

Special topics and intersection of surgery and advanced pharma

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Disclosures:

- I receive a donation of drug and placebo (empagliflozin) from Boehringer Ingelheim for a clinical trial.
- I serve as a site PI for clinical trials from Eli Lilly, and Recordati.
- I serve on advisory board and shareholder for Calorify.
- I consult for Eli Lilly and Abbott on publications.

Support:



National Institute of
Diabetes and Digestive
and Kidney Diseases



National Heart, Lung,
and Blood Institute



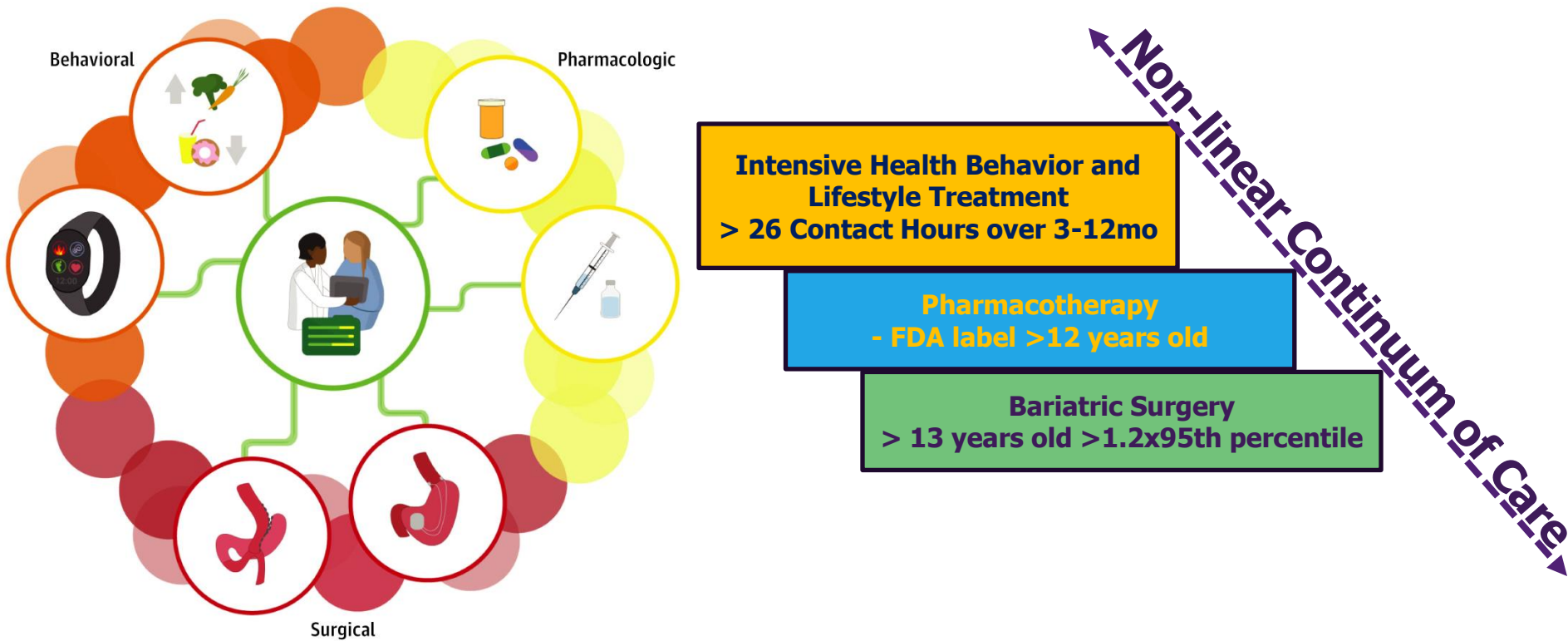
Hot Topics and Questions to Address

- 1) Who is likely to respond to obesity treatment and which one?
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- 4) Are GLP-1s going to put pediatric bariatric surgeons out of business?

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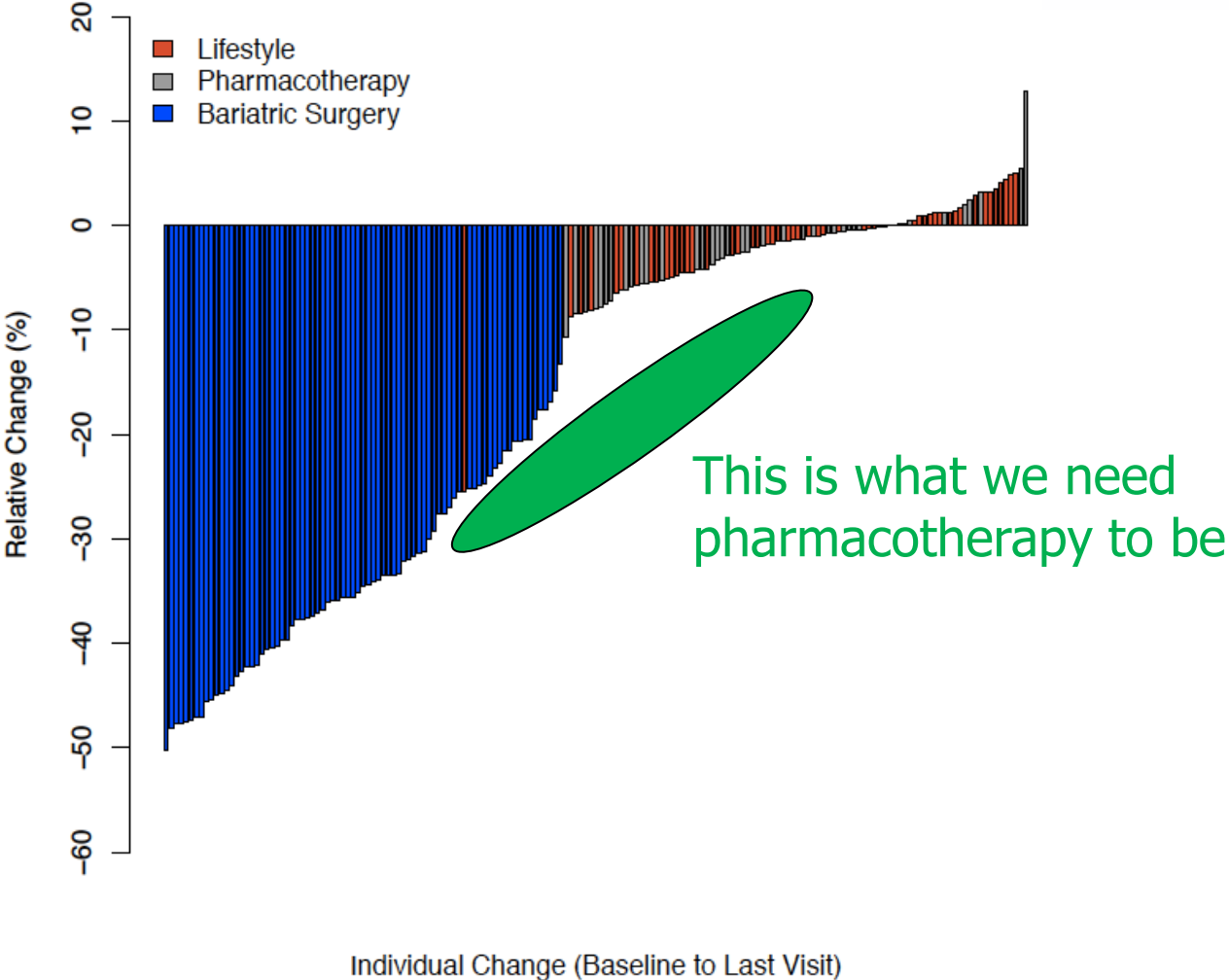
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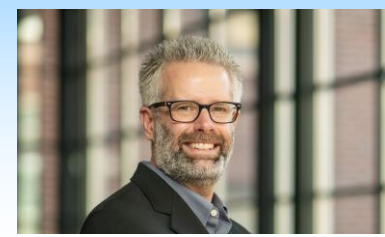
Obesity Clinical Management



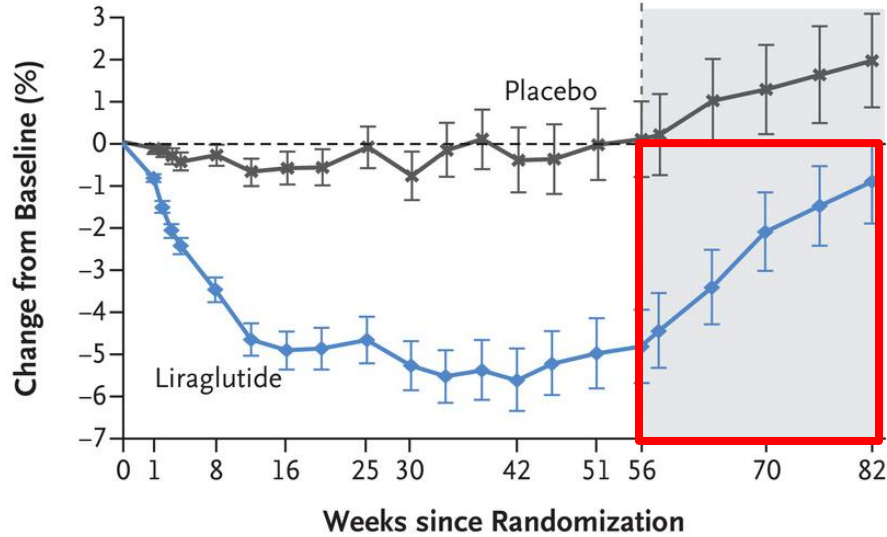
Heterogeneity is Significant!

Figure 1. Panel A: Relative Change in BMI





B Relative Change in BMI

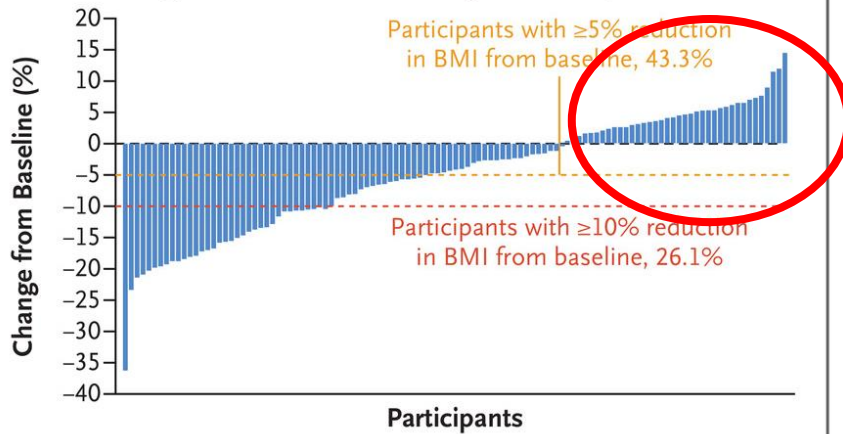


No. of Participants

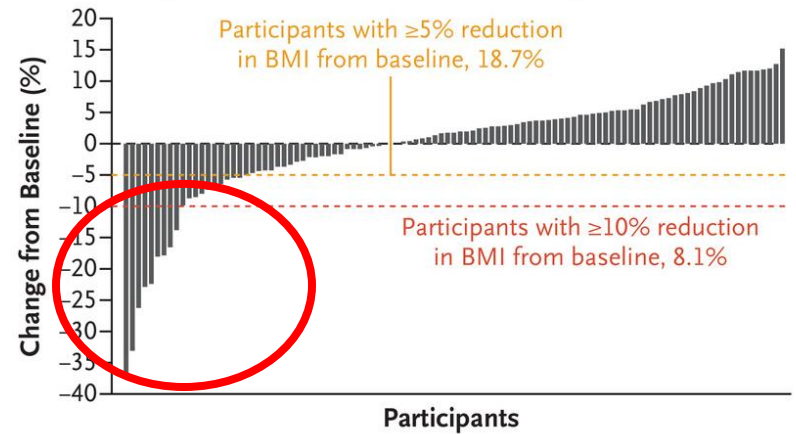
Placebo	126	125	123	116	116	105	101	105	97	102
Liraglutide	125	123	119	118	119	110	107	113	106	112

Obesity is a Disease!
Will require long-term treatment

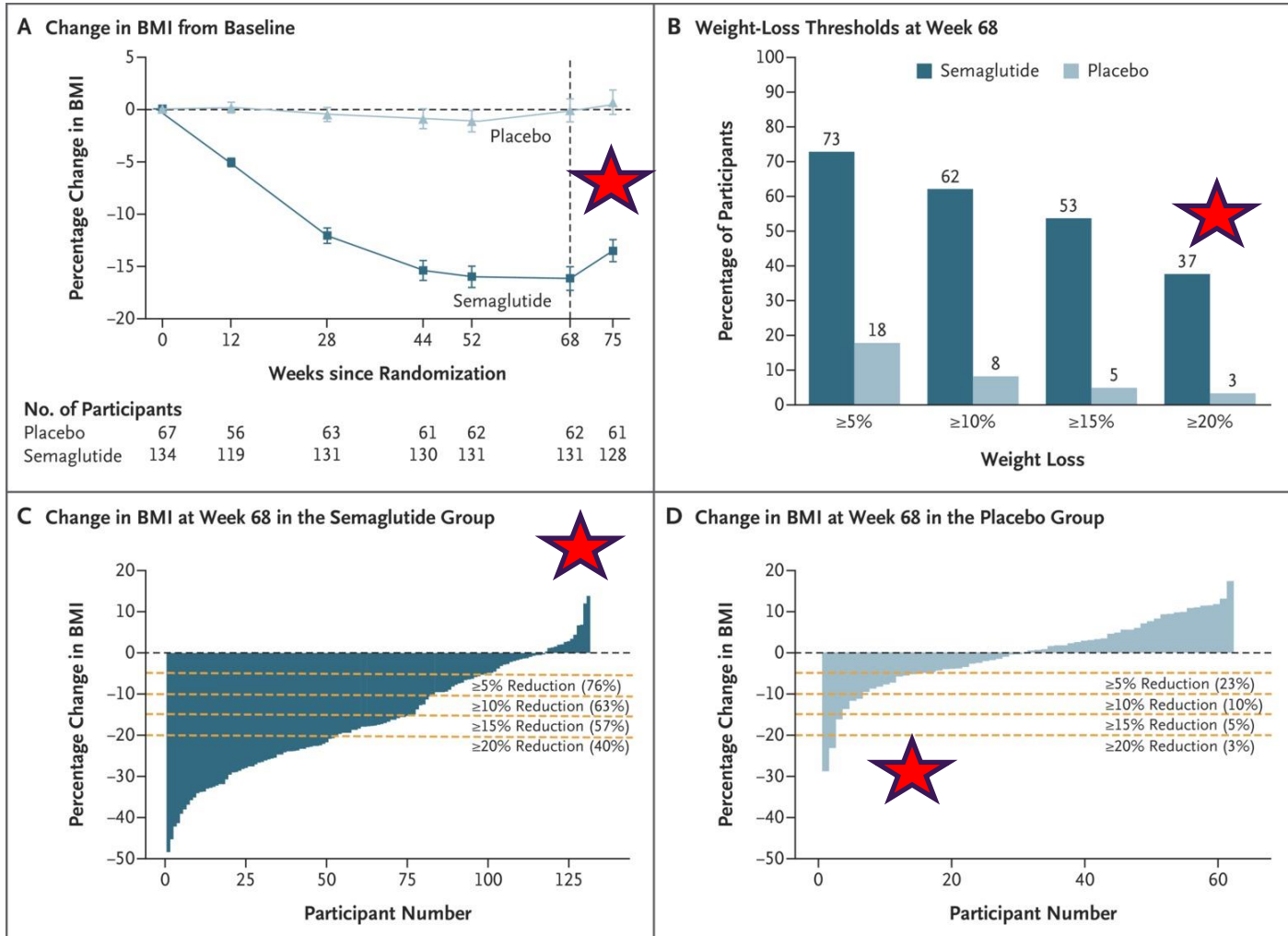
C Relative Change in BMI at Wk 56 in Liraglutide Group



D Relative Change in BMI at Wk 56 in Placebo Group



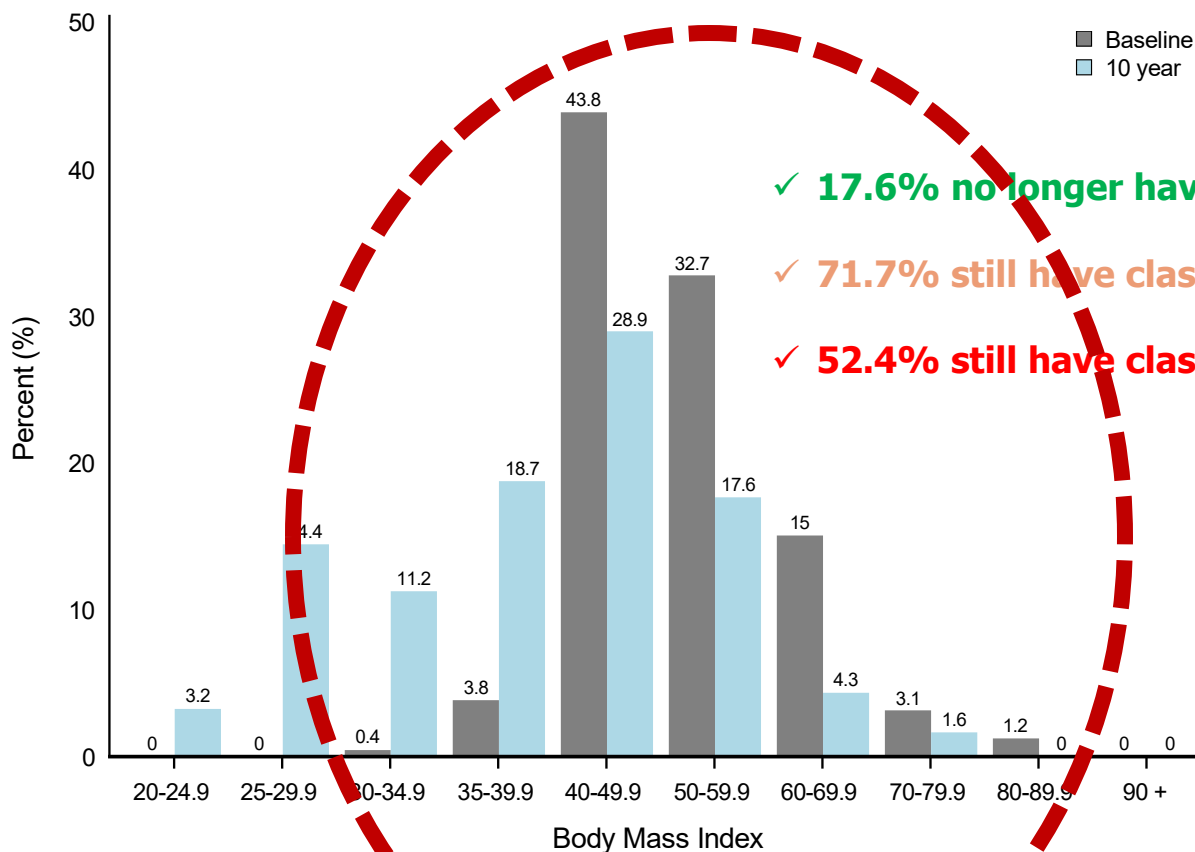
Semaglutide and future longer acting GLP-1RAs will be a game changer.



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BMI distribution by study visit.



✓ 17.6% no longer have obesity

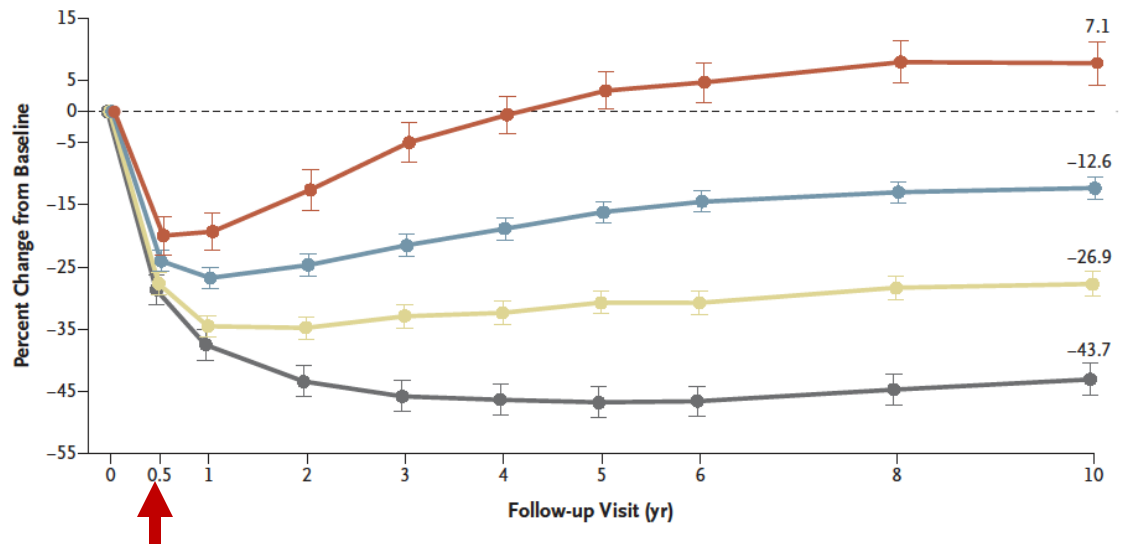
✓ 71.7% still have class 2 obesity at 10 years

✓ 52.4% still have class 3 obesity at 10 years

82.5% still qualify for OMM

Early Response Predicts Long-term Response

B Trajectories of Changes in BMI



- **11% (n=28)**
- **%BMI change at 10 year +7.1%**

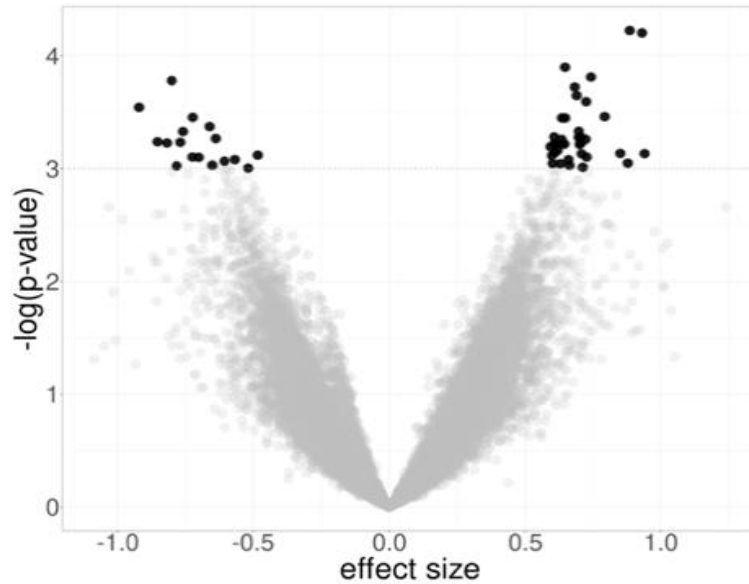
- **38% (n=99)**
- **%BMI change at 10 year -12.6%**

- **33% (n=87)**
- **%BMI change at 10 year -26.9%**

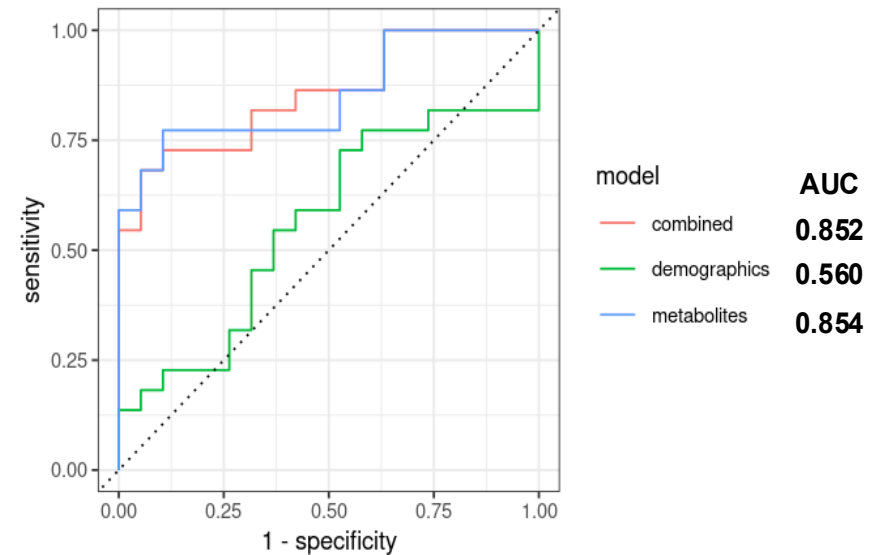
- **18% (n=46)**
- **%BMI change at 10 year -43.7%**

>24% BMI reduction to be black or yellow

Can we Predict at Pre-Op who is going to respond AND need both surgery and OMMs?



Numerous baseline metabolites are associated with long-term weight loss maintenance.

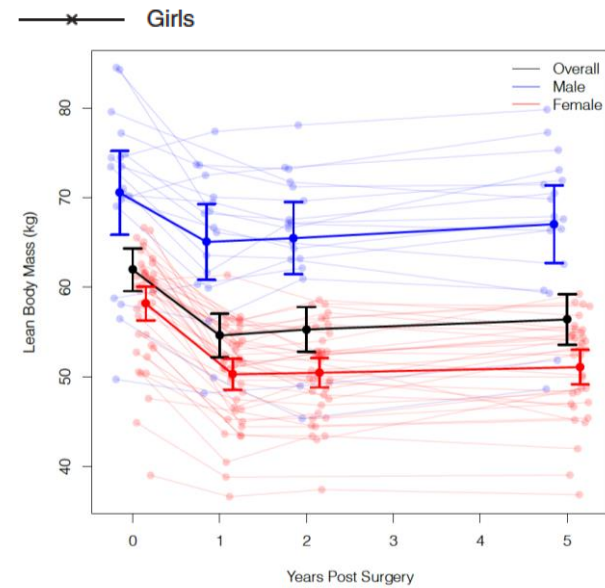
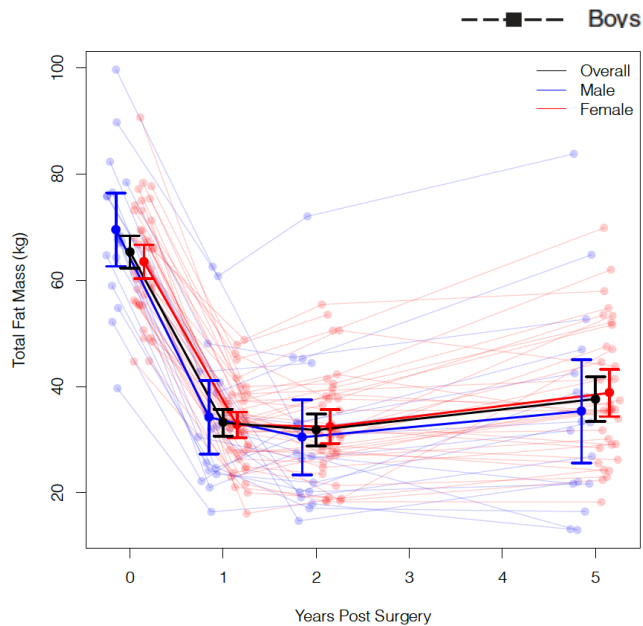
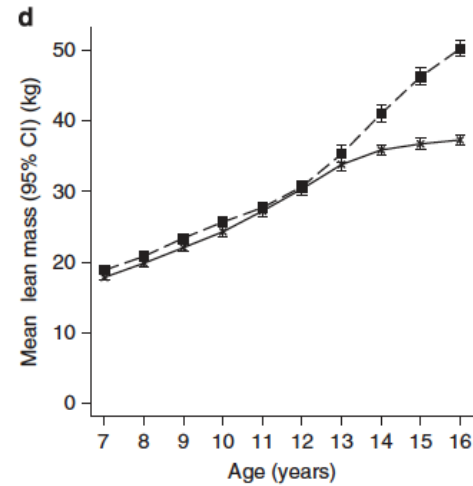
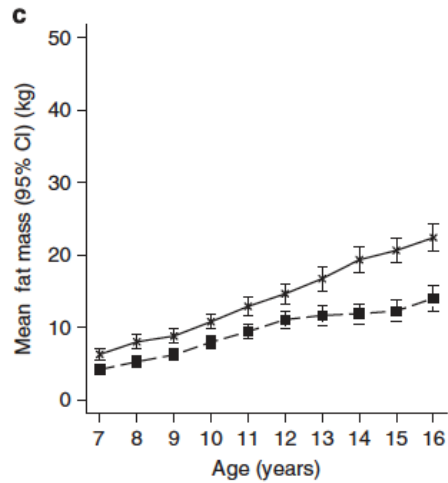


ROC analysis of predictive models for weight loss maintenance.

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Role of Fat Mass and Fat Free Mass Changes

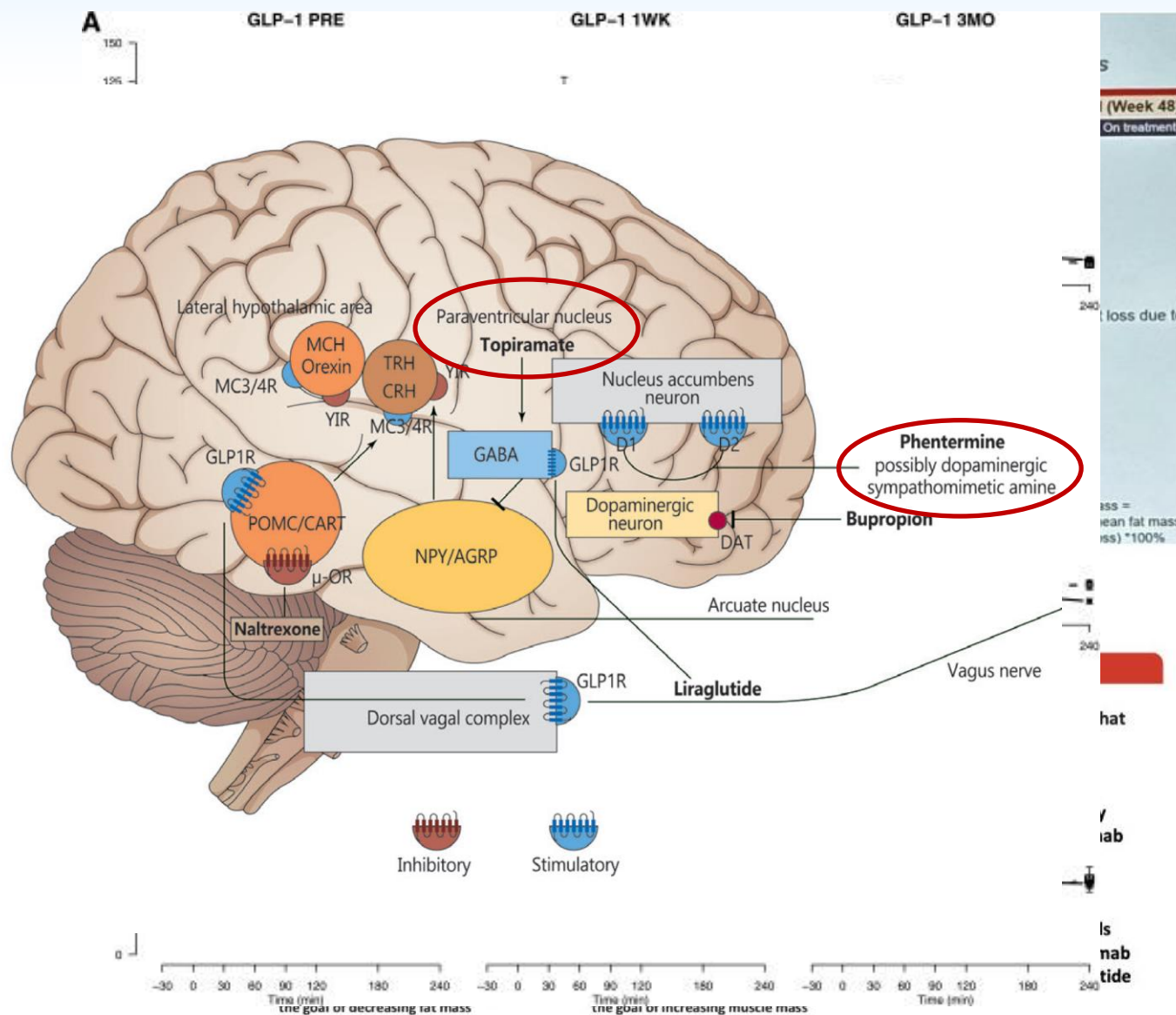


Which pharma do you start with as an add on?

GLP-1RA +
GIP? + Gluc?

Qsymia
(phentermine
/ topirmate)

Wait for
Bimagrumab

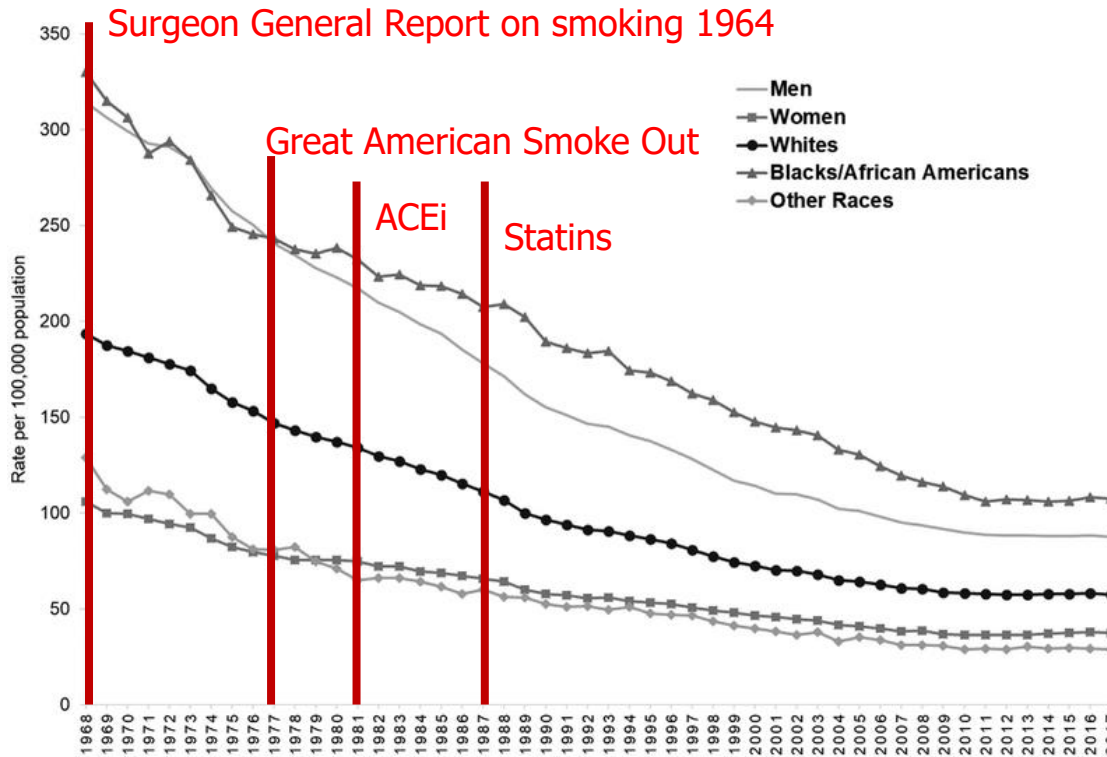


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Will GLP-1s induce a Smoking +Pharma like event on CVD events?

Hard
CVD
events

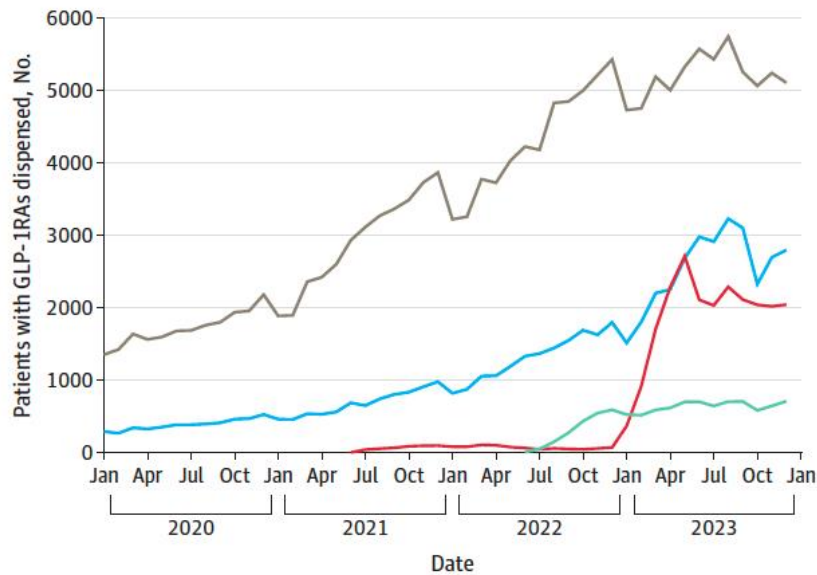


Ritchey et al., 2019 Trends CV Med

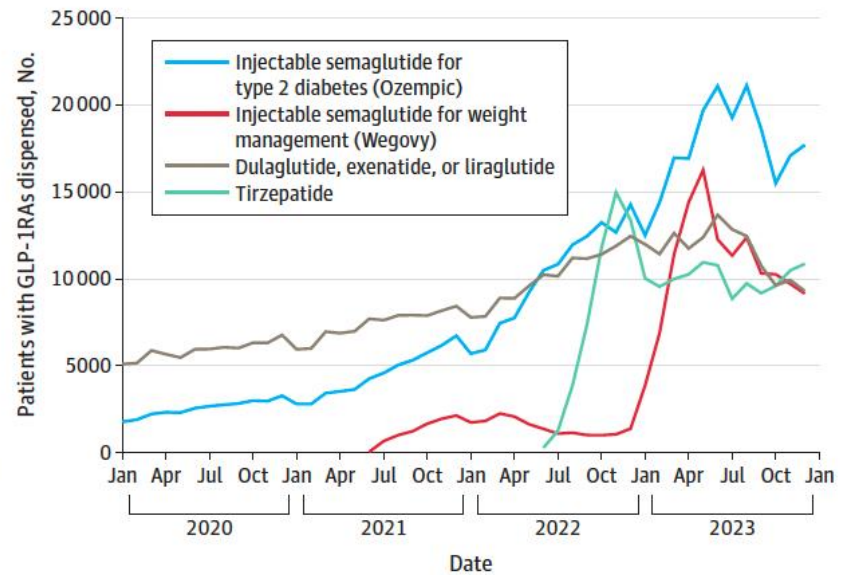
Current use of GLP-1s.....

Lee et al., 2024 JAMA

C Adolescents aged 12-17 y with dispensing of specific GLP-1RAs



D Young adults aged 18-25 y with dispensing of specific GLP-1RAs

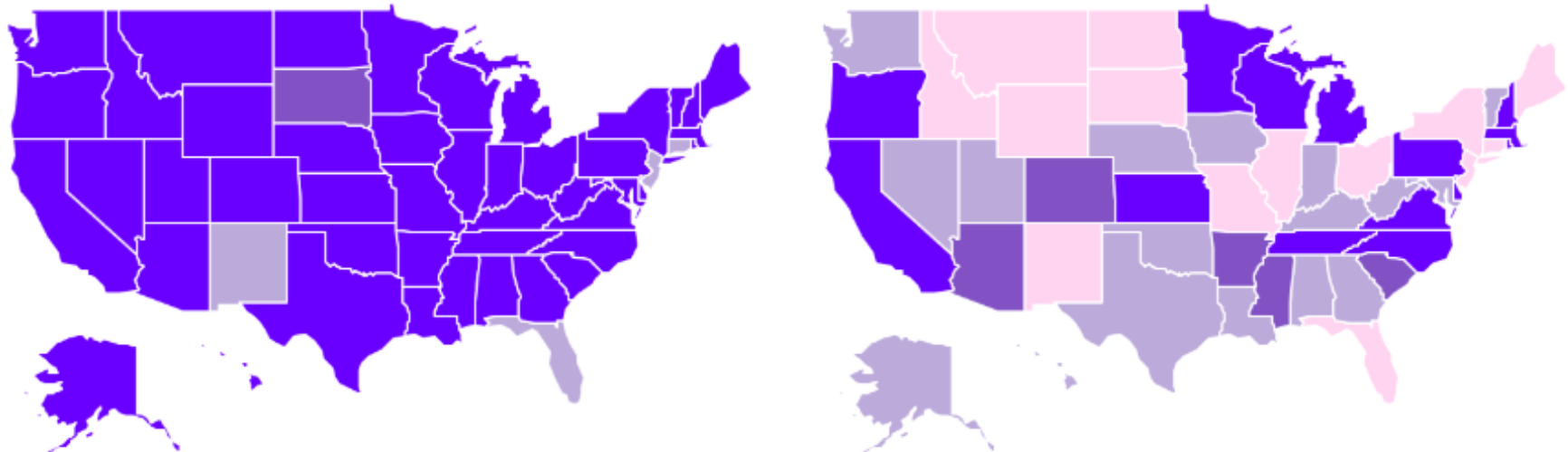


1 in 23 adolescents in USA met the eligibility criteria for MBS (Shapiro et al, 2024, Pediatrics)

~ 1.8mil adolescents

Differences based on diagnosis!

Which State Medicaid Programs Currently Cover GLP-1 Drugs?



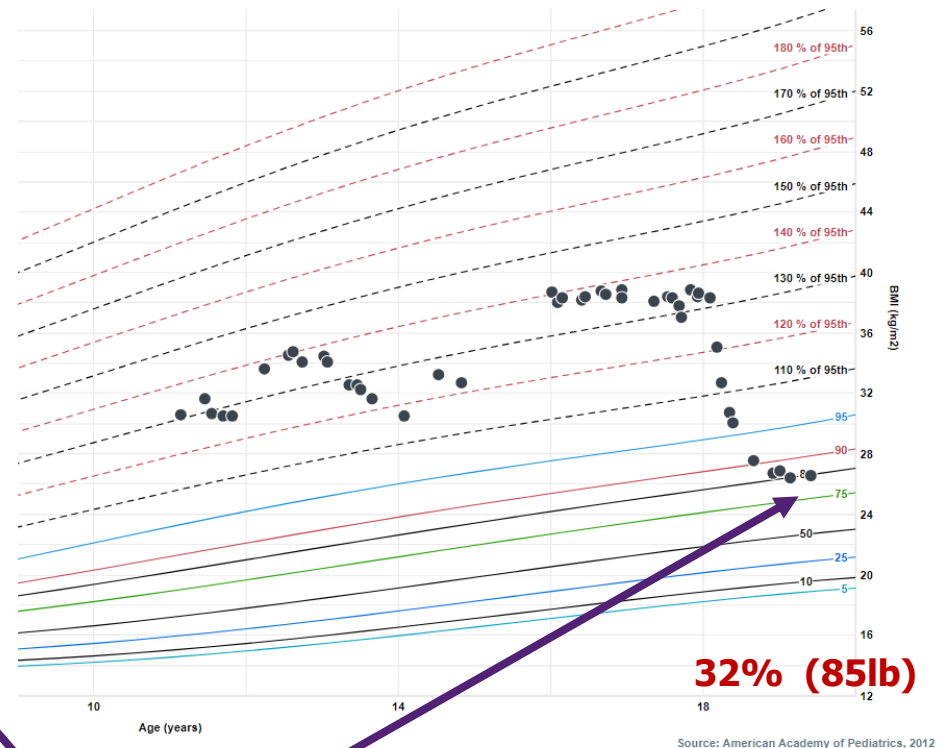
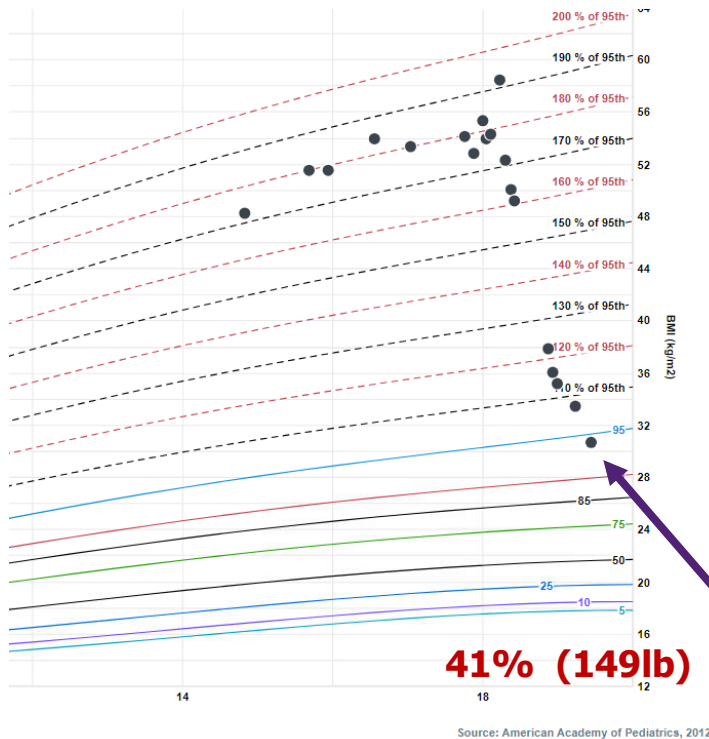
Type 2 diabetes-indicated GLP-1 coverage
(Ozempic, Mounjaro, or Rybelsus)

Obesity-indicated GLP-1 coverage
(Wegovy, Zepbound, or Saxenda)

● None of them ● One of them ● Two of them ● All of them

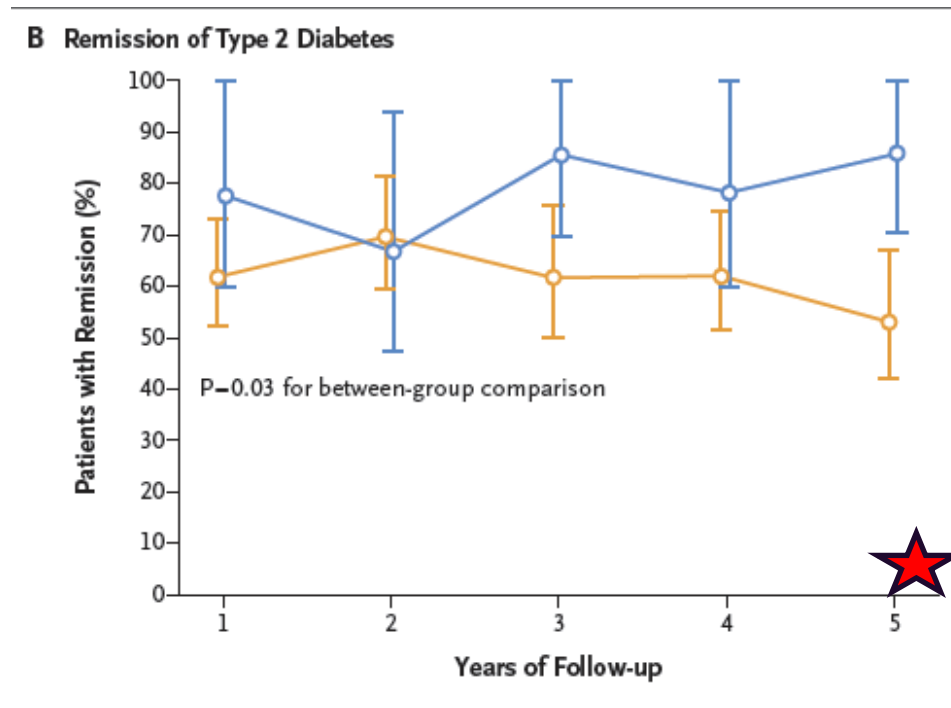
Data Source: IRIS by Real Chemistry | Image Credit: Real Chemistry

You do not see these results with medications



No longer has
obesity

Better at T2D remission than adults



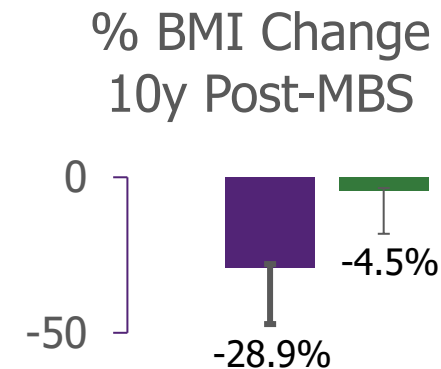
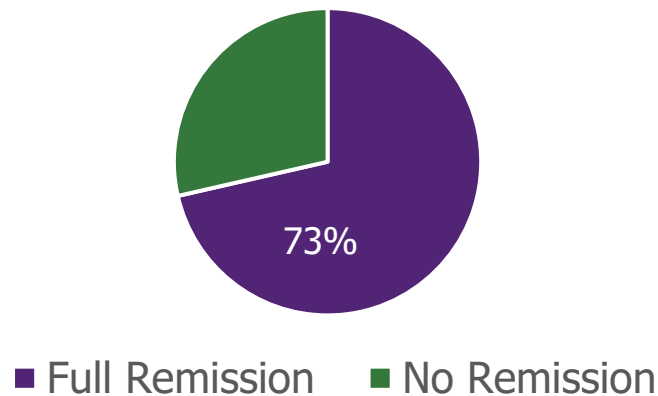
This is with medical management

Inge et al., 2019, NEJM

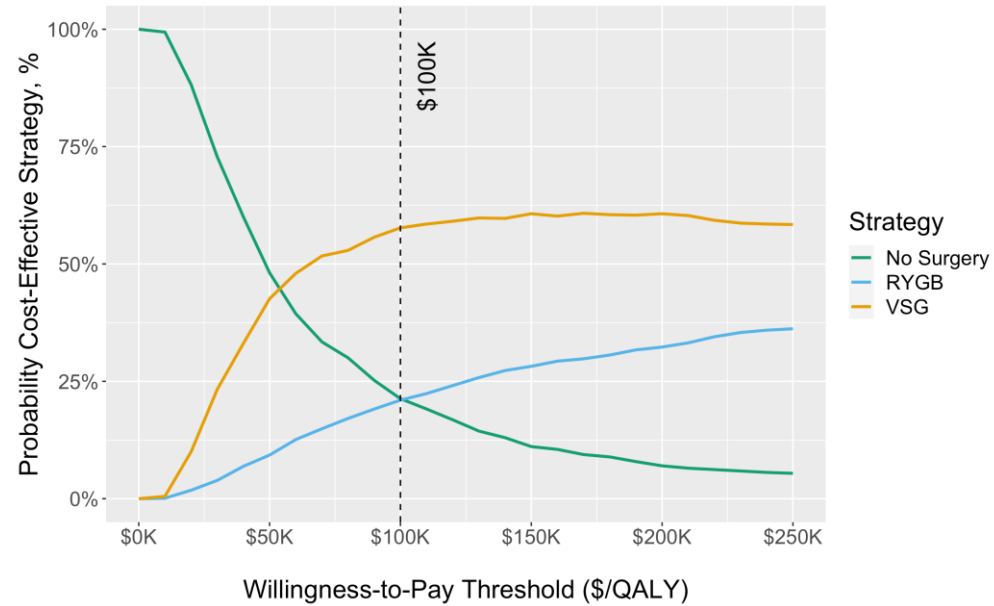
10 year T2D remission rates

Patient Characteristics	Mean (SD) or Median (Q1, Q3)	T2D Remission	No T2D Remission
BMI (kg/m ²) at MBS	53.9 (9.2)	54.6 (9.4)	52.1 (9.3)
HbA1c (%) at MBS	6.3 (5.4, 8.0)	5.9 (5.3, 6.6)	6.8 (6.3, 10.8)
BMI (kg/m ²) at 10 years post-MBS	42.0 (13.2)	38.9 (13.3)	49.7 (10.4)
% Change BMI 10 years post-MBS	-21.9 (20.2)	-28.9 (18.3)	-4.5 (13.7)
HbA1c (%) 10 years post-MBS	5.2 (5.1, 6.4)	5.1 (4.9, 5.2)	9.2 (7.6, 10.8)

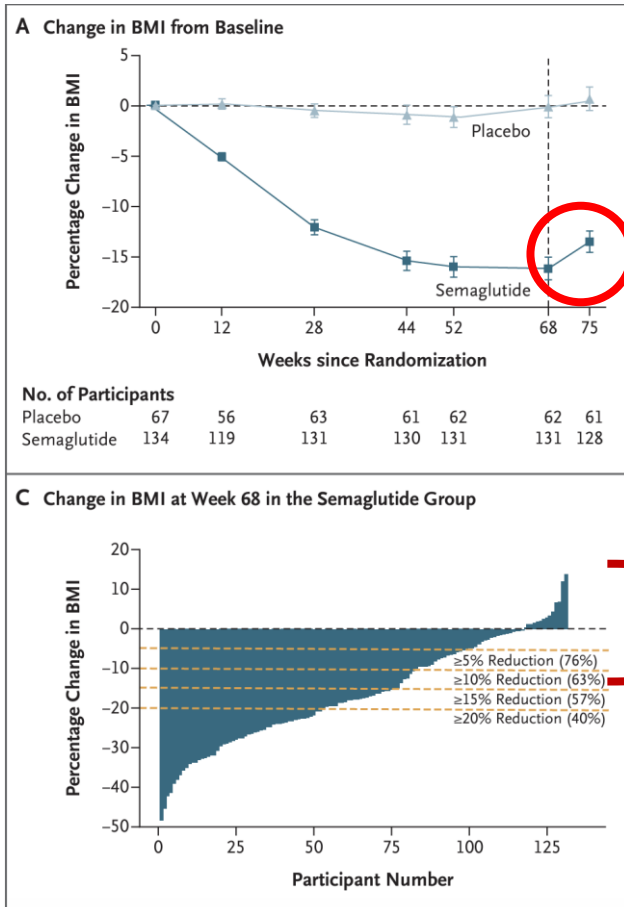
10y Post-MBS Diabetes Status



MBS in adolescents is cost-effective



Strategy	Total Cost (\$)	QALYs	ICER (\$/QALY gained)	
			vs. no surgery	vs. VSG
No surgery	40,882	6.117	REF	
VSG	72,048	6.875	41,164	REF
RYGB	79,626	6.888	50,271	557,751



Unlike with MBS, weight regain off-treatment is almost immediate?
Will this change over 3, 5, 10 years with and without meds?

If they still have severe obesity and/ co-morbidities are these prime surgical candidates?

Some Take Home Points

- Treatment of pediatric obesity has significant variation in response
- Understanding the mechanisms and identifying predictors of response will expedite precision medicine / surgical efforts
- The space is evolving rapidly due to more potent pharmacotherapy being available, these will likely be complementary to surgery not a replacement
- Bariatric surgery will remain the most effective treatment option until medications demonstrate long-term cost-effectiveness

Questions?

Contact info: jryder@luriechildrens.org