Weill Cornell Medicine

Pharmacotherapy in Limited Resources

Tackling Obesity: Multidisciplinary Approaches for Comprehensive Care

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Disclosure Statement

- Speaker:
  - Dr. Beverly Tchang

- Disclosed the following financial/non-financial relationship
  - ➢ Advisor-Novo Nordisk

- **Will be discussing unlabeled/unapproved use of drugs or products**

Objectives

- Identify strategies to overcome resource barriers for obesity pharmacotherapy
- Review the efficacy and safety of obesity pharmacotherapy in low-resource settings
- Design cost-effective obesity treatment plans with off-label pharmacotherapies

“Low-resource setting” is characterized by several factors

- Financial
- Skilled personnel
- Infrastructure and facilities
- Medication
- Technology
- Health system
- Public health
- Geography
- Research and innovation

AOM, anti-obesity medication

Skilled providers, medication supply, health system, and research are resources we need to provide high quality care

Financial	1. How many doctors are skilled in prescribing AOMs?	Infrastructure and facilities	2. Is the supply of medications meeting demand?
Technology	3. Does the system invest in or prioritize care of patients with obesity?	Public health	Geography

4. What research is being done on long-term use of AOMs in Qatar?

AOM, anti-obesity medication

Off-label AOMs can help address these insufficient resources

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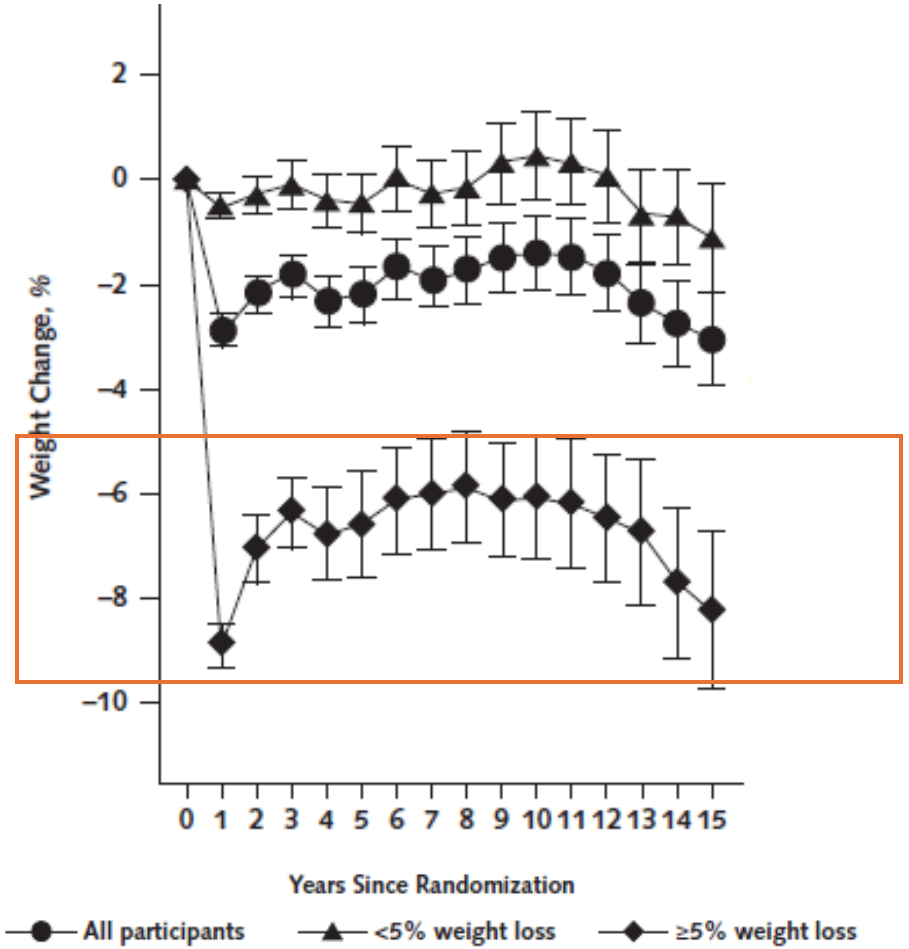
Off-label AOMs	
metformin	1. Familiar to most medical professionals 2. Easy to manufacture, scale up, and distribute 3. Approved for other diseases 4. Longstanding clinical and research experience
topiramate	
bupropion	
naltrexone	

AOM, anti-obesity medication

Metformin

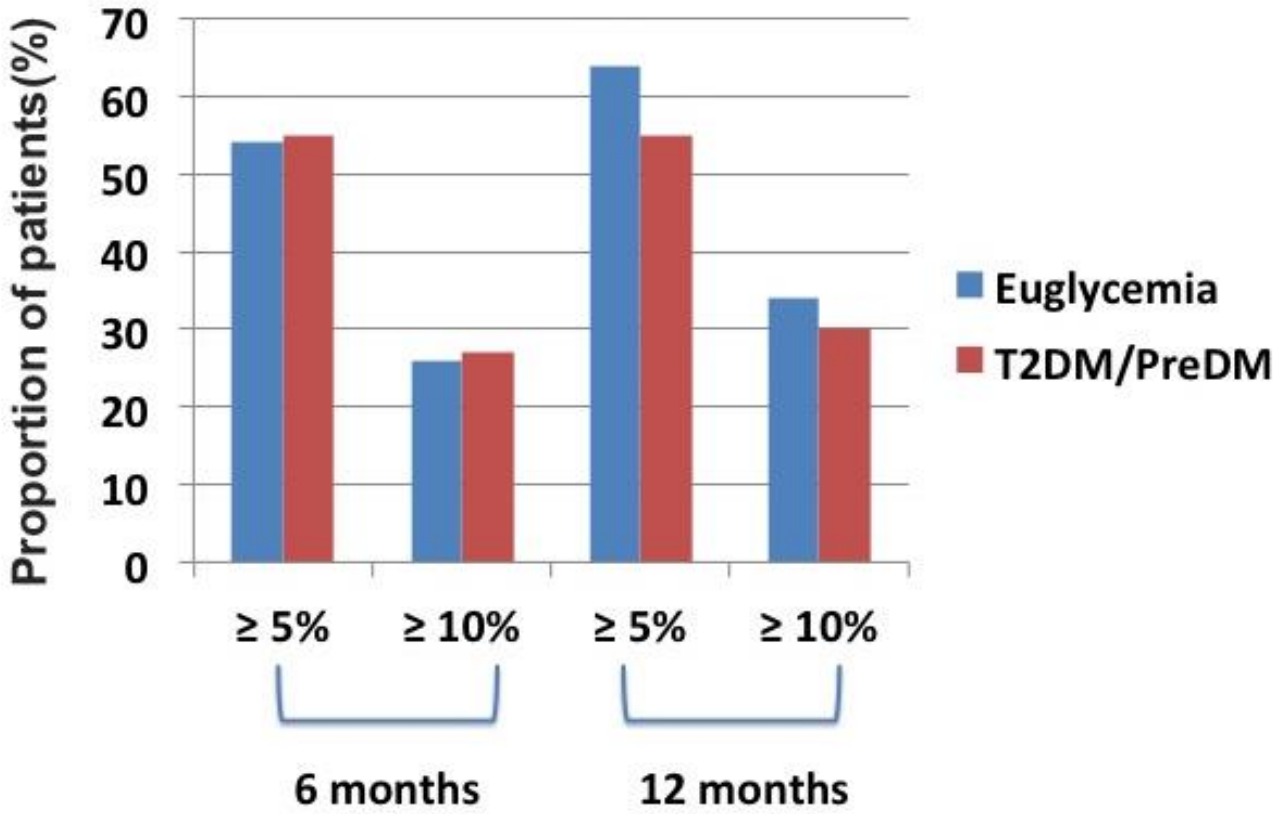
Metformin responders in the DPPOS saw about 7% weight loss with 850 mg BID (1700 mg/d)



DPPOS, Diabetes Prevention Program Observational Study

Diabetes Prevention Program Research Group, Knowler WC et al. Lancet. 2009 Nov 14;374(9702):1677-86; Apolzan et al. Ann Intern Med. 2019 May 21;170(10):682-690

Median dose of 1500 mg/d was associated with 7% weight loss in our patients



Chukir T, Mandel L, Tchang BG, Al-Mulla NA, Igel LI, Kumar RB, Waitman J, Aronne LJ, Shukla AP. Metformin-induced weight loss in patients with or without type 2 diabetes/prediabetes: A retrospective cohort study. Obes Res Clin Pract. 2021 Jan-Feb;15(1):64-68. doi: 10.1016/j.orcp.2020.12.005. Epub 2020 Dec 30. PMID: 33386253.

Start metformin XR 500 mg and increase to at least 1500 mg/d

Wk 1: Start 1 tab daily with breakfast. Wk 2: Take 1 tab twice a day. Wk 3: Take 2 tabs with breakfast and 1 tab with dinner. Wk 4: Take 2 tabs twice a day.

Side effects of metformin are largely gastrointestinal

Nausea

Stomach cramps

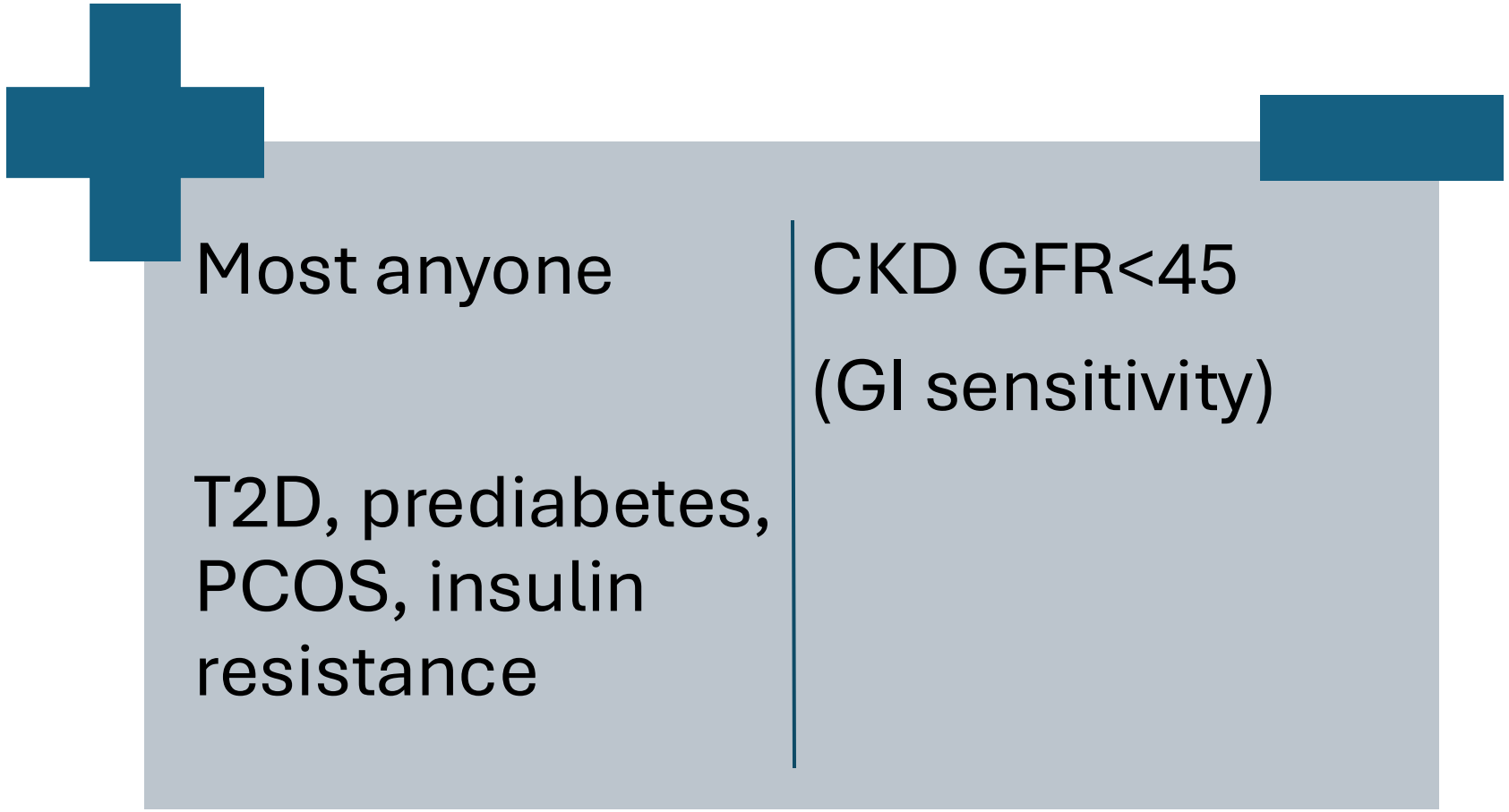
Diarrhea

Vitamin B12 deficiency*

* About 5% of adults with B12 < 295.2 pmol/L have symptoms

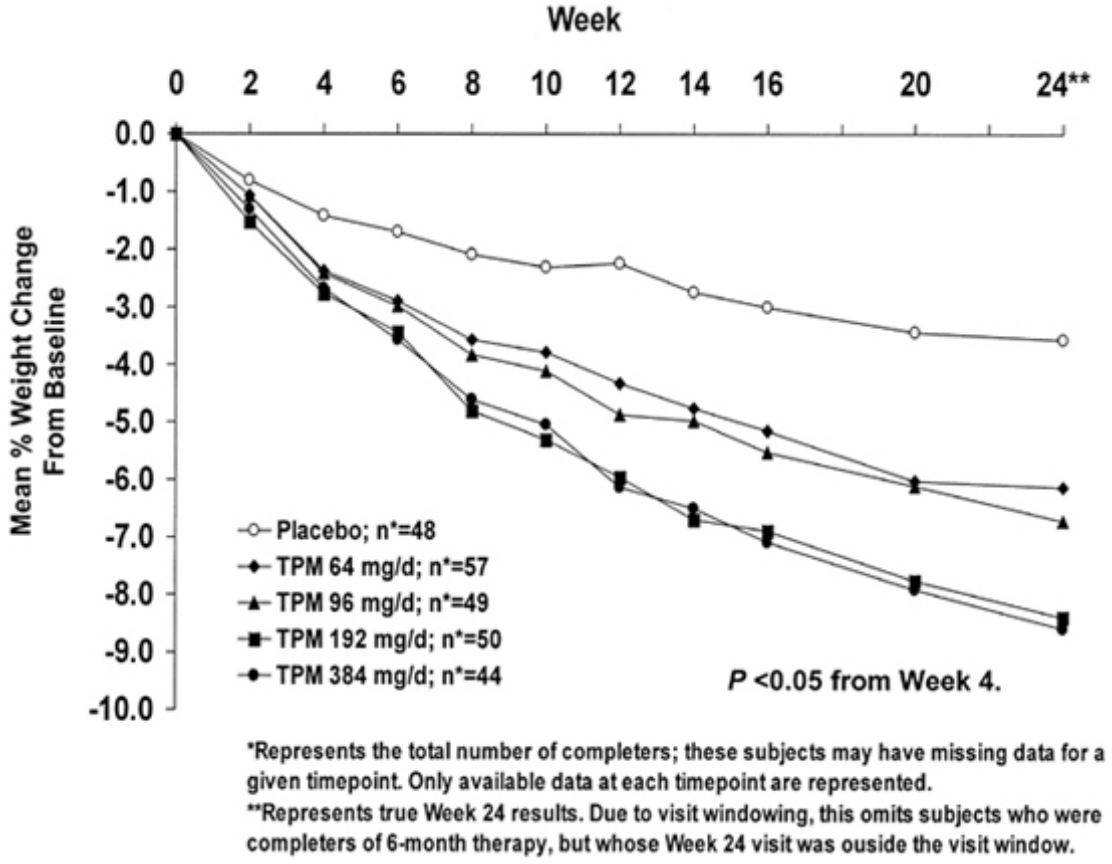
Metformin package insert

Consider metformin our “first-line” off-label AOM



Topiramate

Topiramate up to ~200 mg/d causes 9% weight loss over 6 months



*Represents the total number of completers; these subjects may have missing data for a given timepoint. Only available data at each timepoint are represented.
**Represents true Week 24 results. Due to visit windowing, this omits subjects who were completers of 6-month therapy, but whose Week 24 visit was ouside the visit window.

Bray GA, Hollander P, Klein S, Kushner R, Levy B, Fitchet M, Perry BH. A 6-month randomized, placebo-controlled, dose-ranging trial of topiramate for weight loss in obesity. Obes Res. 2003 Jun;11(6):722-33. doi: 10.1038/oby.2003.102. PMID: 12805393.

Start with topiramate 25 mg and increase to max 200 mg/d

Take 1 tab around dinnertime for 7 days then increase to 2 tabs if tolerated

Double the dose at each escalation to optimize therapeutic effect

Most common side effects of topiramate are neurological

Paresthesias

Drowsiness

Brain fog

Dysgeusia with carbonated drinks

Mood changes

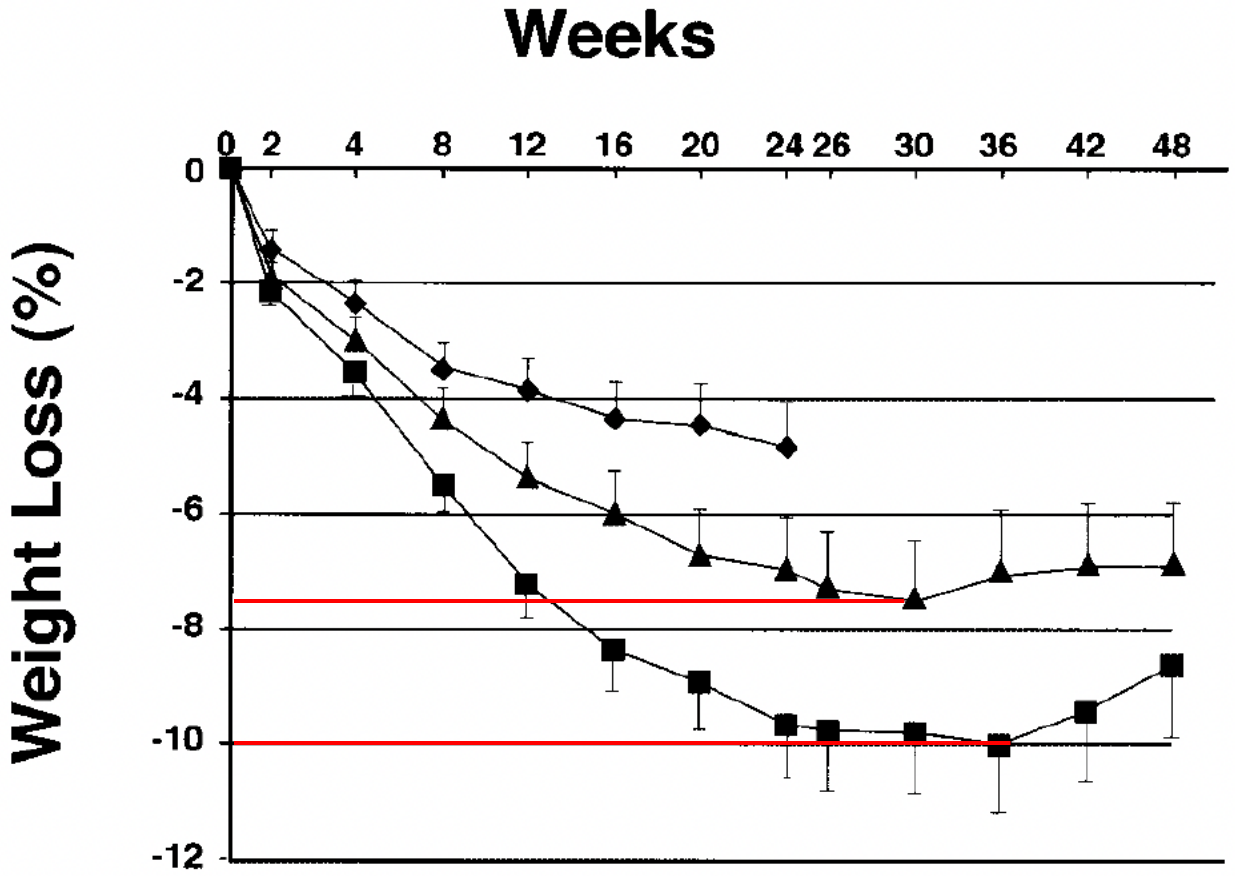
Topiramate package insert

Consider topiramate for binge eating, cravings

Cravings	Kidney stones
Binge eating	Acute angle glaucoma
Migraine prophylaxis	⚠ CrCl<70, child-bearing potential
Seizure disorder	

Bupropion

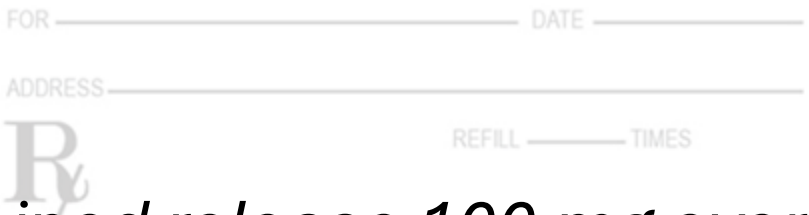
Bupropion 300 mg/d and 400 mg/d caused 7% and 9% weight loss



◆, placebo; ▲, bupropion SR 300 mg/d; ■, bupropion SR 400 mg/d.

Anderson JW, Greenway FL, Fujioka K, Gadde KM, McKenney J, O'Neil PM. Bupropion SR enhances weight loss: a 48-week double-blind, placebo- controlled trial. Obes Res. 2002 Jul;10(7):633-41. doi: 10.1038/oby.2002.86. PMID: 12105285.

Start bupropion 100 mg and aim for 300-400 mg/d



Start bupropion sustained release 100 mg every morning x 7 days then increase to 200 mg if tolerated

→ Follow up appointment to assess tolerance before further dose escalation

Side effects of bupropion are mostly related to the norepinephrine component

Palpitations

Dizziness

Anxiety

Tremor

Insomnia

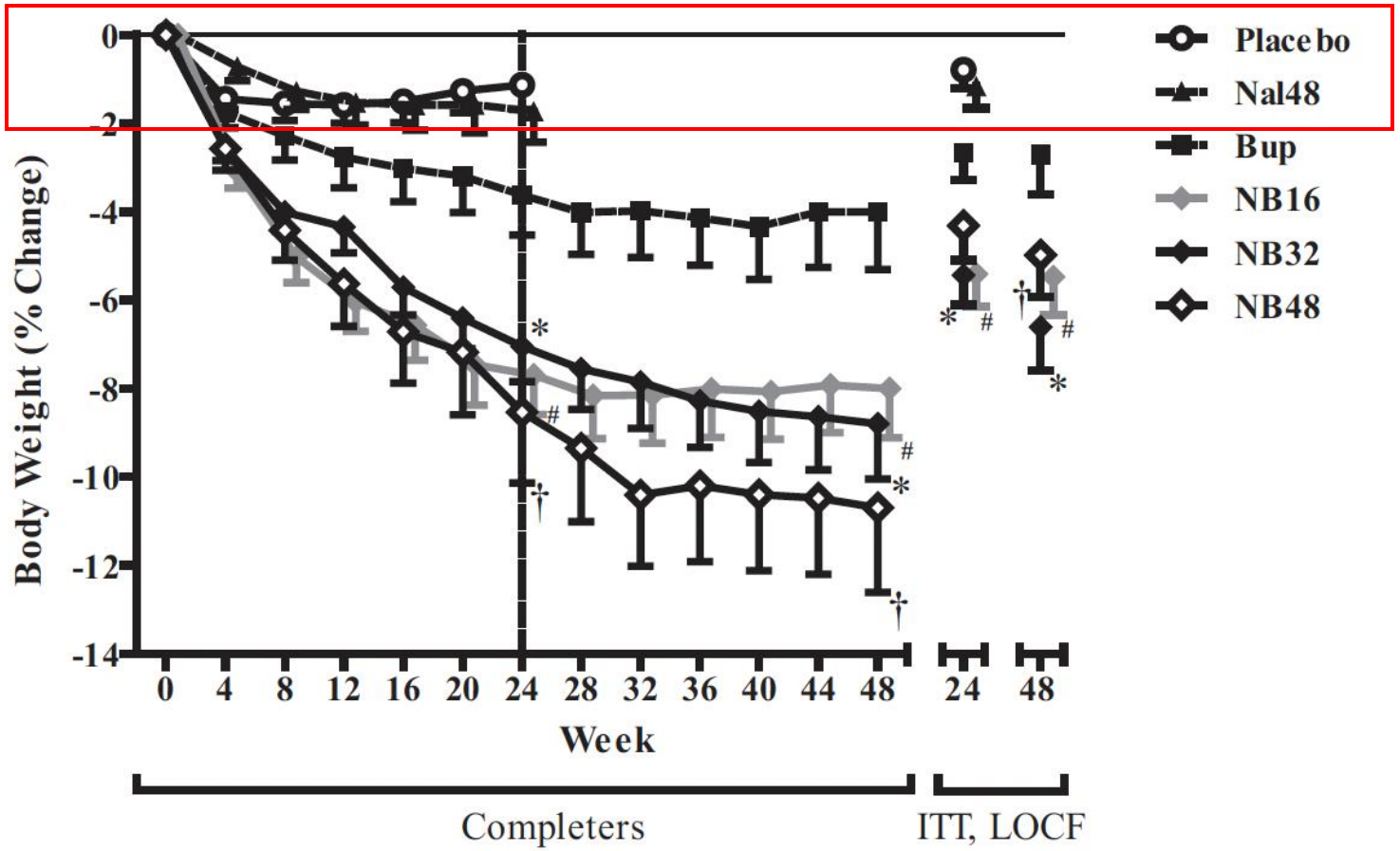
Bupropion package insert

Consider bupropion for cravings, fatigue, low mood

Cravings	Seizures, bulimia
Smoking	Suicidal ideation
Depression	Anxiety
Fatigue	BP>140/90
	⚠ CrCl<60, liver failure

Naltrexone

Naltrexone 50 mg/d monotherapy does not cause weight loss



Greenway FL, Dunayevich E, Tollefson G, Erickson J, Guttadauria M, Fujioka K, Cowley MA; NB-201 Study Group. Comparison of combined bupropion and naltrexone therapy for obesity with monotherapy and placebo. J Clin Endocrinol Metab. 2009 Dec;94(12):4898-906. doi: 10.1210/jc.2009-1350. Epub 2009 Oct 21. PMID: 19846734.

Start with ¼ tab of naltrexone 50 mg and increase to max 50 mg/d

Take ¼ tab once a day for 7 days then increase to ½ tab (25 mg) if tolerated.

Side effects of naltrexone are mostly gastrointestinal

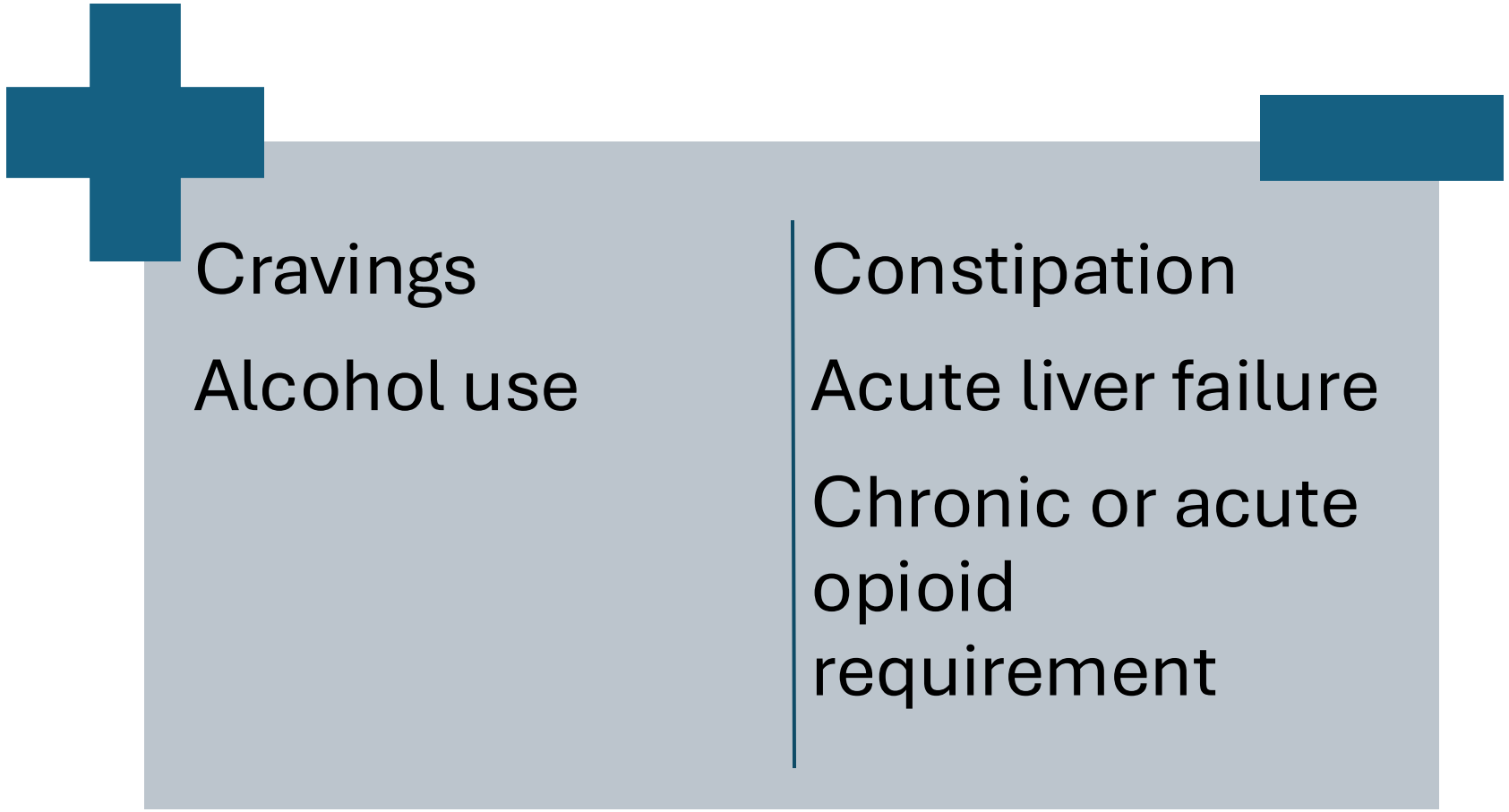
Nausea

Constipation

Mood changes

Naltrexone package insert

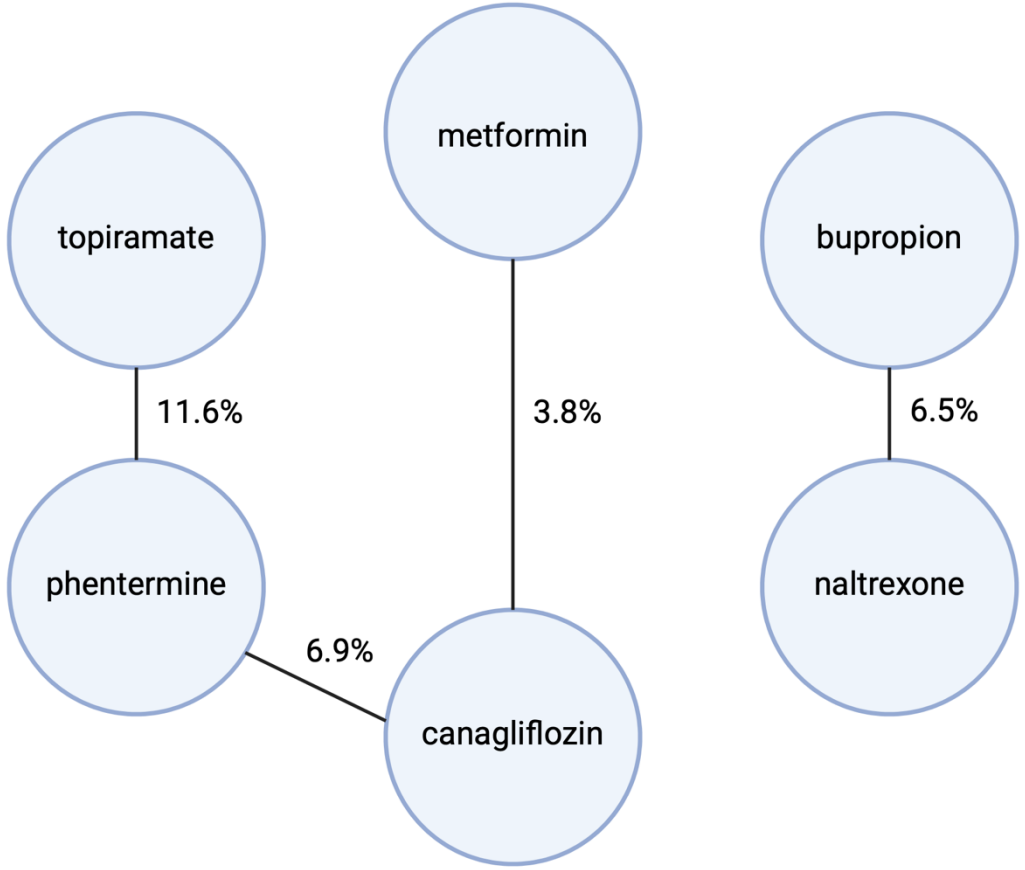
Consider naltrexone as a non-stimulating option for cravings



Combination AOMs

Design cost-effective obesity treatment plans with off-label pharmacotherapies

Few randomized controlled trials establish evidence for combination therapy



Greenway FL, et al. *Obesity (Silver Spring)*. 2009 Jan;17(1):30-9. doi: 10.1038/oby.2008.461. Aronne LJ, et al. *Obesity (Silver Spring)*. 2013 Nov;21(11):2163-71. doi: 10.1002/oby.20584. Hollander P, et al. *Diabetes Care*. 2017 May;40(5):632-639. Hadjadj S, et al. *Diabetes Care*. 2016 Oct;39(10):1718-28.

But rationale for combination therapy is rooted in chronic disease management

Type 2 diabetes

Glycemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Prioritize avoidance of hypoglycemia in high-risk individuals

Hypertension

ctive sleep apnea (snoring, witnessed apnea, excessive daytime sleepi

↓

Pharmacological treatment

Maximize diuretic therapy

Add a mineralocorticoid receptor antagonist

Add other agents with different mechanisms of actions

Use loop diuretics in patients with CKD

and/or patients receiving potent vasodilators (e.g., minoxidil)

↓

Refer to specialist

2024 ADA Standards of Care of Diabetes. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Mean weight loss was 10.4% at 4.4 years with about 2 AOMs per patient

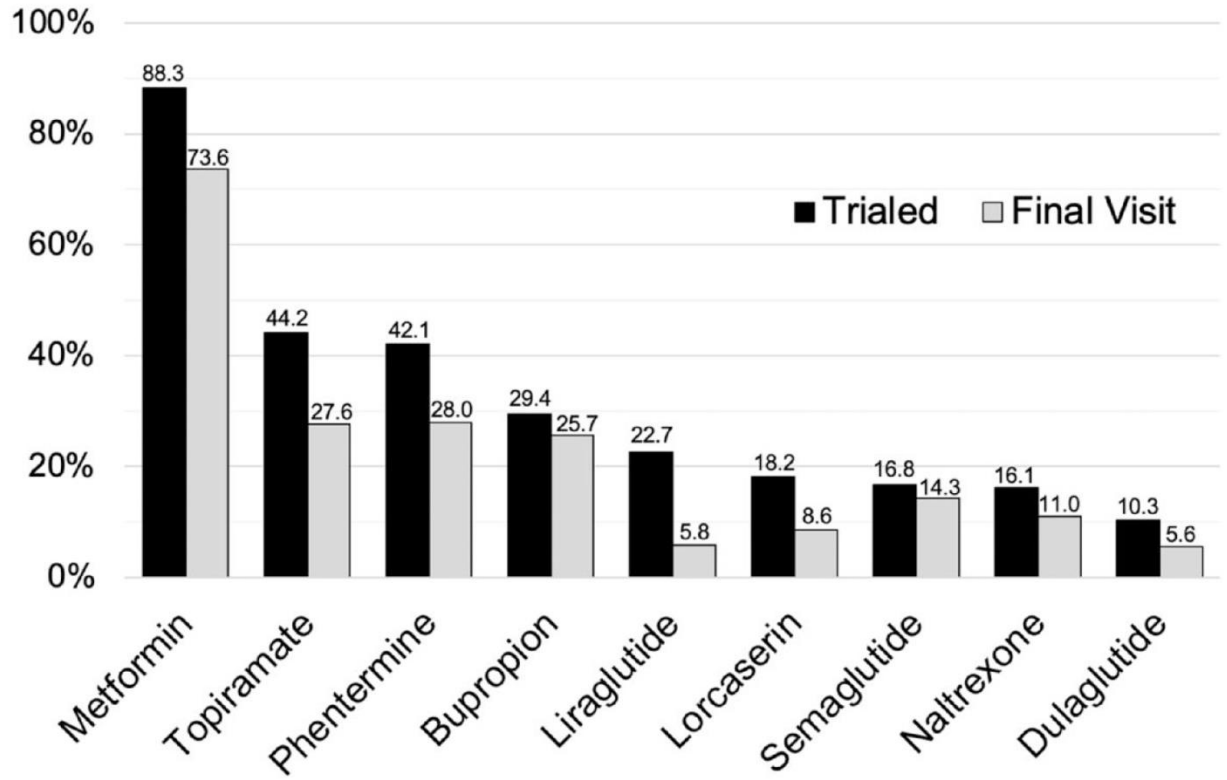


Figure 3. The frequency of antiobesity medications trialed (≥ 1 dose) and taken at final visit are displayed. Antiobesity agents taken at final visit in less than 5% of patients are not shown.

Weintraub MA, D'Angelo D, Tchang BG, Sahagun AD, Andre C, Aronne LJ, Shukla AP. Five-year Weight Loss Maintenance With Obesity Pharmacotherapy. J Clin Endocrinol Metab. 2023 Aug 18;108(9):e832-e841. doi: 10.1210/clinem/dgad100. PMID: 36810608; PMCID: PMC10438886.

Summary

Achieve significant weight loss in low-resource settings with off-label but evidence-based strategies

Metformin, topiramate, and bupropion are effective monotherapy AOMs

Early evidence supports combination regimens