss*
- Low muscle mass (sarcopenia) and weakness with aging should be considered in advising/prescribing weight loss for older adults, *including GLP and other incretin drugs.*



# Acknowledgments

TRI staffs

Paul Coen, Ph.D.

Robert Standley, Ph.D.

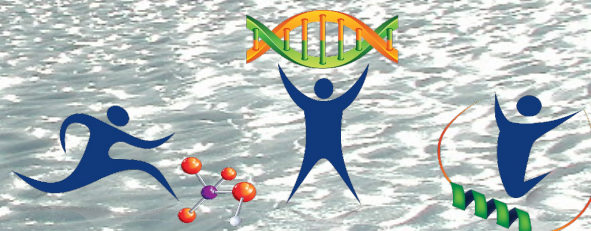
Lauren Sparks, Ph.D.

Elvis Carnero, Ph.D.

Giovanna Distefano, Ph.D.

Andrea Brennan, Ph.D.

David Kelley, M.D.



The Molecular Transducers of Physical Activity  
Consortium (MoTrPAC)

