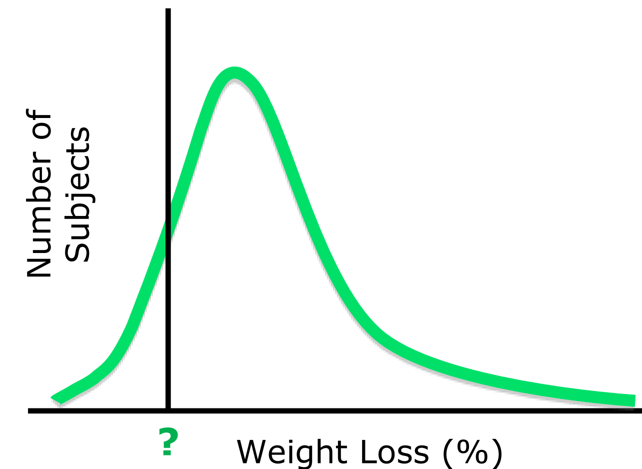
LMKaplan0@gmail.com

Defining the Clinical Response to Metabolic Surgery



Lee M. Kaplan, MD, PhD

Obesity Medicine Section and Dartmouth Obesity Care Center
Geisel School of Medicine at Dartmouth

LMKaplan0@gmail.com

31 August 2023

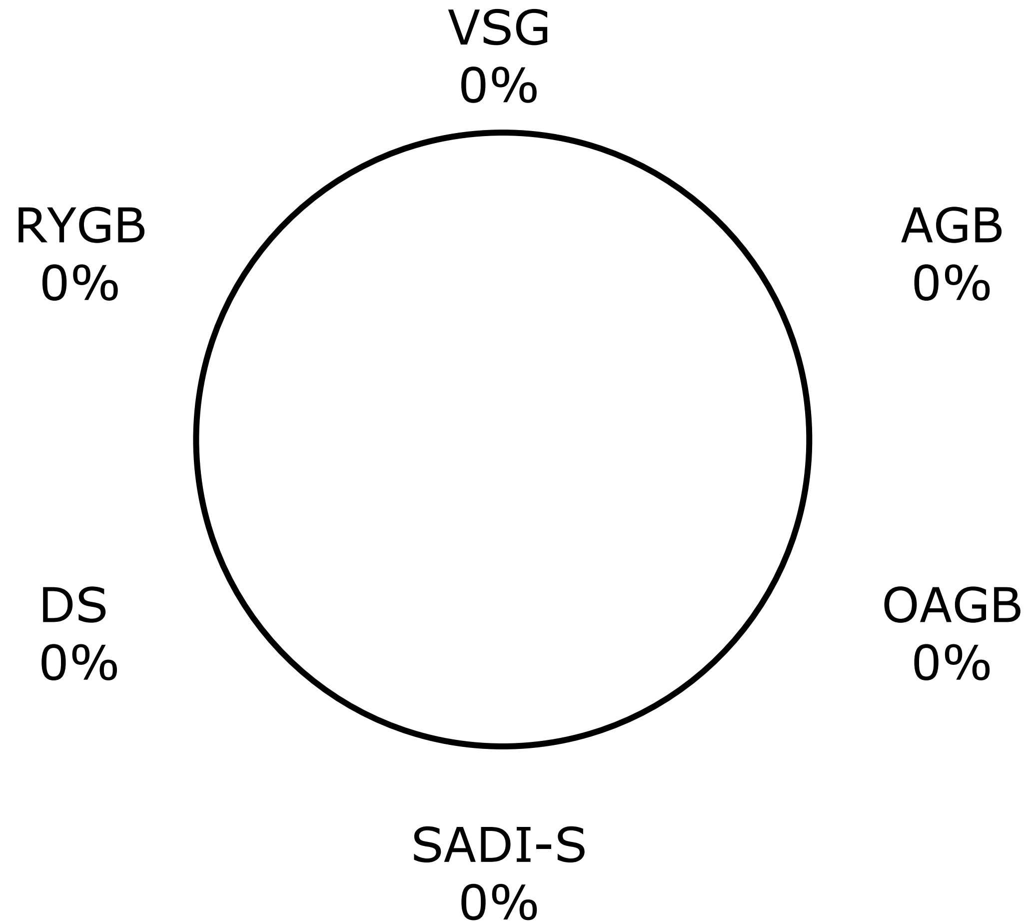
2023 IFSO World Congress

Disclosures

I am currently or have recently been a paid consultant to the following companies and organizations:

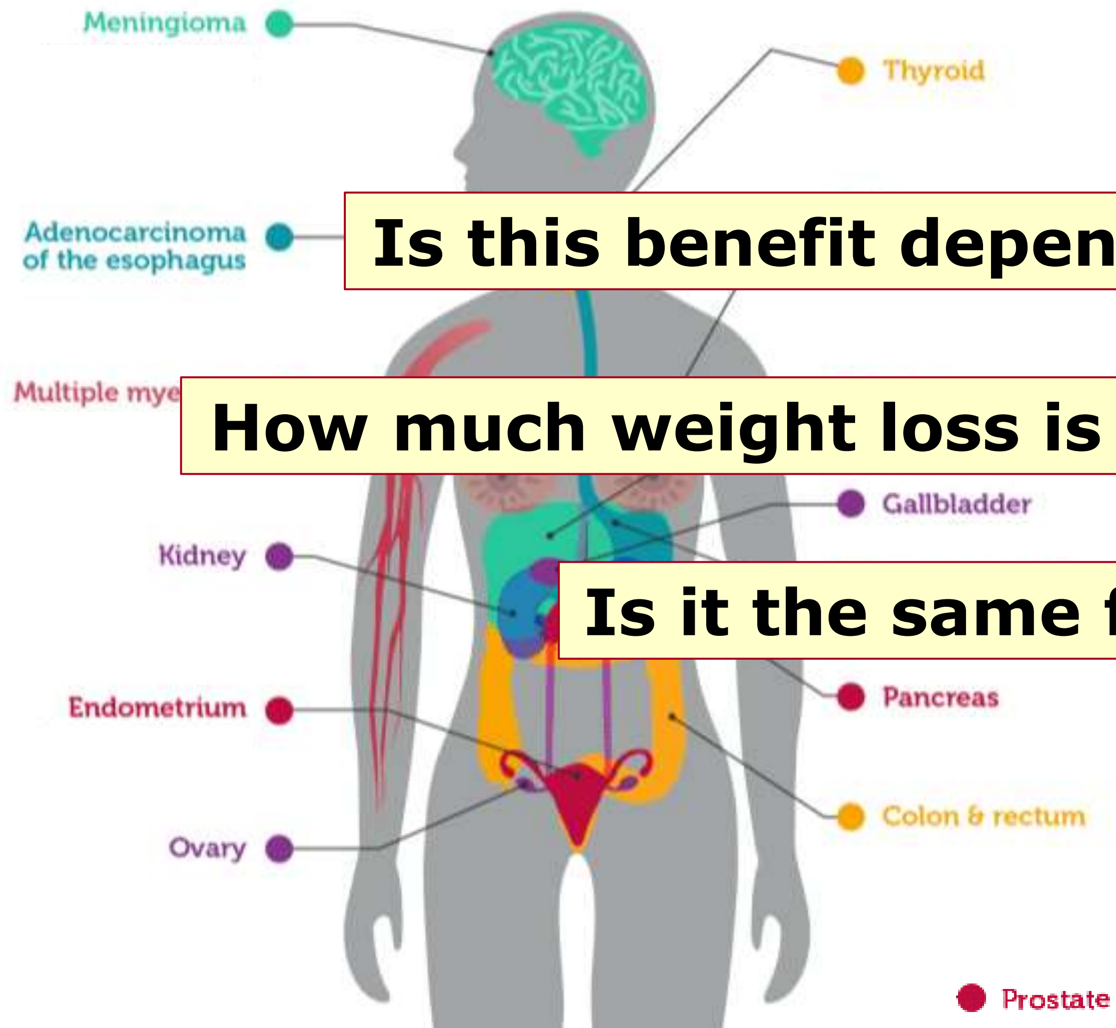
Altimmune
Amgen
Boehringer Ingelheim
Gelesis
Gilead Sciences
Eli Lilly & Company
Novo Nordisk
Pfizer
Rhythm Pharmaceuticals
Sidekick Health
The Obesity and Nutrition Institute
twenty30.health
Xeno Biosciences

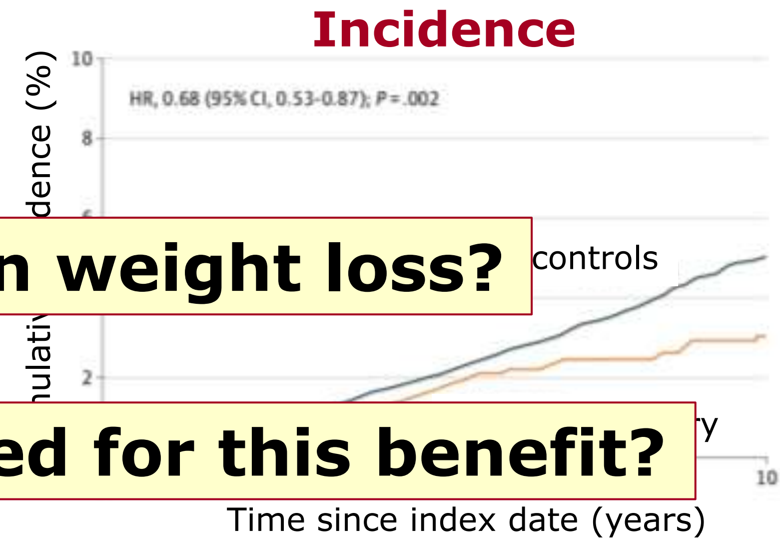
Disclosure of Case Mix



Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Bariatric surgery reduces cancer incidence and mortality

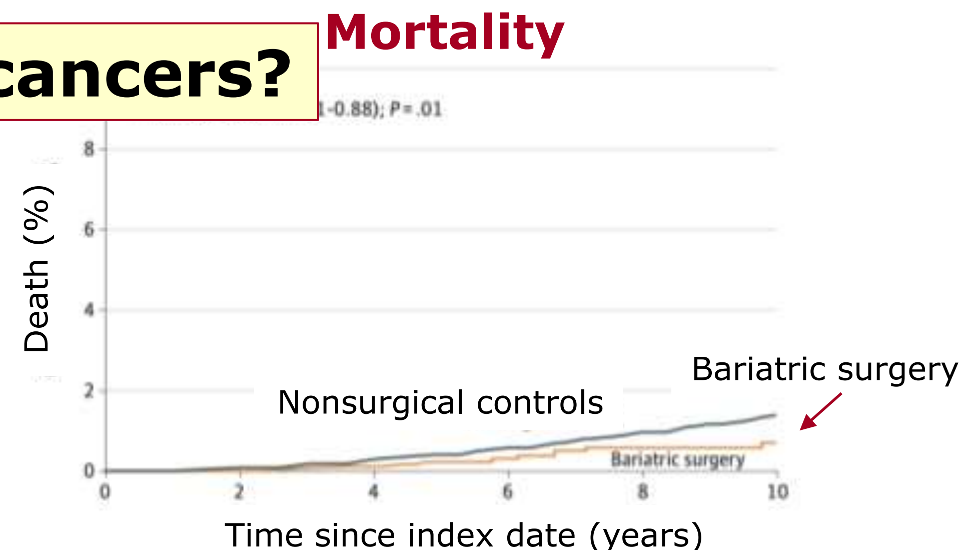




Is this benefit dependent on weight loss?

How much weight loss is required for this benefit?

Is it the same for all cancers?



Adapted from http://www.cancer.gov; Aminian A *et al.*, *JAMA* 2022

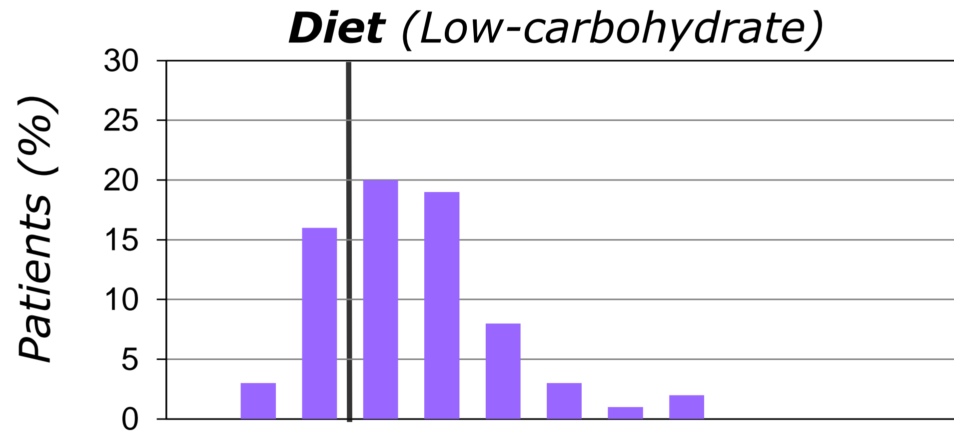
The magnitude of weight loss is important

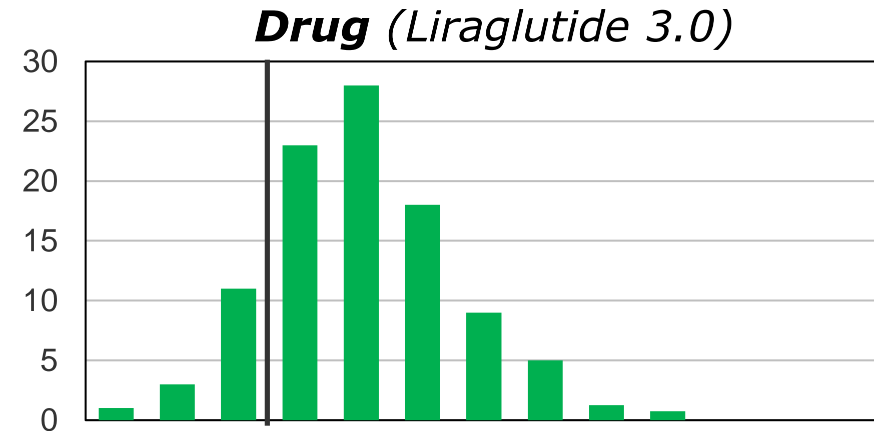
Obesity complication	Weight loss for substantial improvement (%)	Benefits increase with increasing weight loss
Type 2 diabetes	5-15	✓
Hypertension	15	✓
Dyslipidemia	10-15	✓
Fatty liver disease (NAFLD)	10	✓
Sleep apnea	10	✓
Osteoarthritis	5-15	✓
Stress incontinence	5-10	✓
Gastroesophageal reflux	10-15	✓
Polycystic ovary syndrome	10-15	✓

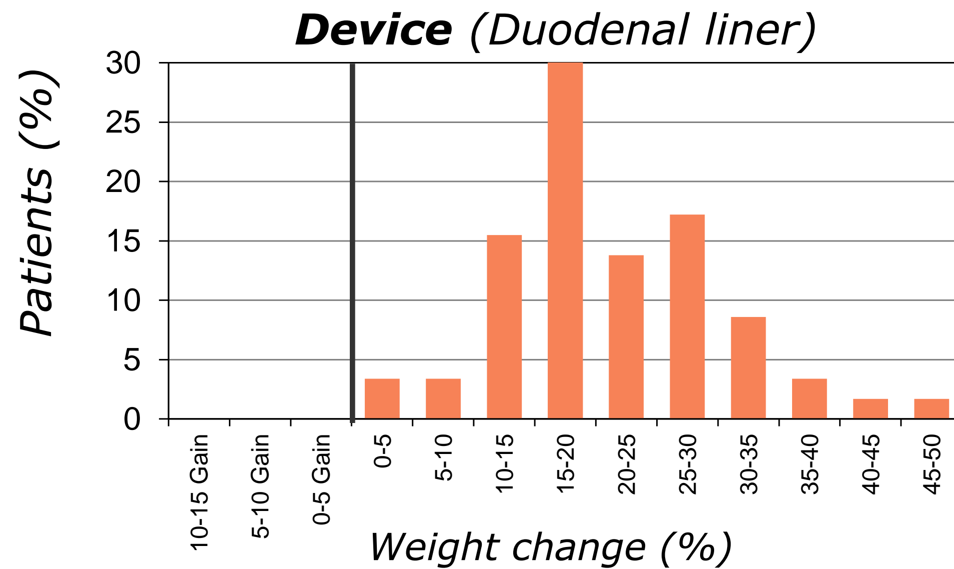
Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

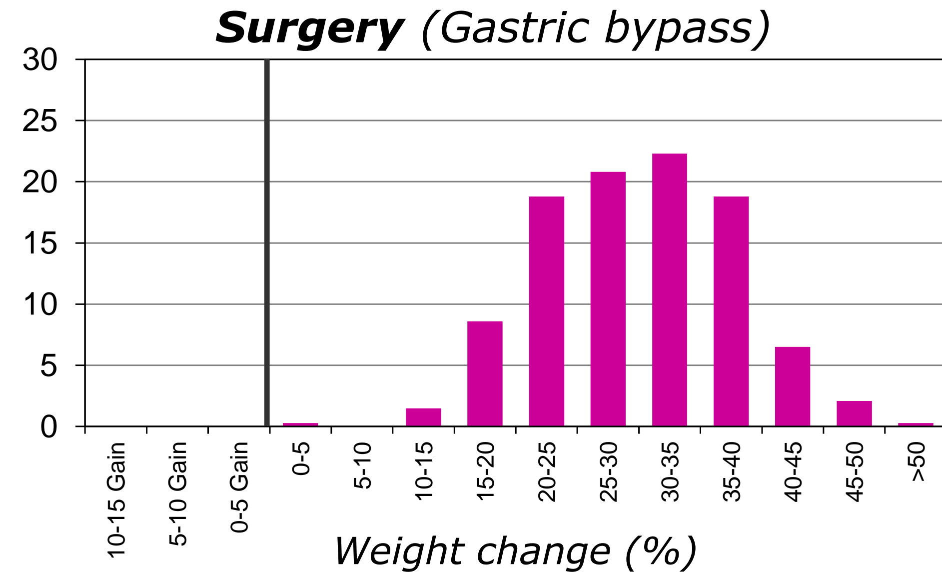
Adapted from Cefalu WT *et al.*, *Diab Care* 2015

Weight loss varies widely among patients









Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Kaplan LM, 2023

Weight loss is associated with remission of steatohepatitis

- Subjects: **293 adults** with NAFLD

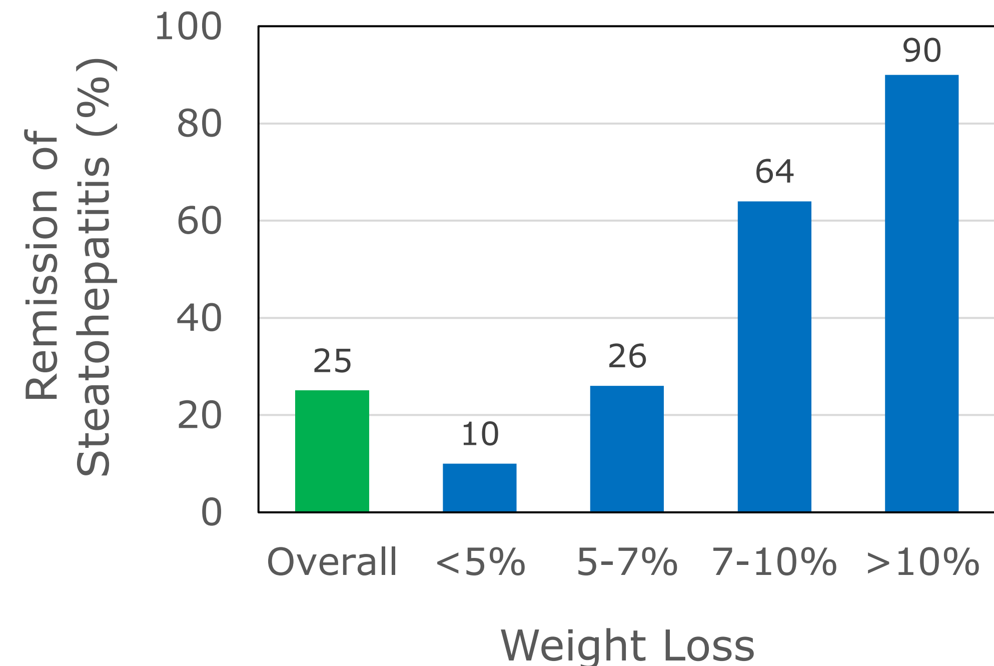
  Average NAS 4.8

  61% F0, 8% F1, 20% F2, 11% F3 (no F4)

- Intervention: 52 week treatment
  750 kcal/day deficit diet
  200 min/week exercise

- Average weight loss **3.8%**
  - **30% with weight loss ≥5%**

- Average change in NAS Score **-1.58**



Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Adapted from Vilar-Gomez E *et al.*, *Hepatology* 2015

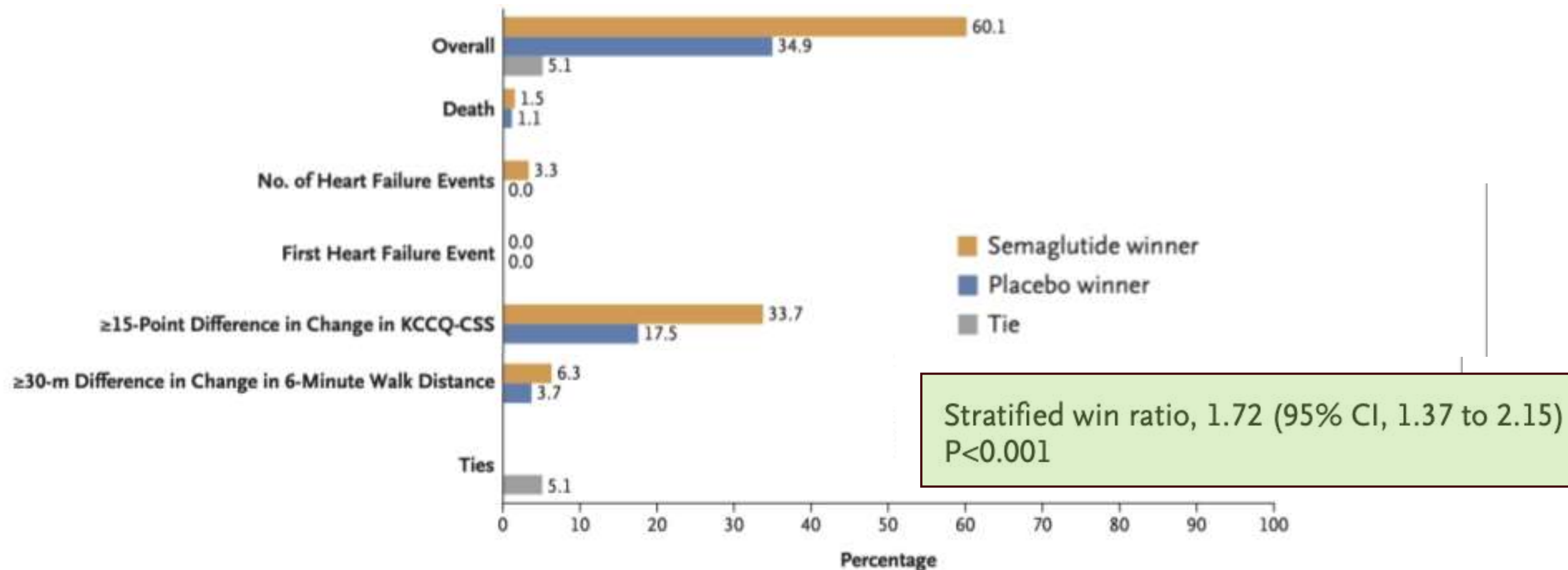
Semaglutide improves cardiac outcomes and reduces major adverse cardiac events in patients with HFpEF

STEP-HFpEF Trial

Phase 4 study of semaglutide 2.4 mg vs. placebo for 52 weeks in people with HFpEF

N=529

Stratified Win Ratio for Hierarchical Composite End Point



Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Kosiborod MN *et al.*, *NEJM* 2023

Weight loss is essential for HFpEF improvement on semaglutide

STEP-HFpEF Trial

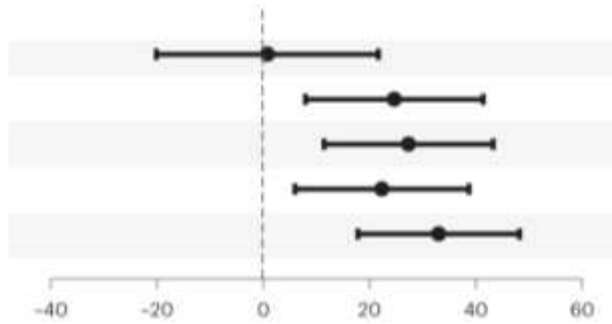
Phase 4 study of semaglutide 2.4 mg vs. placebo for 52 weeks in people with HFpEF

N=529

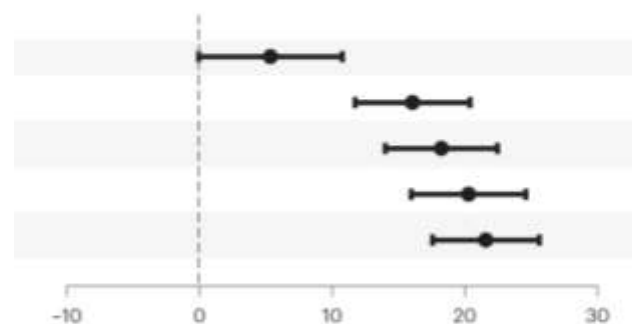
Intention-to-treat analysis

Weight loss	Physical functioning (6MWD)	Patient-reported outcomes (KCCG-CSS)	Inflammation (CRP)

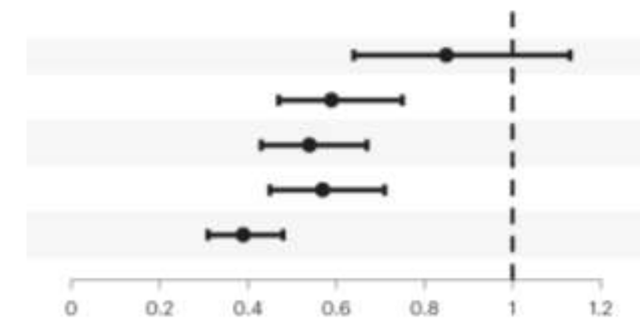
<5%
5-10%
10-15%
15-20%
>20%



Worse ← → Better



Worse ← → Better



Better ← → Worse

Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Adapted from Borlaug BA *et al.*, *Nat Med* 2023

Addressing a suboptimal initial response to surgery

Options

- Substitute for obesogenic medications
- Reinvigorate lifestyle treatment
- Add one or more anti-obesity medications
- Add a bariatric endoscopic intervention
- Modify (revise) metabolic-bariatric operation
- Convert to new metabolic-bariatric procedure

Each option has different benefit, risk and cost characteristics.
Each one can be used alone or in combination with others.

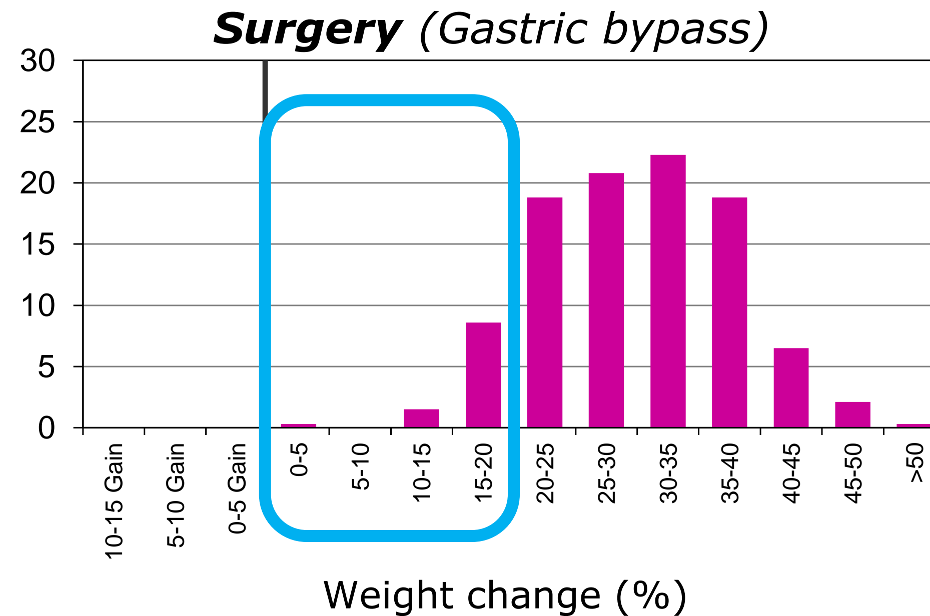
Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Kaplan LM, 2023

Assessing cutoffs for suboptimal initial weight loss

Section 1 - Proposed statement 8

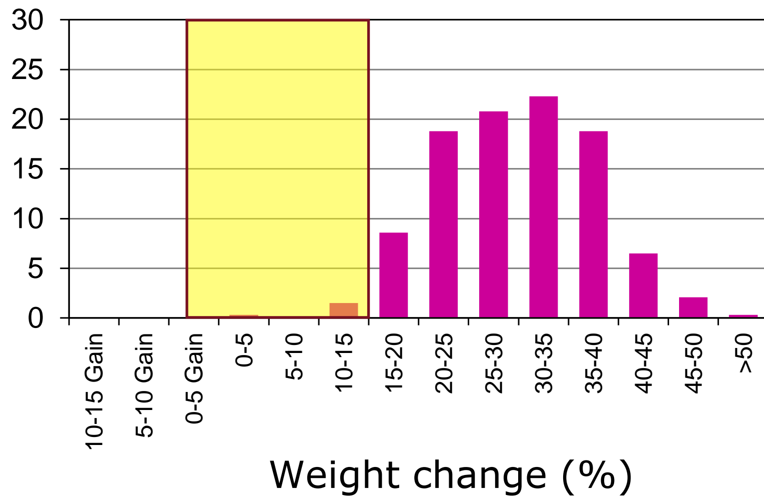
United States

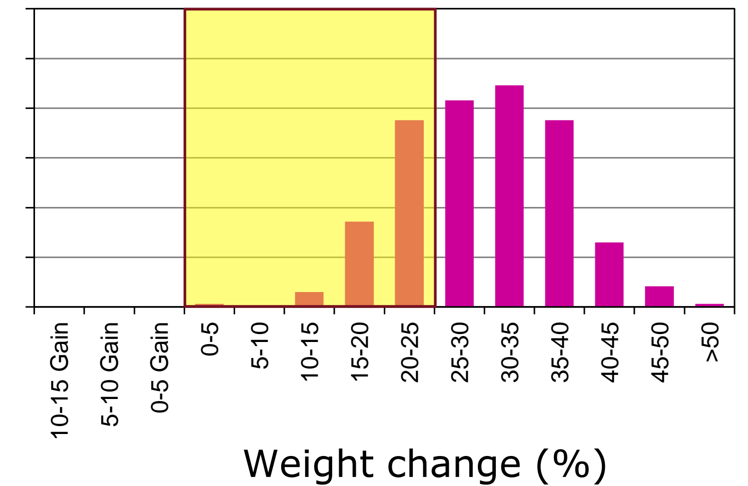


Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Kaplan LM, 2022

Assessing cutoffs for suboptimal initial weight loss

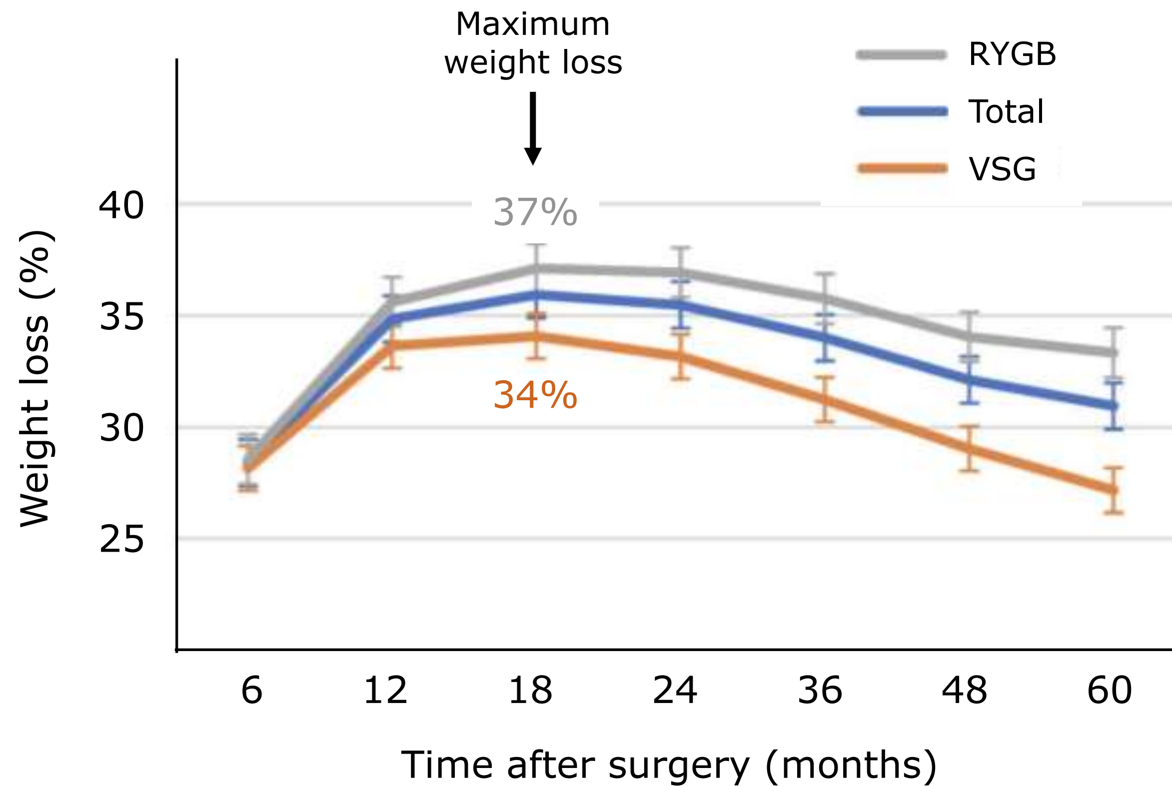




Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Kaplan LM, 2023

Differential 5-year weight loss with RYGB vs. VSG



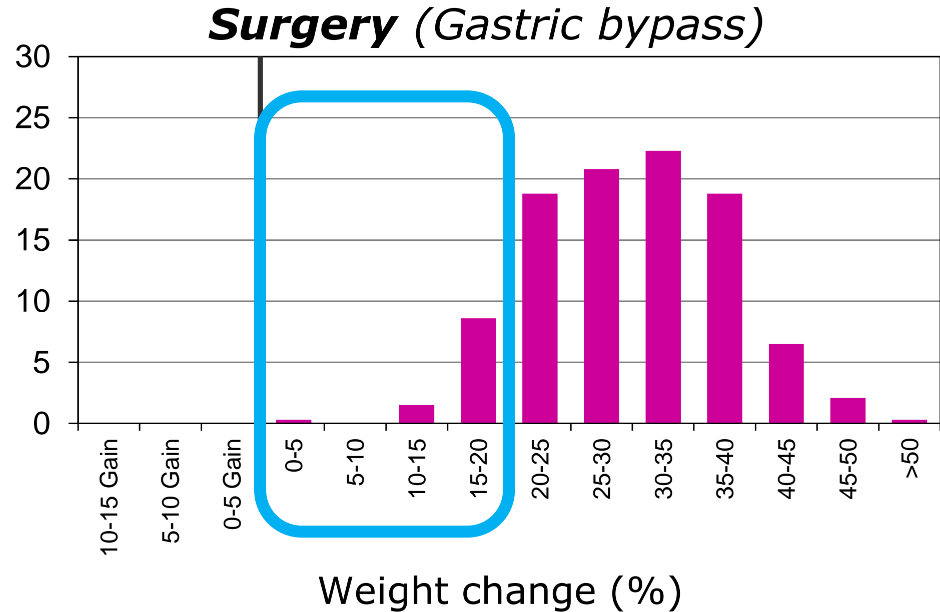
VSG averaged 92% as much weight loss as RYGB

Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Adapted from Sanchez-Cordero *et al.*, *J Clin Med* 2023

Assessing cutoffs for suboptimal initial weight loss

United States



Spain

	<15% TWL	<18% TWL	<20% TWL
	Portion of patients meeting this criterion		
VSG	5.2%	10.4%	18.0%
RYGB	1.8%	7.0%	10.4%

Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Kaplan LM, 2023; Sanchez-Cordero *et al.*, *J Clin Med* 2023

Conclusions

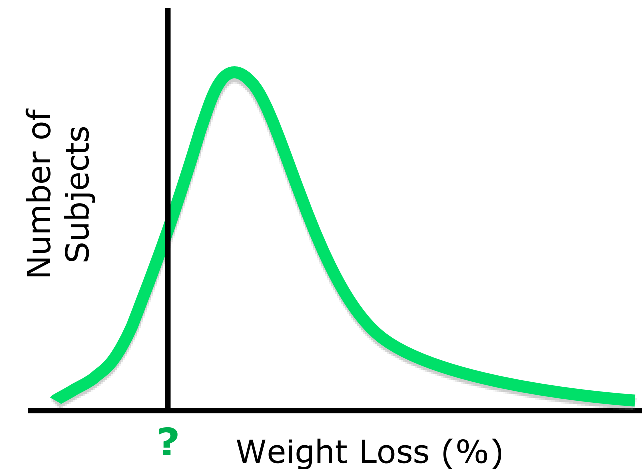
- There is currently no consistent means of determining the optimal clinical response to surgery
- Categorical definitions of “responder” and “non-responder” based simply on BMI or percent weight loss characterize individual patients as “successes” or “failures,” which can reinforce stigma
- ”Suboptimal initial response” to surgery allows for a more continuous description of benefit
- ”Suboptimal initial response” is viewed differently depending on the initial indications for the surgery (e.g., degree of obesity, type and severity of complications, etc.)
- There are widely different efficacy and risk characteristics of different therapeutic approaches to suboptimal initial response (i.e., medications, endoscopic interventions, and revision and conversion surgery)
- Thus, the indications for defining suboptimal clinical response and the approach to further therapy should be individualized based on the patient’s need and the treatment considered

Copyright © 2023 The Obesity and Metabolism Institute. All rights reserved.

Kaplan LM, 2023

LMKaplan0@gmail.com

Defining the Clinical Response to Metabolic Surgery



Lee M. Kaplan, MD, PhD

Obesity Medicine Section and Dartmouth Obesity Care Center
Geisel School of Medicine at Dartmouth

LMKaplan0@gmail.com

31 August 2023

2023 IFSO World Congress