

Webinar Will Begin Momentarily

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Professional Education Series

Support. Inform. Educate. Empower.

Unlocking the Potential of GLP-1 RA: What we've learned and its implications in lifestyle.

TODAY'S AGENDA:

- Welcome
- Speaker Introduction
- Presentation
- Q&A
- Closing



WEBINAR HOST:

Keith Hine, MS, RD

VP of Healthcare, Sports & Professional Education
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WEBINAR PRESENTER:

Angela Manderfeld, MS, RDN, LD, CDCES

Registered Dietitian, Board Certified in Advanced Diabetes
Management

DISCLOSURES

Orgain
Medtronic Diabetes

OUTSMART
YOUR
DIABETES

LEARNING OBJECTIVES

- Identify clients who may benefit of using GLP1 RA
- State 3 possible downsides to the use of this medication
- Nutrition and lifestyle implications that need to be addressed in clients taking this med
- 3 ways to help clients increase their GLP1 without meds



Understanding How GLP1 Works

- GLP 1 is secreted by L Cells in the small intestine particularly after we eat.
- GLP1 binds to receptors in places such as the pancreas, brain, heart and GI tract
- Enhances insulin secretion from beta cells in pancreas, particularly when BG is higher. Less chance of hypoglycemia.
- Inhibits glucagon secretion from pancreatic alpha cells, helping lower glucose
- Slows Gastric Emptying which helps give the feeling of fullness
- Acts on CNS (hypothalamus). Promotes satiety and reduces appetite.
- GLP-1 can improve endothelial function and has vasodilatory effects, which contributes to better cardiovascular health.
- Provides neuroprotection and renal protection. (FLOW trial)

But WAIT, there's MORE



- Reduction in neuroinflammation and improves cognitive function
- Improve gut microbiota which positively impacts metabolic health
- Promotes bone formation/reduces bone resorption.
- Reduce albuminuria and improve renal function markers in patients with diabetes
- May reduce fatty liver and improve liver enzymes, (NAFLD)
- Decrease systemic inflammation (helps CV and DM2)
- Immunomodulation effects
- Reduce symptoms of depression and anxiety

Sounds like we all need more GLP1 in our lives, right?

Who would benefit?

Those with:

- Type 2 diabetes
- CV disease
- High blood pressure
- Kidney disease
- Overweight/Obesity
- Post gastric bypass

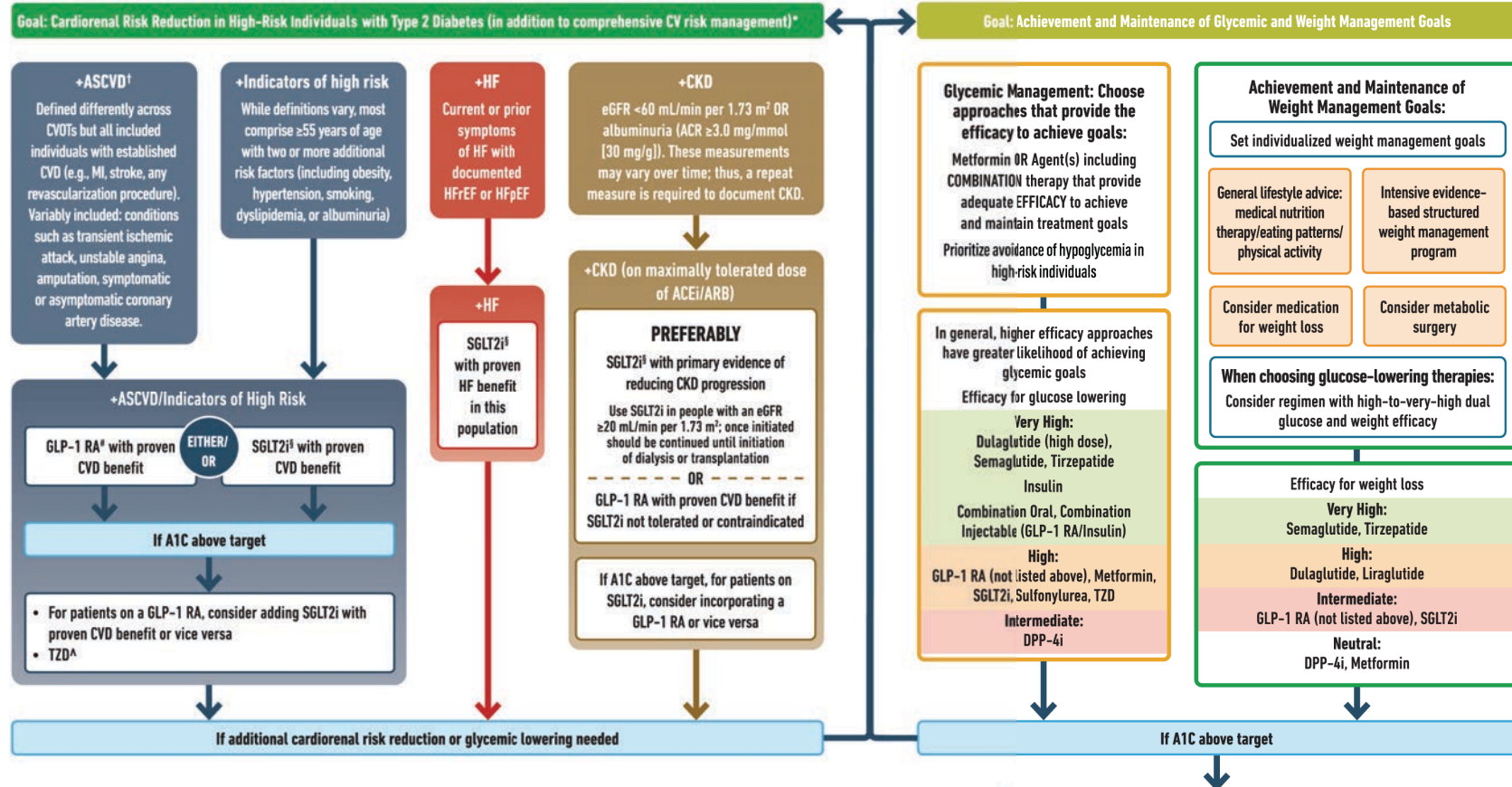


Who would NOT benefit?

- Chronic pancreatitis
- Hx of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2 (MEN2)
- Careful with gall bladder disease
- Pregnant
- Gastroparesis
- Bowel Obstruction
- Inflammatory Bowel Disease

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

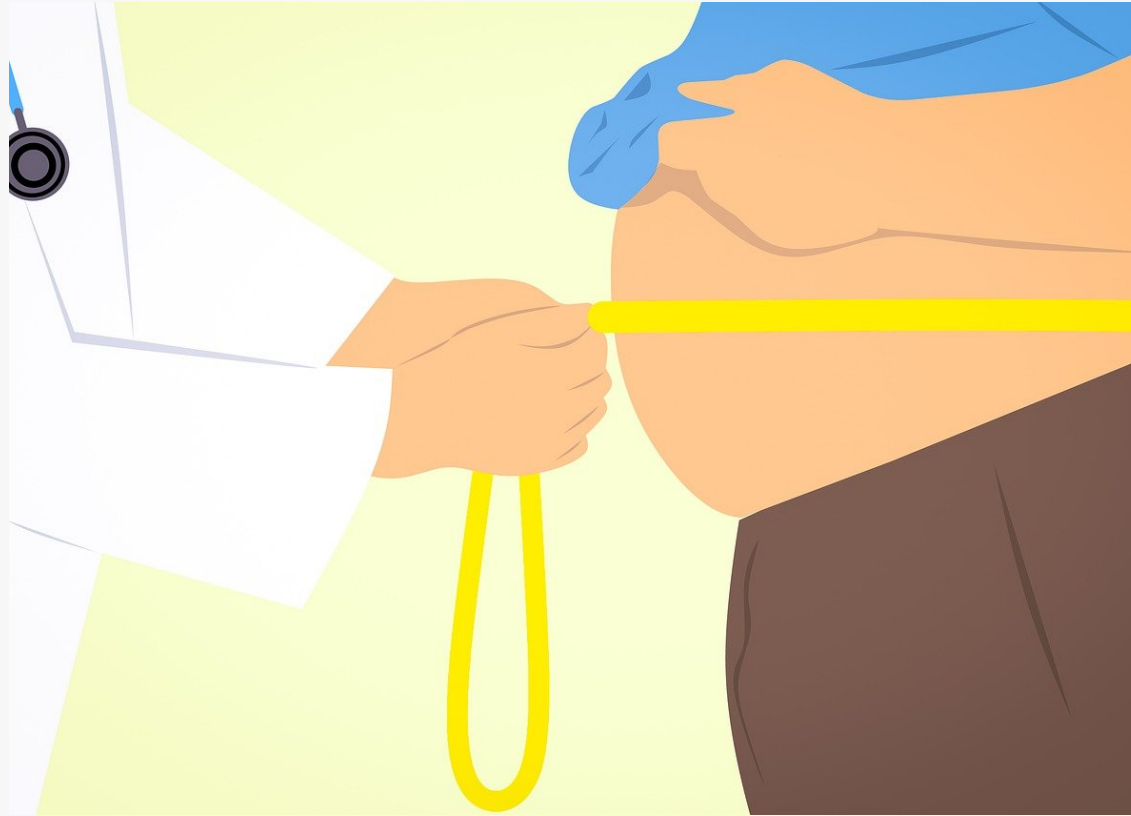
HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)



* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin;† A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details;‡ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HFrEF, and renal outcomes in individuals with T2D with established/high risk of CVD; ¶ For GLP-1 RA, CVDs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

What about people who do not have diabetes?

- *BMI of 30 or higher*
- *BMI of 27 with co-morbidity related to weight (high blood pressure, pre diabetes, high cholesterol, sleep apnea, CV disease)*



 Myths	VS	 Facts
Compounded medications are unregulated and unsafe.		Medications compounded by a 503B Pharmacy are made under strict cGMP guidelines set forth by the FDA, the same administration that oversees commercial manufacturers.
The active pharmaceutical ingredients (APIs) used in compounding are not approved or regulated.		The APIs used by 503B pharmacies are procured from FDA-registered and Current Good Manufacturing Practices (cGMP)-regulated facilities, ensuring their quality and purity. These ingredients must also have a USP-NF monograph.
Compounding pharmacists operate without oversight and can act independently of regulations.		503B pharmacies are heavily regulated by federal and state authorities.
Compounded medications can be made and distributed without prescriptions.		All compounded medications must be prepared under the supervision of licensed pharmacists and must be based on valid prescriptions. However, medications prepared at 503B facilities can be distributed to medical offices without individual prescriptions.
Compounded medications are unnecessary and inferior to commercially available drugs.		Compounded medications allow patients to continue their treatment when name-brand drugs are not commercially available due to shortages.

Compounding Pharmacies

Key takeaways:

- Compounds are custom-made medications available through specialized pharmacies. They're often prescribed when an FDA-approved medication, dose, or dosage form is unavailable.
- Due to shortages, some pharmacies are making compounded versions of GLP1's ***Unregulated GLP1 products are also being sold without a prescription.***
- Consumers should be aware that some Semaglutide products are being made with semaglutide salts (chemicals for research use only) or ingredients from unregistered manufacturers, which do not meet FDA safety requirements.

<https://www.olympiapharmacy.com/blog/understanding-compound-glp-1/>

<https://www.goodrx.com/classes/glp-1-agonists/compounded-semaglutide>

<https://www.fda.gov/drugs/quick-tips-buying-medicines-over-internet/besaferx-your-source-online-pharmacy-information>

What about kids?

In January 2023, the American Academy of Pediatrics urged aggressive treatment of childhood obesity, including using US Food and Drug Administration (FDA)–approved medications such as GLP-1 agonists combined with lifestyle and dietary modifications.



Cost effectiveness study: Lim F, Bellows BK, Tan SX, et al. Cost-Effectiveness of Pharmacotherapy for the Treatment of Obesity in Adolescents. *JAMA Netw Open*. 2023;6(8):e2329178. doi:10.1001/jamanetworkopen.2023.29178
<https://acestoohigh.com/got-your-ace-score/>



CASE STUDY: Pediatric

35 YEAR OLD, FEMALE

- Mom (white)struggles with weight, realtor
- Dad (hispanic) struggles with weight/ DM2/ he is the main cook, works from home
- Has 2 younger sisters who are not overweight
- Very self conscious, especially about going on walks (worried about how others perceive her)
- Checking weight is a “demotivator” for pt, she always felt bad if the scale didn't move
- Scared of needles, often skipping doses
- Pt was resistant to increasing to 2mg dose
- Skipping breakfast - not hungry, but still had to function at school
- Parents were busy didn't always oversee meds
- Starting Wt: 306.2, ending weight 298#, Ht: 5'2”, BMI 56
- Feelings of defeat, like she is doing something wrong
- Not very social at school due to weight and confidence
- Provider said that pt is “cheating on her diet” and “sneaking food”, pt would cry at the doctor appt and was always fearful of being weighed
- Eventually mom and daughter were “fired” from that practice.
Encouraged them to see a functional med NP who specializes in endocrinology.

SHORT-TERM

- Nausea
- Diarrhea
- Constipation
- Reflux/ Fizzy Stomach
- Abdominal pain

MORE SERIOUS

- Pancreatitis
- Bowel Obstruction
- Gastroparesis
- Careful with gall bladder disease
- Thyroid and Medullary Thyroid Cancer
- Acute Kidney Injury (dehydration from n/v)



The use of GLP-1 receptor agonists is associated with an increased risk of thyroid cancer

GLP-1 receptor agonists and the risk of thyroid cancer

Bezin J., Gouverneur A., Pénichon M., Mathieu C., Garrel R., Hillaire-Buys D., Pariente A., Faillie J-L.

Nationwide population-based study on French SNDS database

3,746,672 individuals with type 2 diabetes treated with second-line antidiabetes drugs between 2006-2018



2,562 cases of thyroid cancers



45,184 matched control subjects

	Case subjects <i>n</i> = 2,572	Control subjects <i>n</i> = 45,184	Adjusted hazard ratio (95%CI)*
GLP-1 receptor agonists			
No use	2,255 (88.0)	40,836 (90.4)	Reference
Cumulative use ≤1 year	117 (4.6)	1,767 (3.9)	1.22 (0.99 to 1.50)
Cumulative use 1-3 years	112 (4.4)	1,419 (3.1)	1.58 (1.27 to 1.95)
Cumulative use >3 years	78 (3.0)	1,162 (2.6)	1.36 (1.05 to 1.74)
DPP-4 inhibitors			
No use	1,522 (59.4)	27,406 (60.7)	Reference
Cumulative use ≤1 year	333 (13.0)	5,209 (11.5)	1.12 (0.99 to 1.28)
Cumulative use 1-3 years	310 (12.1)	5,918 (13.1)	0.96 (0.84 to 1.10)
Cumulative use >3 years	397 (15.5)	6,651 (14.7)	1.19 (1.04 to 1.35)

* Adjusted for social deprivation index, goiter, hypo- and hyperthyroidism in the last year, and use of other antidiabetes drugs in the last 6 years considered in therapeutic class.

GLP1 RA OPTIONS

MEDICATION NAME	HOW OFTEN?	DIABETES	WEIGHT LOSS	GLP1 or GIP	OPTION FOR "CLICKS"
♥ Semaglutide	Daily and Weekly	Ozempic 1x/wk Rybelsus daily pill	Wegovy 1x/wk	GLP 1	Yes
Exenatide	Daily and Weekly	Byetta 2/d Bydureon BCise 1/wk		GLP 1	No
Dulaglutide	Weekly	Trulicity 1x/wk		GLP 1	No
Liraglutide	Daily	Victoza 1x/d	Saxenda 1x/d	GLP 1	Yes
♥ Tirzepatide	Weekly	Mounjaro 1x/wk	Zepbound 1x/wk	GLP 1 & GIP	No

♥ = crowd favorites

GLP1 RA DOSING

MEDICATION NAME	HOW OFTEN?	DIABETES DOSING	WEIGHT LOSS DOSING
Semaglutide	Weekly Daily	Ozempic: .25mg/.5mg/1mg Rybelsus (pill): 3mg/7mg/14mg <i>(take at least 30 min before 1st meal)</i>	Wegovy: .25mg/.5mg/1mg/1.7mg/2.4mg
Exenatide	Weekly Daily	Bydureon/Bydureon BCise: 2mg Byetta: 5 mcg/10mcg <i>(twice daily up to an hour before eating)</i>	N/A
Dulaglutide	Weekly	Trulicity: .75mg/1.5mg/3mg/4.5mg	N/A
Liraglutide	Daily	Victoza: .6mg/1.2mg/1.8mg	Saxenda: .6mg/1.2mg/1.8mg/2.4mg/3mg <i>(titrated weekly, dosed any time of day)</i>
Tirzepatide (GLP1/GIP)	Weekly	Mounjaro: 2.5mg/5mg/7.5mg/10mg/ 12.5mg/15mg	Zepbound: 2.5mg/5mg/7.5mg/10mg/12.5mg/ 15mg

CASE STUDY: Insulin Adjustments

66 YEAR OLD, FEMALE

-357#, 5' BMI 69.7

-Has CGM

-Came to me at the beginning of Aug 2023 and told me she needed to lose weight because she had to fly at the end of August for a doctor's appt.

- PAH, DM2, Shingles, Abdominal hernia, Asthma, Fibromyalgia, Allergic to many medications, Arthritis R knee (bone on bone), Sleep Apnea, IBS

- Had been told to eat a bedtime snack so her blood sugar wouldn't go low in the night 🍪

- Aug 8—> 88u tresiba/ Aug 18—> 76u (12# wt loss)/ Sept 19 —>50u Tresiba

- End of July/early Aug CGM avg was 140mg/dl, Sept CGM avg 125mg/dl

- October, switched from 2mg Ozempic to 5mg Mounjaro, down to 44u Tresiba

- Fast Forward: June 2024: Wt is 302# (lost 55.1# total) 15mg Mounjaro, 16 u Tresiba- lost ~15% total body weight

There's more to it than this....

Digestion
mindfulness
stress

Weights/Cardio

Protein

Fiber

Hydration





CASE STUDY: Adult

Q9 YEAR OLD, FEMALE

- Starting Wt 182#, Current weight 137# (initial goal weight was 146#) ~ 25% weight loss overall (15 months)
- Has Hashimoto's, high blood pressure, anxiety, IBS, high cholesterol, mild sleep apnea, prediabetes
- Initially started on Saxenda .6mg (Dec 2022), March 2023 switched to Wegovy got up to 2.4mg dose (March '23 to March'24 lost 30#)
- Notes the 2.4mg dose of Wegovy has completely stopped her appetite.
- Has seen some hair loss.
- Taking fiber supplement. Has always struggled with getting enough protein (even prior to GLP1). But has noticed with high dose she struggles to even eat meals
- Exercises consistently 3-5 days per week. Mostly cardio, is better with weights when she works with trainer.
- Pt wonders if she should go off Wegovy. Recommend she talk with provider about decreasing to 1.7mg dose and not to stop cold turkey.
- Consistently reinforcing protein and weight training during sessions

CAN PATIENTS EVER COME OFF THE MEDICINE WITHOUT WEIGHT COMING BACK?



Slowly Titrate Down

Just as we slowly titrate up, in order to be successful, you must slowly titrate down as well. How?

Behavior Modification

Thinking ahead to any barriers, focusing on behaviors rather than scale. Mindset shift.

Lifestyle

Exercise plan is locked in. Nutrition is priority and making healthy choices feels easy.

Supplements & Tech

Plants/Herbs, Good Bacteria, Omega 3's, Hume Health Body Pod, CGM, Oura Ring

Wilding JPH, Batterham RL, Davies M, Van Gaal LF, Kandler K, Konakli K, Lingvay I, McGowan BM, Oral TK, Rosenstock J, Wadden TA, Wharton S, Yokote K, Kushner RF; STEP 1 Study Group. Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. Diabetes Obes Metab. 2022 Aug;24(8):1553-1564. doi: 10.1111/dom.14725. Epub 2022 May 19. PMID: 35441470; PMCID: PMC9542252.<https://pubmed.ncbi.nlm.nih.gov/35441470/>

How to Increase our own GLP-1

Foods to Increase Akkermansia Muciniphila

- Raw green bananas
- Onions
- Garlic
- Raw asparagus
- Jicama
- Chicory root
- Jerusalem artichoke
- Leeks
- Cold cooked potato
- Dandelion root
- Berries, vegetables (polyphenols)
- Fatty Fish
- Flax
- Hemp seed oil

Foods that contain or help produce butyrate

Butyrate containing foods:

Hard cheeses (like Parmesan and pecorino), butter, full-fat yogurt, and fermented foods, such as kimchi, sauerkraut, pickles, and tempeh.

Ways to help your body produce butyrate:

Eat ground flax, chia seeds, beans and lentils; high-pectin fruits, such as apples and berries; and vegetables like garlic and onions.

Work on sleep- sleep disorders affect butyrate production.

Fasting at least 13 hr overnight from dinner to breakfast is beneficial for butyrate production.

Bonus: Butyrate helps reduce leaky gut



FIBER

Flax, chia, beans, lentils

PROTEIN

Fatty fish, hard cheeses, full-fat yogurt

FRUITS & VEGETABLES

Berries, apples, raw asparagus, onions, garlic, jicama, leeks, cold cooked potato, raw green bananas, kimchi, tempeh, sauerkraut

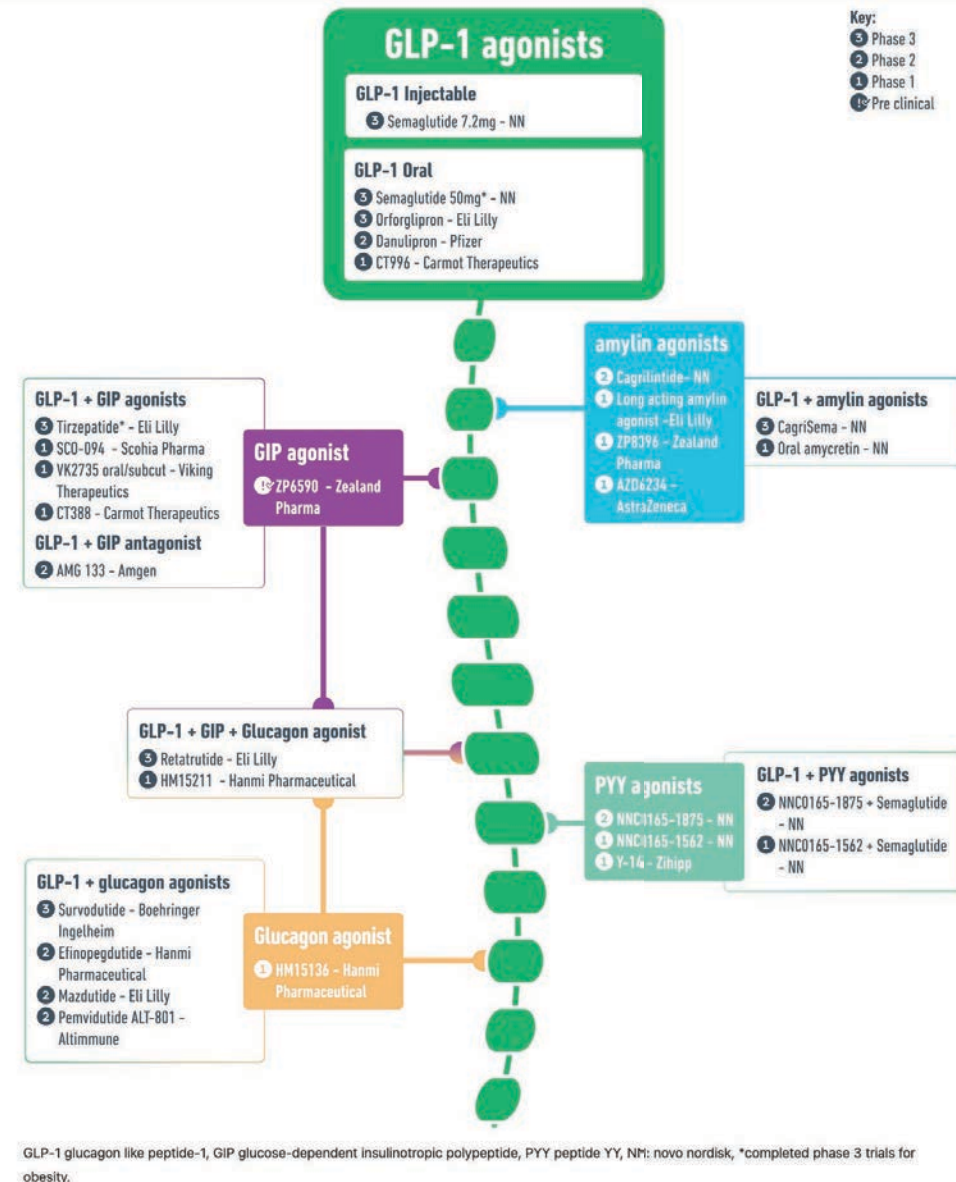
SUPPLEMENTS

Berberine/Metformin, curcumin, ginseng all help increase Akkermansia

More to Come....

- Adding a muscle preserving agent to GLP1
- Additional hormones: Amylin agonists, GIP agonist, GLP1/glucagon, GLP1/GIP/ glucagon triple agonists, Peptide YY agonsits/ GLP1/PYY dual agonists
- Implanted GLP1 for DM2 (rejected by FDA)
- More pill versions of GLP1

Melson, E., Ashraf, U., Papamargaritis, D. *et al.* What is the pipeline for future medications for obesity?. *Int J Obes* (2024). <https://doi.org/10.1038/s41366-024-01473-y>



Key Takeaway

I honestly believe there will never be a replacement for eating healthy and moving our bodies.

We can develop every drug, supplement concoction under the sun, but there is no “hack” that will ever replace lifestyle. Lifestyle is always the foundation in the journey to healing our bodies.

It's great to have “tools”, but they should not be confused with the actual “fix”.

Resources

- Jian H, Liu Y, Wang X, Dong X, Zou X. *Akkermansia muciniphila* as a Next-Generation Probiotic in Modulating Human Metabolic Homeostasis and Disease Progression: A Role Mediated by Gut–Liver–Brain Axes? *International Journal of Molecular Sciences*. 2023; 24(4):3900. <https://doi.org/10.3390/ijms24043900>
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- Aronne LJ, Sattar N, Horn DB, Bays HE, Wharton S, Lin WY, Ahmad NN, Zhang S, Liao R, Bunck MC, Jouravskaya I, Murphy MA; SURMOUNT-4 Investigators. Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. *JAMA*. 2024 Jan 2;331(1):38-48. doi: 10.1001/jama.2023.24945. PMID: 38078870; PMCID: PMC10714284.

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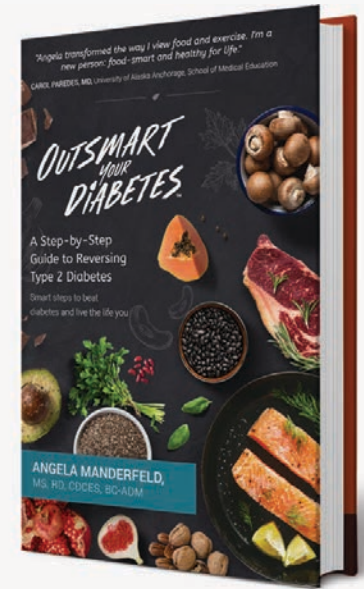


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THANK YOU

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