Obesity Therapy Update

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Disclosure

I have no financial interests or relationships to disclose.

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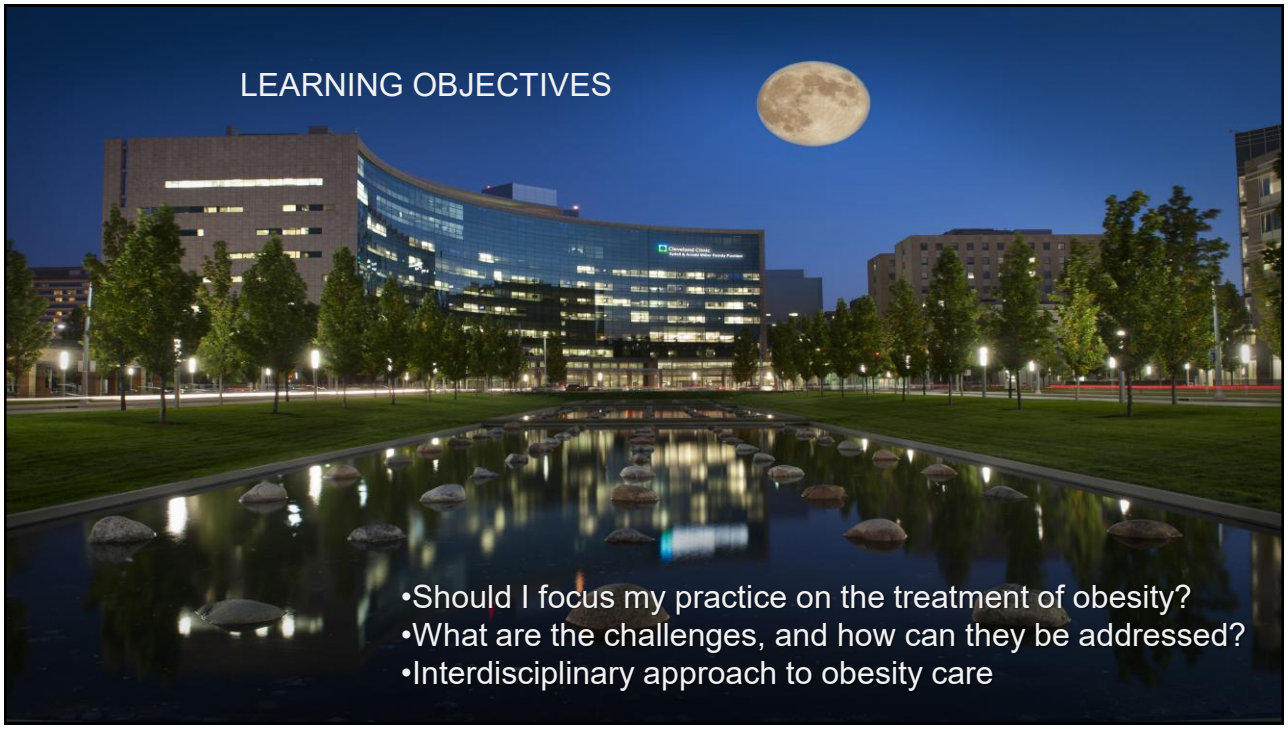

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Why Should We Care About Obesity?

Obesity Is Responsible for Many Medical Problems

- Development of T2D (90%) and HTN (50%) of cases
- Dyslipidemia (70%)
-
- Depression (50%)
- Osteoarthritis (>25%)
- More than 50% of patients with OSA have obesity

NCD Risk Factor Collaboration. Lancet. 2017;10113:2627-2642
WHO Technical Report Series. 894. Geneva, Switzerland, 2000
World Health Organization. Obesity and Overweight Fact Sheet
Aronow WS et al. Annals of Translational Medicine. 2017;5(17):350
Luppino FS et al. Arch Gen Psychiatry. 2010;67(3):220–229
Romero-Corral A et al. Chest. 2010;137(3):711–719

4

These Were the Top 10 Most Searched Health Trends of 2024, According to Chatgpt

Obesity Is Affecting Our Lives in Many Ways

1. Weight control, nutrition, and diet trends
2. Exercise trends and home training
3. Mental health, burnout, and stress management
4. Management of chronic diseases(diabetes, obesity, and cardiovascular health)
5. Telehealth and digital health services
6. Cancer treatment
7. Sleep health and sleep disorders
8. Skin health and cosmetic dermatology
9. Long COVID and vaccination protocols
10. Anti-obesity medications

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The New York Times

From nobody wanting to treat obesity → to everyone considering themselves an expert in it

Every minute there are 70,000 health-related consultations

Only 1 out of 10 reaches a reliable source

Daniel Forero

OPINION
GUEST ESSAY

Are We Thinking About Obesity All Wrong?

The Situation Has Become a Bit Confusing

HUFFPOST HIGHLINE TWITTER | FACEBOOK | SUBSCRIBE

Everything You Know About Obesity Is Wrong

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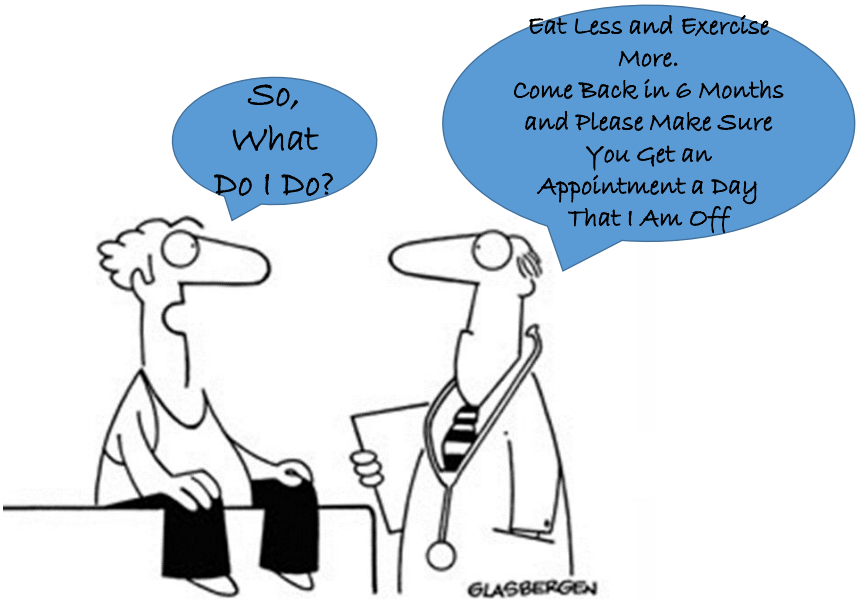

Frustration (and confusion) with their medical care (40% with obesity)

7

Platforms That Provide Virtual Treatment with GLP-1 Analogues

- Noom Med
- Calibrate
- Sesamo Care
- PlushCare
- Ro
- Strut Health
- Henry Meds
- Reflex MD
- K Health
- Quick MD

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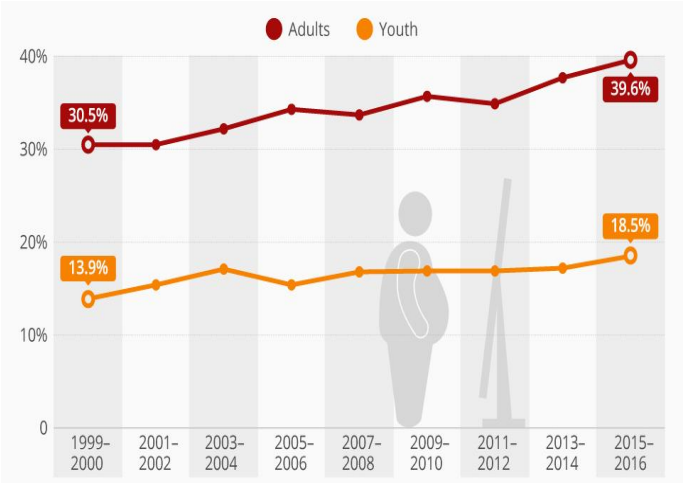
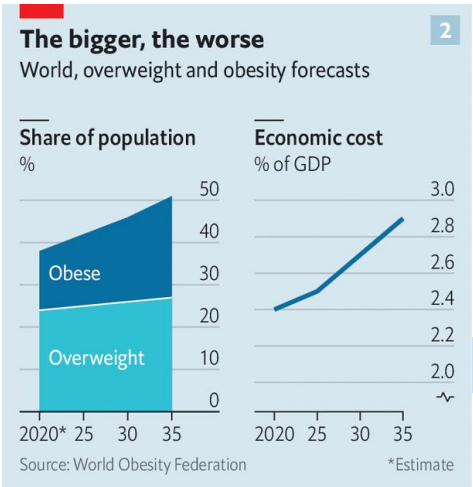
Prevalence of Obesity + Rising Costs





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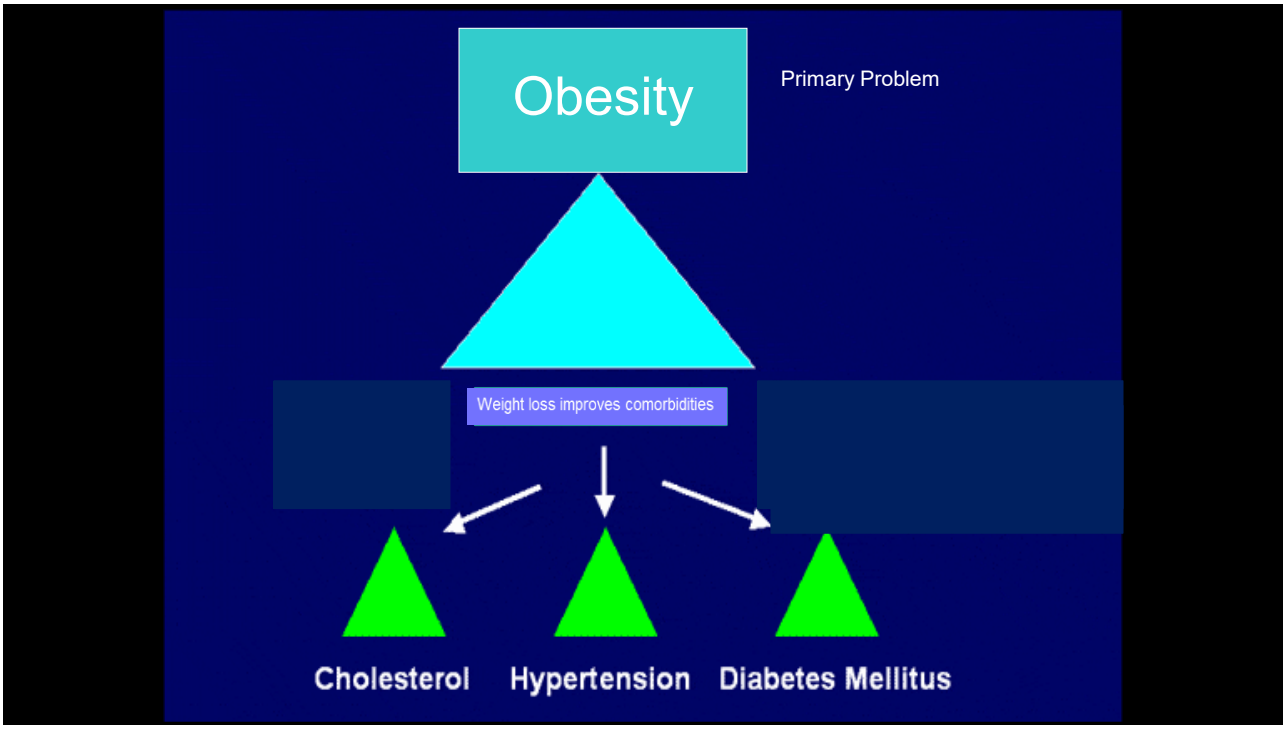

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- How Can I Improve the Care of Patients Suffering Obesity?

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All Patients Seeks the Same:

- Seek to be heard
- Support and empathy
- Not to be judged
- Easy access and follow-up
- Information & Direct communication
- Personalized Treatment
- Results at Affordable Cost

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All Doctors Face Similar Challenges:

- ⬆ Cost of maintaining a private/Hospital
- Difficulty consolidating a team
- Institutional support
- Higher expectations
- Online programs
- “Everyone is an expert in obesity”
- Lower payments from Insurance & State
- New medications -> expensive and poorly covered

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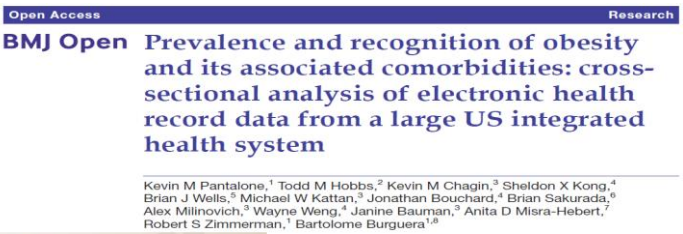
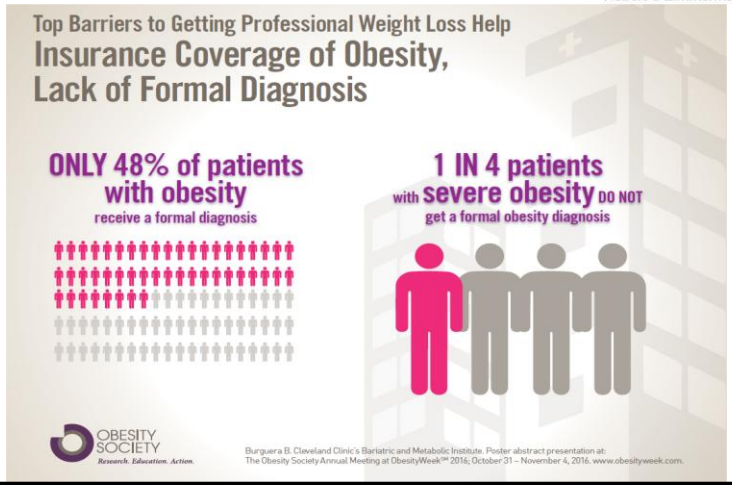
We Do Not Pay to Much Attention to Establish a Diagnosis of Obesity



Open Access Research

BMJ Open **Prevalence and recognition of obesity and its associated comorbidities: cross-sectional analysis of electronic health record data from a large US integrated health system**

Kevin M Pantalone,[1] Todd M Hobbs,[2] Kevin M Chagin,[3] Sheldon X Kong,[4] Brian J Wells,[5] Michael W Kattan,[3] Jonathan Bouchard,[4] Brian Sakurada,[6] Alex Milinovich,[3] Wayne Weng,[4] Janine Bauman,[3] Anita D Misra-Hebert,[7] Robert S Zimmerman,[1] Bartolome Burguera[1,8]



Obesity Is Often Not Targeted in the Medical Setting

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1-MINUTE CONSULT

CME CREDIT *LEARNING OBJECTIVE:* Readers will customize a pre-visit questionnaire to facilitate obesity conseling during office visits

JOHN A. ZAMBRANO, MD, MHS
Department of Internal Medicine, Harvard Vanguard Medical Associates, Atrius Health, Boston, MA

BARTOLOME BURGUERA, MD, PhD
Bariatric and Metabolic Institute, Cleveland Clinic

Q: Can effective obesity counseling fit into the 20-minute appointment?

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A: Yes,

- Pre-visit questionnaire:
  - weight hx, eating habits, level of physical activity and ROS
- We need to center on:
  - Optimization of patient's diet
  - Personalized physical activity program
  - Appetite control
  - Optimization of sleeping habits
  - Addressing: depression, anxiety, stress and eating disorders

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Will They Come to See Us When They Can Easily Find on the Internet the Treatment They Believe Can Help Them?

What Can We Do About It?

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"Back to Basics":

Give Up the Usual Demands, Simplify Your Approach and Maintain Transparency

- Importance of empathy
- Facilitate access
- Direct communication
- Personalized treatment
- Multidisciplinary and holistic approach

Programs based on scientific evidence, with respect for the patient, facilitating accessibility, ensuring long-term treatment, and incorporating AI will succeed

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Specific Areas to Consider:

- Rethink your efforts
- Maximize time
  - Templates
  - Shared Medical Appointments (SMAs)
- Interdisciplinary Teams
- Close follow-up
- Concierge Medicine
- Artificial Intelligence

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Cleveland Clinic

Weight Management-Obesity Programs

OUTPATIENT VISIT

PRIMARY CARE PHYSICIAN:

Age: _____ Sex: _____ Height (inches): _ Weight (lbs.):____ BMI: ____

Have you been referred to us □ Yes □ No

If yes, by whom_____

At what age did you begin to develop a significant weight problem?_

What is your primary reason for making an appointment at this time?

Please describe any events you believe are related to your weight gain?
Event Minimum weight Maximum weight Age of Onset

Your ideal body weight? Weight at graduation from high school?

What contributes to your weight? (check as many that apply)
□ Portion sizes
□ Medications
□ Eating too much fat and sugar
□ Compulsive eating
□ Emotional eating
□ Stress eating
□ Lack of exercise
□Lack of knowledge about healthful eating and exercise

FAMILY HISTORY

Age	Appx. Wt.	Significant illness
Mother		
Father		
Maternal Grandmother		
Maternal Grandfather		
Paternal-Grandmother		
Paternal Grandfather		
Siblings		

Are you adopted? □Yes □No
With whom do you live at home?

Weight loss medications

Name	Start Year	Length (months)	Pounds lost

TEMPLATES

Diet Name	Start Year	Length (months)	Starting Weight	Pounds lost	Length of time weight stayed off	How much weight regained

What do you usually have for :
Breakfast:
Lunch:
Dinner:

Number of snack per day?:
Frequency of skipping meals per day:

What do you usually drink? water, tea , pop , juice , energetic drinks, coffee other:
Do you drink alcohol? What type of drink? How many drinks per week?

PHYSICAL ACTIVITY: What are you currently doing as activity or exercise?
How many times per week? How long at each session?
Do you have any Limitations to exercise?

APPETITE: Is your appetite well-controlled at this time? Yes or No

QUALITY OF SLEEP: Are you sleeping well at night? Yes or No
How many hours of sleep per night?
Do you fell rested when I wake up in the morning? Yes or No
Do you have sleep apnea? Do you use CPAP?

LEVEL OF STRESS: What is level of stress in your life currently?
Scale of 1-10 with 10 being the most stressed:
How is your general mood? Depressed—OK

Do you have any heart trouble? Have you ever had a Stress test:
Chest pain, shortness of breath, or fatigue when you walk: YES NO

History of eating disorders: negative, bulimia nervosa, binge eating disorder, anorexia nervosa

Associated medical conditions? thyroid disease, diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, congestive heart failure, gallbladder disease, pulmonary disease, sleep apnea, osteoarthritis, depression, Liver problems, kidney problems or other:

Associated medications: none, antidepressants, tablets for diabetes, insulin, steroids, antiepileptics or other:
Cardiovascular risk factors: none, smoking, positive family history, hyperlipidemia, diabetes mellitus, obesity, sedentary life style, hypertension, type A personality, stress, CAD, CVA/TIA's or other:

Have you ever tried Medications for weight loss (list medications—including prescription, over the counter, herbal, supplements)

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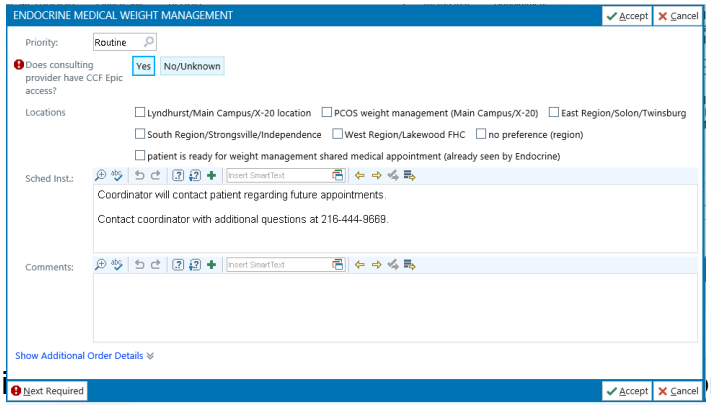
Referral Process – Endocrine

- (#2131446 **ENDOCRINE MEDICAL WEIGHT MANAGEMENT**)



- Communi ne call
- Follow-up will happen via e-mail, MyChart, and telephone
- Initial visit may consist of MD/NP, dietitian, and possibly EP

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Obesity Shared Medical Appointments (SMAs) at Cleveland Clinic

- Groups of 8-10 patients meet monthly with an obesity specialist and registered dietician
- 90-minute SMAs
  - 15-minutes educational activity
  - Take turns addressing individual patient concerns around the room
- Members of the group are constant and determined by chosen diet type

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Mayo Clin Proc. 2019 ;94:957-960

MAYO CLINIC

PERSPECTIVES AND CONTROVERSIES

What to Offer the 99% of Patients With Severe Obesity Who Do Not Undergo Bariatric Surgery?

Check for updates

Bartolome Burguera, MD, PhD; Philip Schauer, MD; and Scott Kahan, MD, MPH

Interdisciplinary Lifestyle Intervention Program

An Intensive Life-Style Program Offered to Patients with Severe Obesity, Who Are Not Candidates or Not Interested in Undergoing Bariatric Surgery

in the Context of Shared Medical Appointments

team: Endocrinologist, Exercise Physiology, Social Worker, Psychologist, Nutritionist, Nursing, Surgeon

objective: To Develop an Optimal Medical Weight Loss Program: Patients with BMI > 35 Non-Surgical Candidates

program Included in CCF Health Plan

goal to Accomplish a 5-10% Weight Loss After 12 Months of Intervention

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Benefits of SMAs

Patient Benefits[1-4]	Provider Benefits[3,4]
• Decreased wait times	• Increased efficiency
• Increased face-time with physician	• Decreased redundancy
• Access to additional learning resources	• Potential cost savings
• Enhanced learning though repetition	• Improved satisfaction
• Improved clinical outcomes	
• Improved satisfaction	

1. Kaidar-Person Oet al. Shared medical appointments: new concept for high-volume follow-up for bariatric patients. The Journal of cardiovascular nursing 2010;25(1):13-19; 2. Housden LM, Wong ST. Using Group Medical Visits With Those Who Have Diabetes: Examining the Evidence. *Curr Diab Rep*. 2016;16(134).; 3. Edelman D, et al. Shared Medical Appointments for Chronic Medical Conditions : A Systematic Review. *VA Evidence-based Synth Progr Reports*. 2012.; 4. Bronson DL, Maxwell RA. Shared medical appointments: Increasing patient access without increasing physician hours. *Cleve Clin J Med*. 2004;71(5):369-377

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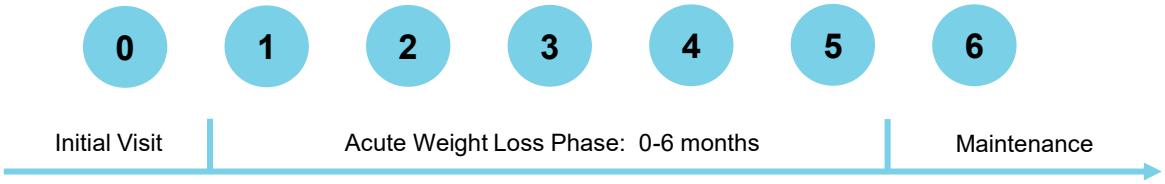
Interdisciplinary Obesity Treatment Algorithm



- Blood test
- Questionnaires
- DEXA

- Body Composition
- Consults

- In-person
- Group Visits
- Virtual


Obesity:
Are shared medical appointments part of the answer?
REVIEW
KELLY SHIBUYA, BS KEVIN M. PANTALONE, DO, ECNU, FACE BARTOLOME BURGUERA, MD, PhD
CLEVELAND CLINIC JOURNAL OF MEDICINE VOLUME 85 • NUMBER 9 SEPTEMBER 2018

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Obesity Center (Department of Endocrinology)

- Significant Growth: doubling each year
- More than 1,500 consultations conducted monthly
- Team:67 endocrinologists
- 10 obesity medicine specialists
- 35 APPs (30 dedicated to obesity management)
- 12 dietitians
- 4 exercise physiologists
- 2 pharmacists
- 3 psychologists
- 3 social workers
- 30 group medical visits per month

- Philanthropic Funds

- **Body Composition Technology**
- 2 body composition machines
- DXA: research & composition analysis
- **Community Presence**
- Locations: LH, Lutheran, Euclid, STJ
- **Collaborations**
- Surgery
- Hepatology
- Orthopedics
- Maternal–Fetal Medicine
- Internal Medicine / Family Medicine
- Vascular Clinic / Lipedema
- Hematology / Oncology

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"Concierge Medicine" Vs. Increase Patient's Volume

- Medical care (membership): exclusive and personalized, with accessibility and convenience
- Fixed monthly fee: unlimited visits and telehealth
- Direct access to a phone line
- Membership fees: $1,200 to $10,000 per year
- In 2013: 50 offices → >1,500 in 48 states

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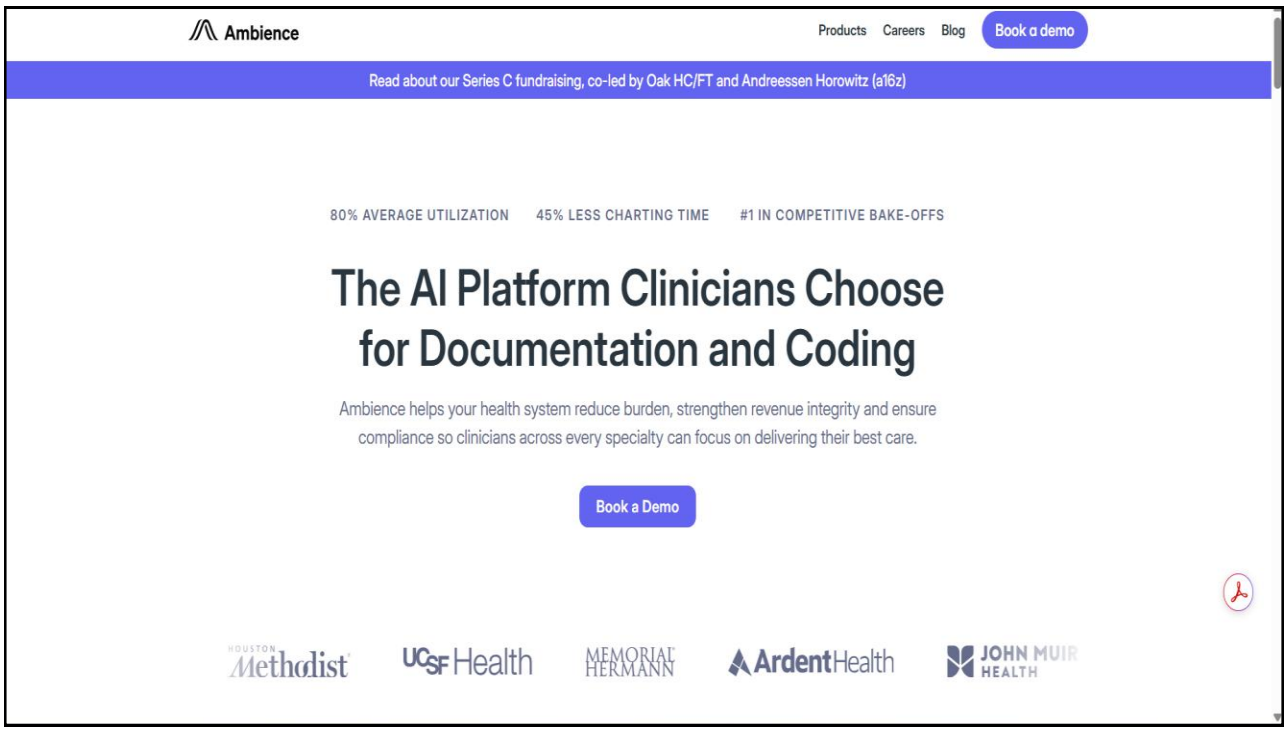

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Spend Time Informing Our Patients About:

- Obesity main health problem
- Set point (appetite threshold)
- Basal metabolic rate
- Effectiveness of medications
- Cardiovascular risk reduction (CVR)
- Muscle maintenance
- Importance of physical activity
- Taking responsibility

Emphasis On:

We provide tools ➔ control

1.- Nutrition: quality, quantity, portions, drinks

2.- Physical Activity: personalized exercise programs

GOALS: short and midterm

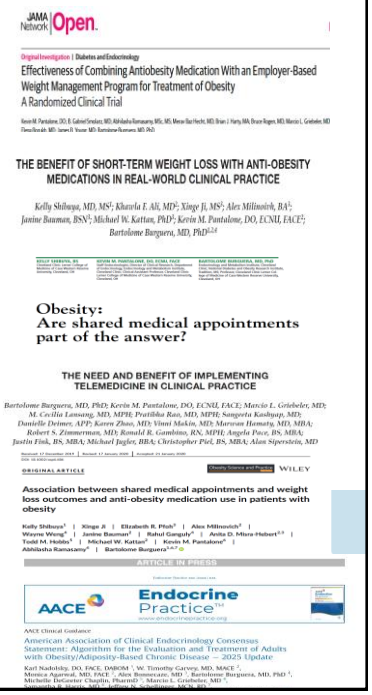
3.- Appetite control: weight loss medications

4.- Sleep patterns. R/o OSA

5.- Stress. Depression. Anxiety

6.- Social aspects

Metabolic surgery, if a medical approach is not successful


JAMA Network Open.

Effectiveness of Combining Antiobesity Medication With an Employer-Based Weight Management Program for Treatment of Obesity
A Randomized Clinical Trial

THE BENEFIT OF SHORT-TERM WEIGHT LOSS WITH ANTI-OBESITY MEDICATIONS IN REAL-WORLD CLINICAL PRACTICE

Obesity:
Are shared medical appointments part of the answer?

THE NEED AND BENEFIT OF IMPLEMENTING TELEMEDICINE IN CLINICAL PRACTICE

Association between shared medical appointments and weight loss outcomes and anti-obesity medication use in patients with obesity

AACE Endocrine Practice

American Association of Clinical Endocrinology Consensus Statement: Algorithm for the Evaluation and Treatment of Adults with Obesity/Adiposity-Based Chronic Disease — 2025 Update

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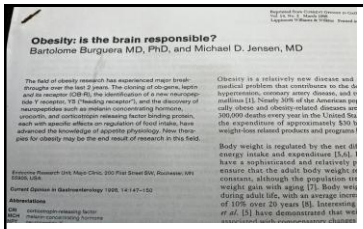
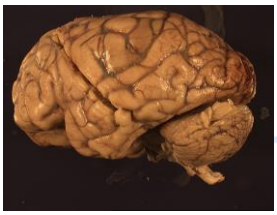
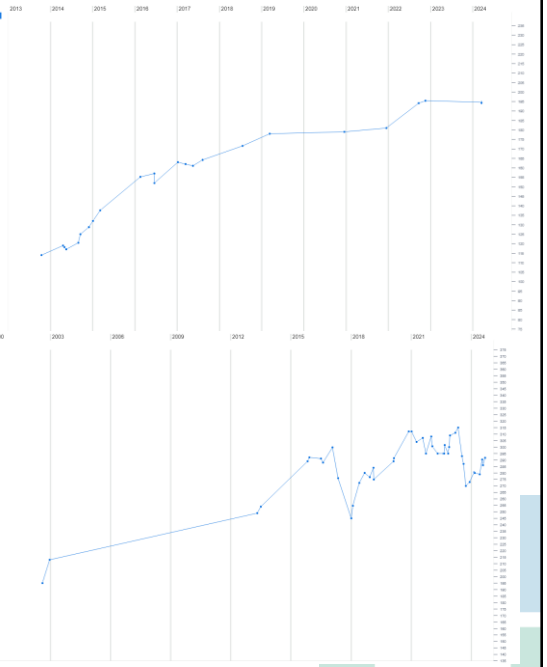

Obesity: is the brain responsible?
Bartolome Burguera MD, PhD, and Michael D. Jensen, MD

Set-Point of Weight





- Factors
  - Genetics
  - Stress, sleep
  - Nutrition, physical activity
  - Hours of light exposure
  - Flora in the gut
  - Medications
  - Menopause

- Losing weight is not complicated
- Challenge is to maintain weight loss

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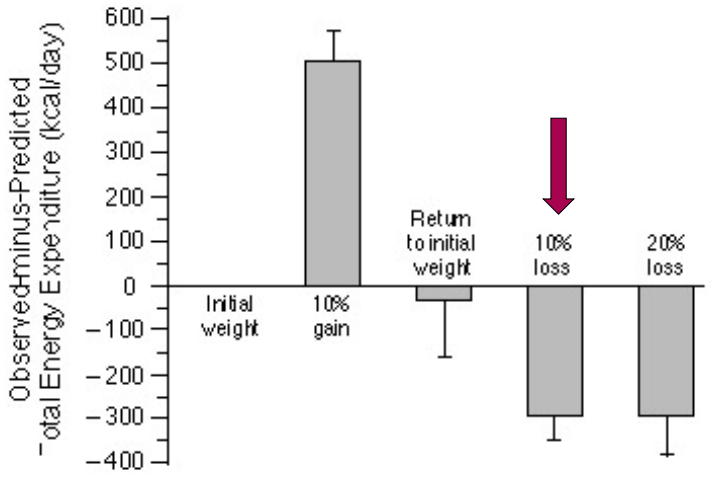
Metabolic Adaptation Occurs with Weight Loss



Leibel RL Et Al. N Engl J Med 1995;332:621-628.

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History of Anti-Obesity Drugs

Date	Drug	Results
1893	Thyroid Hormone	Hyperthyroidism
1934	Dinitrophenol	Cataracts; neuropathy
1937	Amphetamine	Addiction
1967	Rainbow pills	Death
1978	Collagen-based VLCD	Death
1997	Fenfluramine/phenterm	Valvular Insufficiency
1998	Dexfenfluramine	Pulmonary HTN
2008	Rimonabant	Depression, suicide
2010	Sibutramine	Death
2020	Lorcaserin	Cancer

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Obesity Pharmacotherapy

Agents	Action	Approval
Phentermine	• Sympathomimetic	• 1959
Orlistat	• GI lipase inhibitor	• 1997
Phentermine/ Topiramate ER	• Sympathomimetic/Anticonvulsant (GABA receptor modulation?)	• Approved, Summer 2012
BupropionER/ Naltrexone	• Dopamine/noradrenaline reuptake inhibitor/Opioid receptor antagonist	• Approved, September 2014
Liraglutide 3 mg/day	• GLP-1 receptor agonist	• Approved, December 2014
Semaglutide 2.4 mg/week	• GLP-1 receptor agonist	• Approved, June, 2021
Tirzepatide 15 mg/week	• GLP-1 / GIP receptor dual agonist	• Approved in 2022 (T2D) Obesity 2023

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Objective Assessment of Obesity Care Status

- We have the scientific knowledge
- Interest & need
- What teams need to get involved
- Infrastructure
- Medications with unprecedented efficacy and safety

- Lack of access to these evidence-based medications
  - Bias and ignorance
  - High costs of these medications

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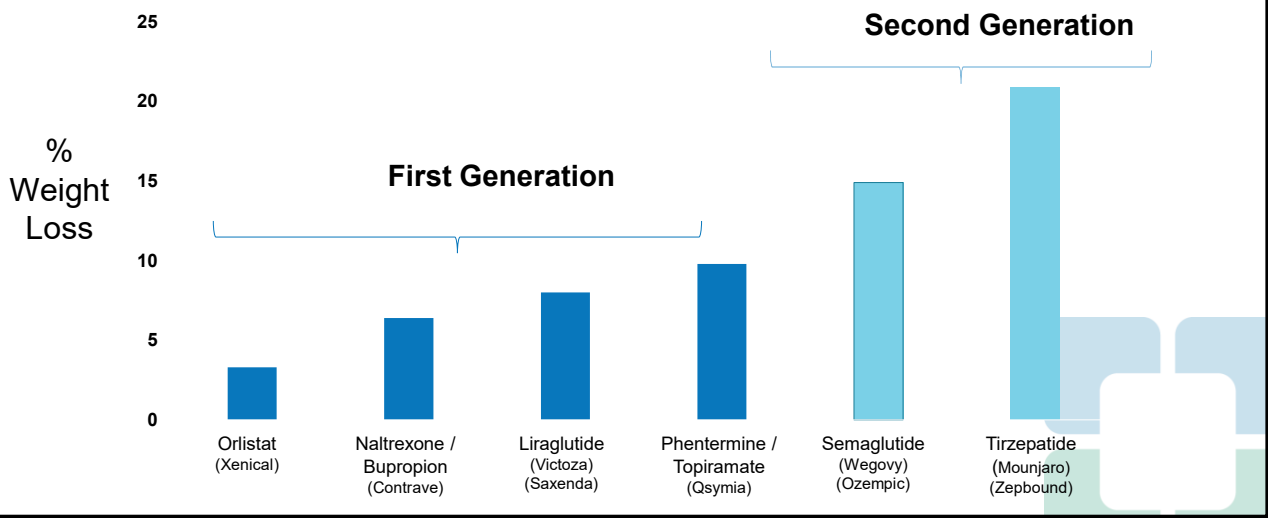
Medications Available to Treat Obesity: Transformational in Terms of Efficacy and Safety



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AACE Endocrine Practice™
www.endocrinepractice.org

AACE Clinical Guidance

American Association of Clinical Endocrinology Consensus Statement: Algorithm for the Evaluation and Treatment of Adults with Obesity/Adiposity-Based Chronic Disease – 2025 Update

Karl Nadolsky, DO, FACE, DABOM [1], W. Timothy Garvey, MD, MACE [2], Monica Agarwal, MD, FACE [2], Alex Bonnecaze, MD [3], Bartolome Burguera, MD, PhD [4], Michelle DeGeeter Chaplin, PharmD [5], Marcio L. Griebeler, MD [4], Samantha R. Harris, MD [6], Jeffrey N. Schellinger, MCN, RD [7], Juliana Simonetti, MD, DABOM [8], Reshmi Srinath, MD [9], Volkan Yumuk, MD, FACE [10]

- This 2025 algorithm for the medical care of adults with obesity underscores that ABCD is a complex, chronic disease that necessitates long-term treatment and care
- Emphasis on optimizing health rather than just weight reduction
- Achieving clinical goals other than a singular focus on body mass index (ie, complication-centric care)
- Choice of interventions and intensity of treatment should be individualized, taking disease severity
- Equality of care and reducing weight bias and stigma

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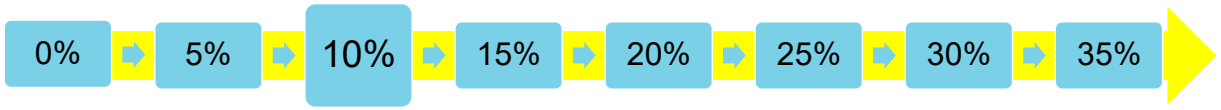
Comorbidities Improve with Weight Loss



% Weight Loss

- Physical function
- Type 2 diabetes
- Cardiovascular risk reduction
- Hypertension
- Sleep apnea
- Fatty liver improvement

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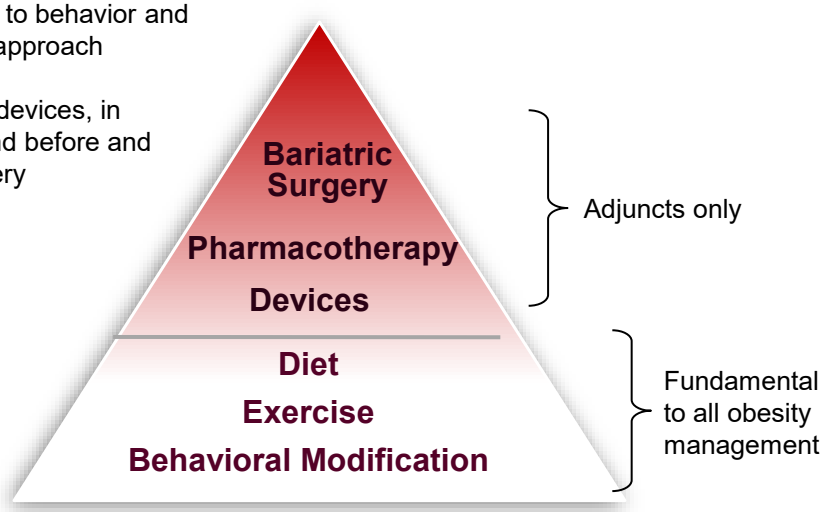
Fundamentals of Care

- Drugs are adjuncts to behavior and a multidisciplinary approach
- Can be used with devices, in combo together, and before and after bariatric surgery



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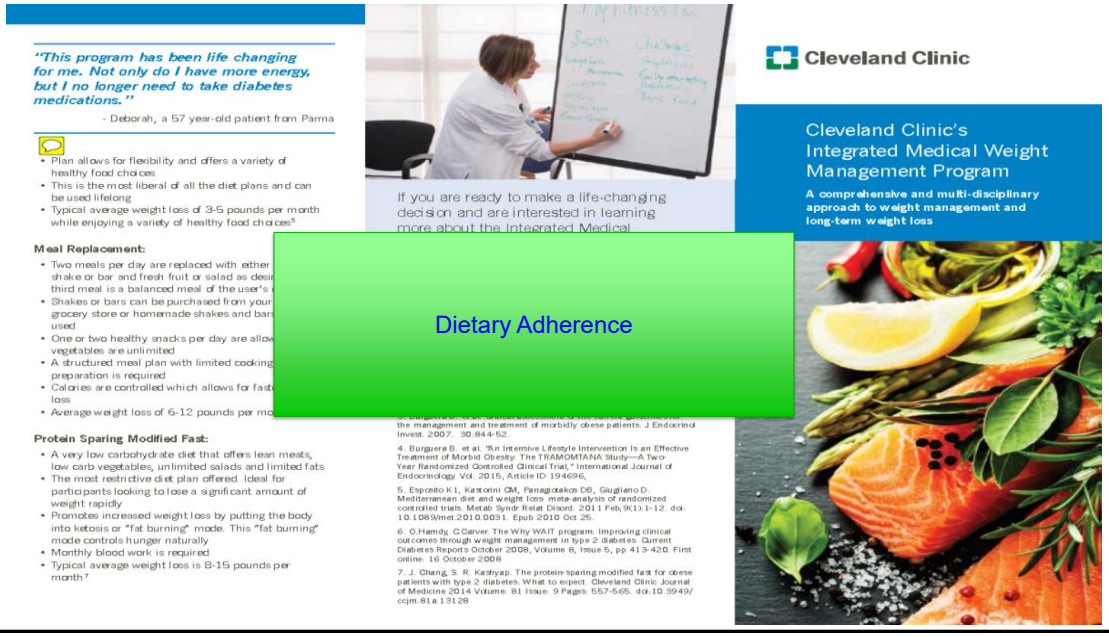
1. Nutrition.



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2.- Regular Physical Activity

- Personalized program:Assess Mobility
  - Walking
  - Upper body exercises
  - Swimming
  - Integrated in daily activities
  - Short term goal
  - Plan a head

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Practical Exercise Prescription (Obesity Care)

🏃 **Aerobic (5x/week):**
- Brisk walk 30 min/day
- OR 10 min walk after meals
- Goal: 150 min/week

💪 **Resistance (2–3x/week):**
- Chair squats (3×10)
- Wall push-ups (3×10)
- Band rows (3×12)
- Step-ups (2×10 each leg)
- Shoulder press (2×12)

🧘 **Flexibility & Balance (Daily):**
- Stretching, yoga, balance drills
- 5–10 minutes per day

✅ **Take-home Message:**
- Exercise is medicine: consistency matters.
- Aerobic + strength training = best results.
- Walking after meals helps weight & sugar.

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Very Enjoyable Life Burning Less Than 400 Cal

- Get up
- Open the door for the dog to get out
- Hit the remote to open the garage door
- Drive to work
- Catch the elevator to your office
- Work/eat in front of the computer all day
- Stop for Chinese/McD food (drive through in the way home
- Read, or if interested in sports ..
- Watch Real Madrid or Liverpool
- Go to bed

If Exercise Is Not a Part of Our Patient's Lives, They Will Probably Develop Significant Health Problems

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Study: M… Pos… …egularly …01

- Body weight control
  - Helps maintain a healthy e…
  - Prevents overweight and o…
  - Facilitates fat loss and pres…
- Metabolic health
  - Improves insulin sensitivity
  - Reduces the risk of metabo…
  - Regulates glucose and trig…
- General health and l…
  - Reduces the risk of premat…
  - Improves immune function…
  - Decreases the risk of type …
- Cardiovascular risk
  - Lowers blood pressure and…
  - Reduces the risk of heart a…
  - Improves endothelial functi…
- Productivity:
  - Increases concentration, m…
  - Improves energy and efficie…
  - Reduces absenteeism.
- Self-esteem and me…
  - Decreases anxiety and dep…
  - Improves mood and self-pe…
  - Strengthens body image ar…

7,000 STEPS A DAY FOR BETTER HEALTH

Walking about 3.5 miles (7,000 steps) per day could significantly **boost your health** based on new analysis of over 50 studies

- Early death –47%
- Heart disease –25%
- Cancer mortality –37%
- Type 2 diabetes –14%
- Dementia –38%
- Falls in older adults –28%

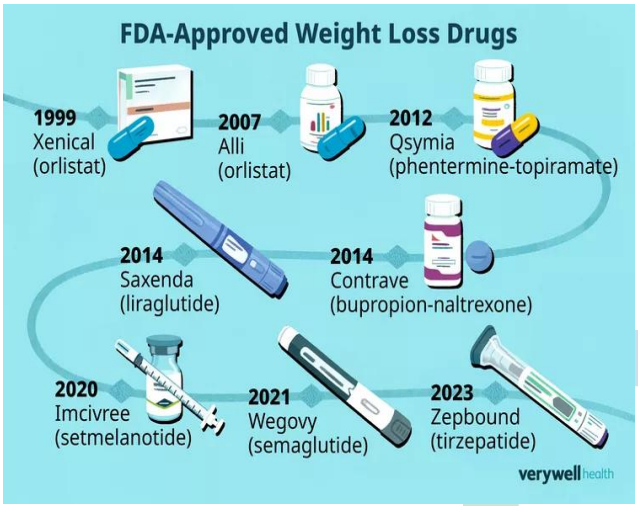
Even modest increases in step count can lower the risk of serious diseases

…nction.
…d sexual dysfunction.
…tive sleep.
…reduces daytime fatigue.
…ng the risk of osteoporosis.
…d balance, preventing falls.
…and chronic pain.
…alth:
…rain plasticity.
…and cognitive decline.
…nd memory.
…anisms that reduce cortisol.
…ional resilience.
…ess.
…group activities.
…munication skills.

43

Appetite Control. It Is Very Difficult to Help People to Lose Weight Without Reducing Their Appetite These Medications Are Useful to Reduce the Patient's Appetite Set Point in the Brain FDA Approved

3. Appetite control: weight loss medications.



44

4. Healthy Sleeping Habits

- Lack of sleep is associated to increased appetite
- Referrals to sleep clinic to r/o restless leg syndrome, obstructive sleep apnea, or other sleeping disorders
- Many patients are not aware of the circumstance
- Increases the risk of suffering a heart attack, a stroke, hypertension and hypogonadism

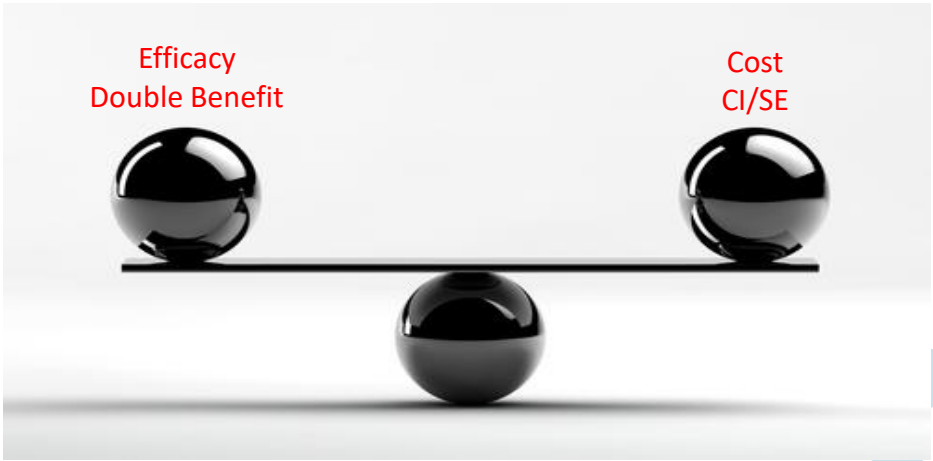
45

5. Try to Improve the Level of Stress in Our Patients' Life

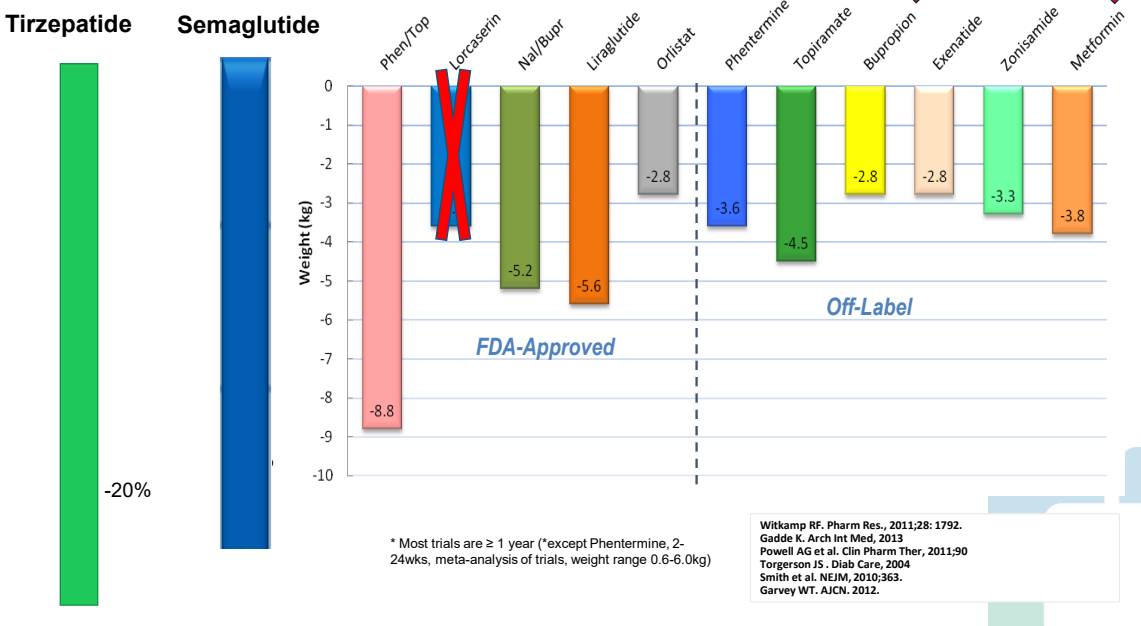
- Collaborate with our Psychology colleagues to assist us with the behavior modification component
- The prevalence of eating disorders, anxiety, depression and other psychiatric disorders is significant in the patients with morbid obesity
- Many of these patients may benefit from antidepressant therapy
- Psychotherapy in the context of SMAs, is also very helpful to address issues related to food addiction, bulimia and binge eating disorders

46

Choice of Appropriate Medication Is Balanced



47



48

Orlistat

- Works in the gut: inhibits the pancreatic lipase
- Approved for long term use
- 4-6% weight loss on average
- Lowers HbA1c 0.3%, reduces risk of developing diabetes, lowers triglycerides

- Pregnancy
- Chronic malabsorption syndrome
- Cholestasis

- Oily spotting
- Flatus with discharge
- Fecal urgency and incontinence

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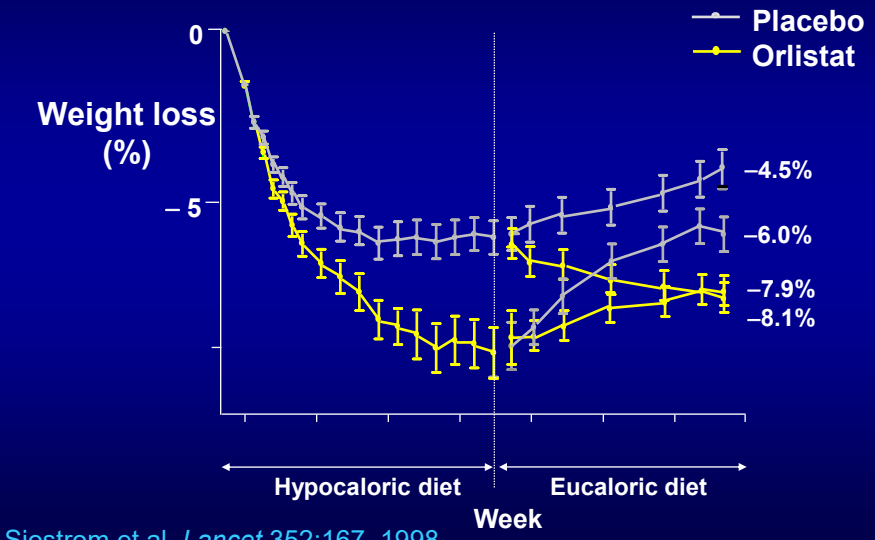
Effect of Orlistat on Body Weight



Sjostrom et al. *Lancet* 352:167, 1998

50

Phentermine/Topiramate ER

Mechanism of Action

- Central noradrenergic effects
  - Phentermine: immediate-release sympathomimetic—affects appetite
  - Topiramate ER: delayed-release gabanergic—affects satiety

Indications

- Adjunct to diet and exercise in patients with
  - BMI ≥30 kg/m^2
  - BMI ≥27 kg/m^2 with ≥1 weight-related comorbidity
    - Hypertension
    - T2D
    - Dyslipidemia

Dosing

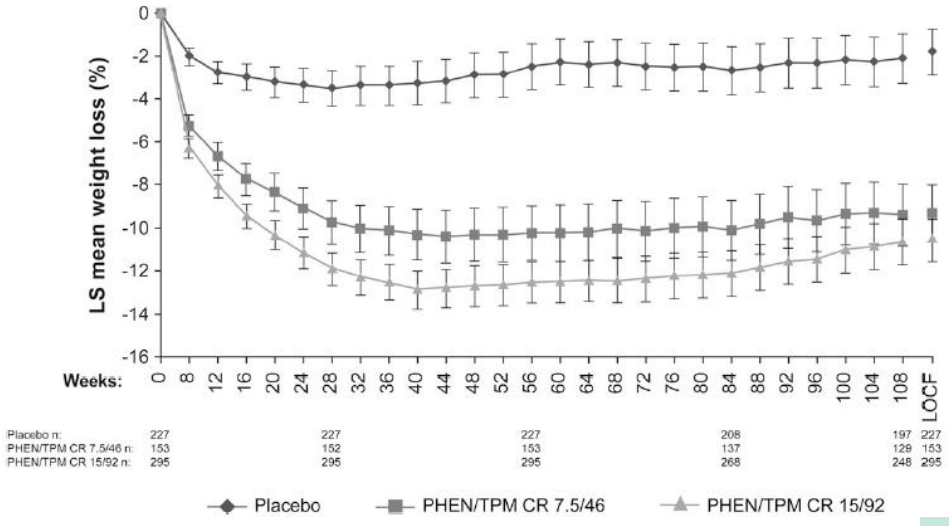
- Once daily in morning
  - Starting dose: phentermine 3.75/topiramate ER 23 mg for 14 days
  - Usual dose: 7.5/46 mg
  - Maximum dose: 15/92 mg
- If <3% weight loss after 12 weeks on usual dose, either discontinue medication or advance to maximum dose (transition dose phentermine 11.25 mg/topiramate ER 69 mg for 2 weeks)
- If <5% weight loss after 12 weeks on maximum dose, then discontinue the medication (to discontinue take every other day for one week)
- Schedule IV Controlled Substance

T2D = type 2 diabetes.

Qsymia prescribing information. Mountain View, CA: Vivus, Inc.; 2012.

51

Phen/Top (Qsymia) 2 Year Data on Weight: SEQUEL Trial

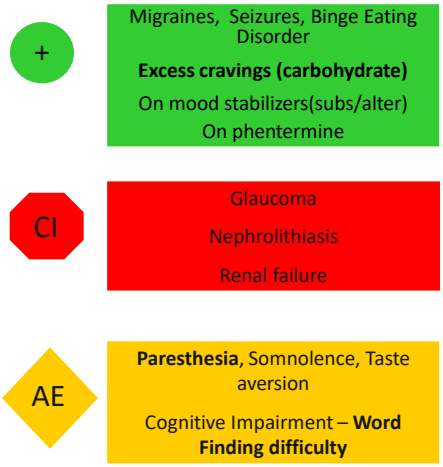


Am J Clin Nutr 2012;95:297–308

52

Off-Label

Topiramate (Topamax®)



Mechanism/Action: *Unclear*

- AMPA and kainate receptors(craving)
- Carbonic anhydrase (modification of lipogenesis, taste aversion)
- GABA (increase energy expenditure)

Dosing:

- Start 25mg daily
- Range: 25-150mg/d

Advice/Precautions:

- Take at night > dinner, Avoid sleeping meds
- May interact with oral contraceptive pills
- Interaction w/ Metformin
- Use BIRTH CONTROL/ (increased risk of oropalatal clefts)

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Naltrexone/Bupropion

- Bupropion: Reduces food intake by acting on adrenergic and dopaminergic receptors in the hypothalamus
- Naltrexone is an opioid receptor antagonist with minimal effect of weight loss when used alone
- Naltrexone blocks the inhibitory influences of opioid receptors activated by the β-endorphins released by the hypothalamus
- Blocking of β-endorphins amplifies the effects of bupropion leading to an anorectic effect

Contraindications

- Uncontrolled hypertension
- Seizures, anorexia, or discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs
- Chronic opioid use
- Use of other bupropion products or monoamine oxidase inhibitors
- Pregnancy

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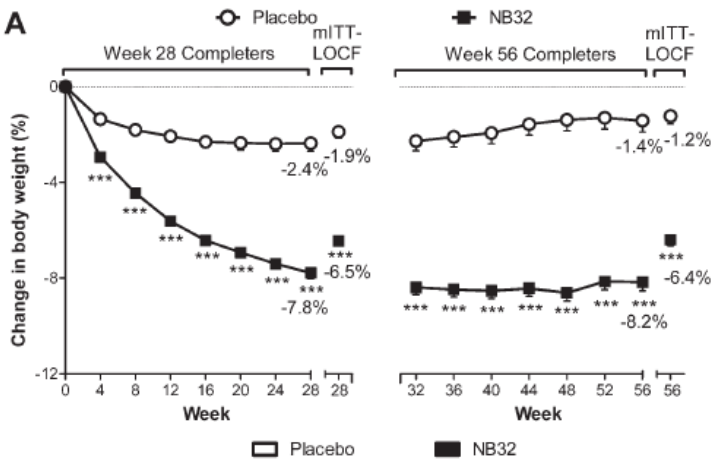
Naltrexone SR/Bupropion SR: COR II Trial



TG decreased 9.8%
HDL increased 3.6%
LDL decreased 6.2%

1,496 subjects, 54% follow up at 1 year

Obesity (2013) 21, 935-943.

55

Bupropion

+	Used to Treat Depression and Seasonal Affective Disorder, It Also Supports Smoking Cessation and Weight Management
CI	**Seizure disorder** . Uncontrolled hypertension Anorexia, or discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs Chronic opioid use
AE	Dry mouth, sore throat, stuffy nose; ringing in the ears; blurred vision; nausea, vomiting, stomach pain, **loss of appetite**, constipation; sleep problems (insomnia); tremors, sweating, feeling anxious or nervous

Mechanism/Action:

- **Inhibition of norepinephrine reuptake**
- Inhibition of dopamine reuptake
- No direct effect on serotonin reuptake inhibition, reducing the risk of sexual dysfunction**, weight gain,** and emotional blunting.
- Nicotine receptor antagonism

Dosing:

- Start 75mg daily
- Range: 75-300 mg/d

Advice/Precautions:

- Avoid if hx **seizures, eating disorder,** or sudden discontinuation of alcohol, seizure medication, or sedatives
- Some young people (up to 24 years of age) may have thoughts about suicide when first taking this medicine
-)

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Liraglutide 3mg

- GLP-1 agonist already used for glucose lowering in diabetes
- 3 mg dose approved for weight loss by FDA on 12/23/2014
- 6-8% weight loss. Reductions in prevalence of Met S
- Side effects: nausea, diarrhea, vomiting, pancreatitis, questions about medullary thyroid carcinoma risk

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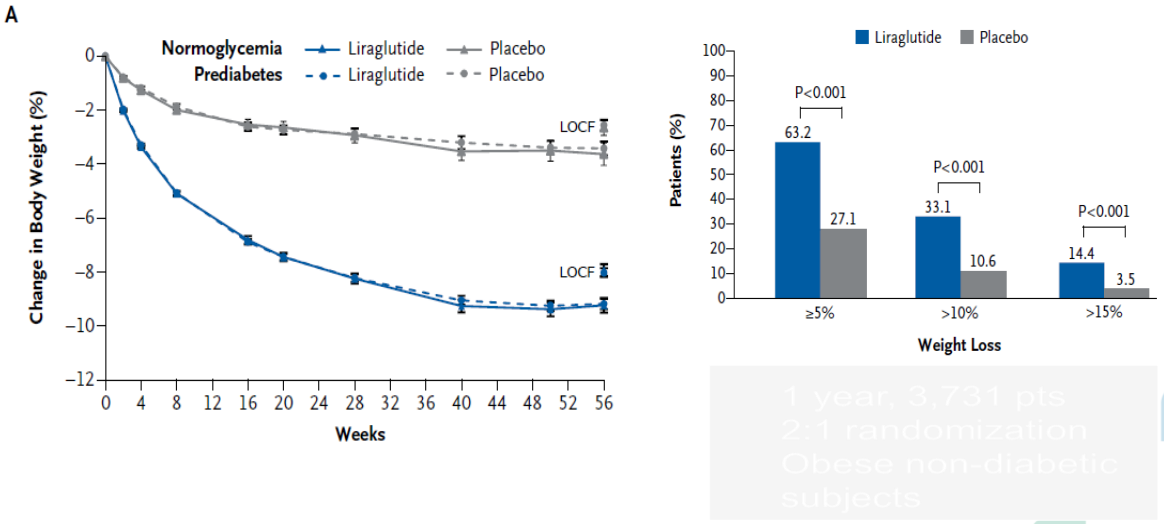
Liraglutide 3 Mg in Obesity



1 year, 3,731 pts
2:1 randomization
Obese non-diabetic subjects

N Engl J Med 2015;373:11-22.

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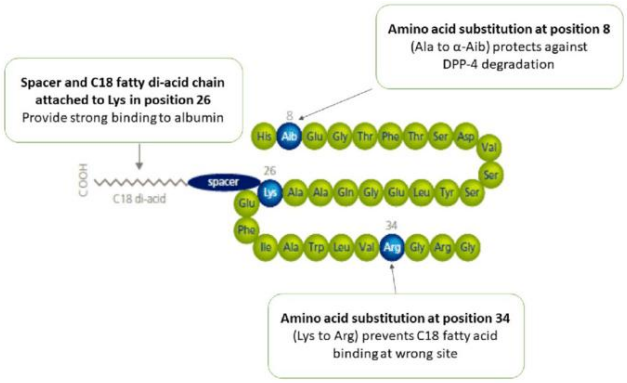
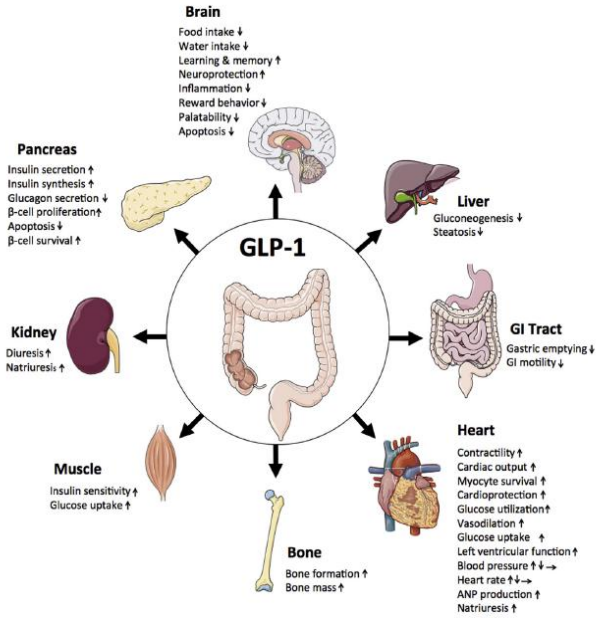
Structure of Semaglutide and Actions of GLP-1

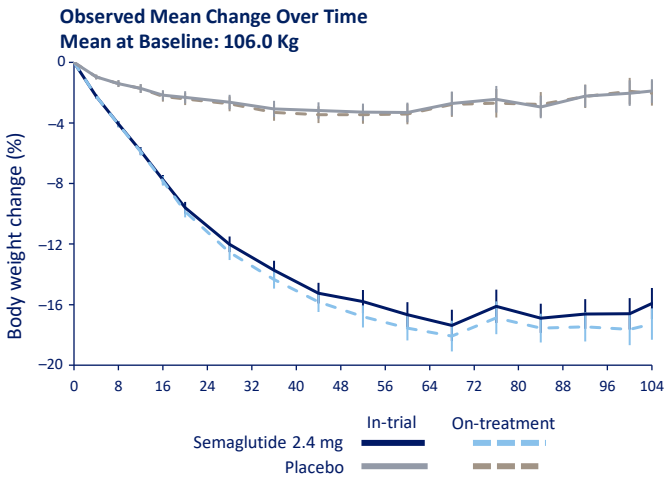




Muller T et al. Molecular Metabolism 2019;30:72-130

59

Two Year Efficacy of Semaglutide 2.4 Mg in the STEP 5 Trial: Change in Body Weight Over 2 Years (%)

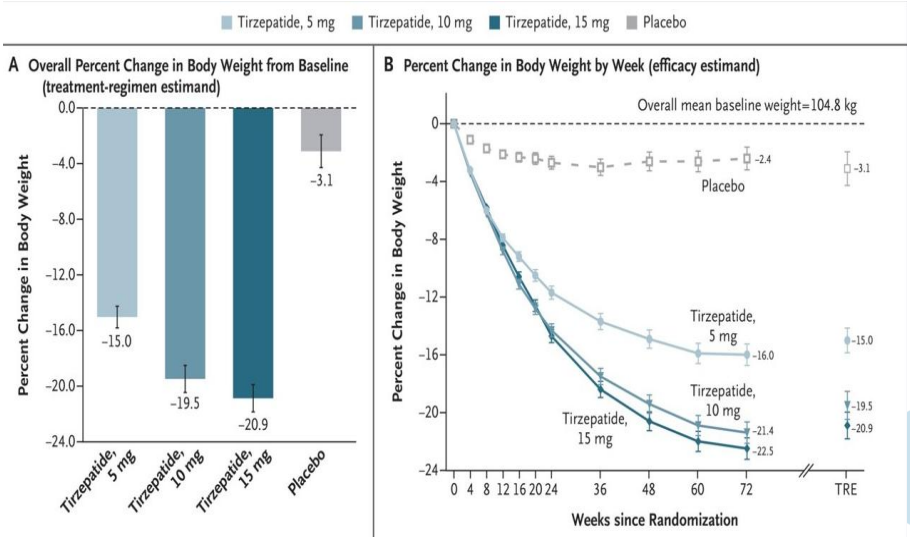


**Treatment policy estimand (assesses treatment effect regardless of treatment discontinuation or rescue intervention); †Trial product estimand (assesses treatment effect if trial product was taken as intended). CI, confidence interval; ETD, estimated treatment difference.*

Garvey WT et al. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. Nature Medicine 2022 Oct;28(10):2083-2091

60

Effect of Once-Weekly Tirzepatide, as Compared with Placebo, on Body Weight



Jastreboff AM et al. N Engl J Med2022;387:205-216

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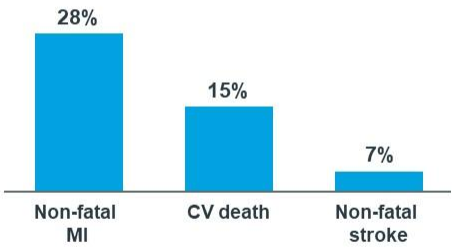
Figure 1
SELECT trial: primary and confirmatory secondary endpoints

Beneficial effects of semaglutide 2.4 mg on cardiovascular risk vs. placebo

Primary endpoint
(top-line readout, 8 Aug. 2023)

20%
relative risk reduction in MACE-3 events
(statistically significant)

MACE-3 components
(relative risk reduction)



17,604 adults with overweight or obesity, without diabetes and had a diagnosis of cardiovascular disease, including prior myocardial infarction, stroke, and/or peripheral artery disease

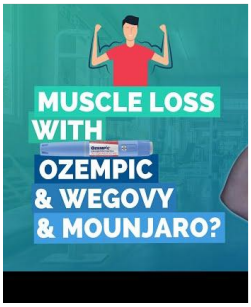
* Including cardiovascular death, urgent heart failure visits and hospitalisations

Source: Lincoff A, Brown-Frandsen K, Colhoun H, et al. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. N Engl J Med. DOI: 10.1056/NEJMoa2307563.; IQVIA EMEA Thought Leadership

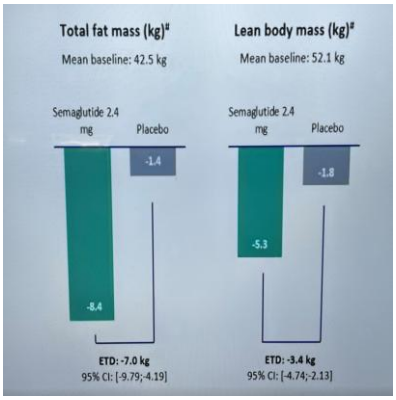
IQVIA

62

Importance of Keeping Muscle Mass



During GLP-1 treatment, it is important to consider getting **adequate amounts of protein, (up to 1.2-1.6 gr/kg),** vitamin B12, vitamin D, iron, and calcium



Aerobic (5x/week):
- Brisk walk 30 min/day
- OR 10 min walk after meals
- Goal: 150 min/week

Resistance (2–3x/week):
- Chair squats (3×10)
- Wall push-ups (3×10)
- Band rows (3×12)
- Step-ups (2×10 each leg)
- Shoulder press (2×12)

Flexibility & Balance (Daily):
- Stretching, yoga, balance drills
- 5–10 minutes per day

Take-home Message:
- Exercise is medicine: consistency matters.
- Aerobic + strength training = best results.

Wilding JPH et al. N Engl J Med 2021:384:989-1002

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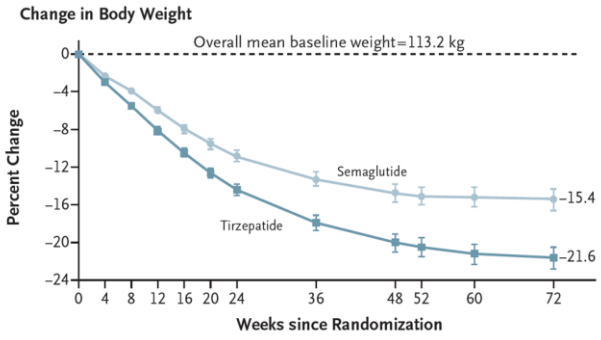
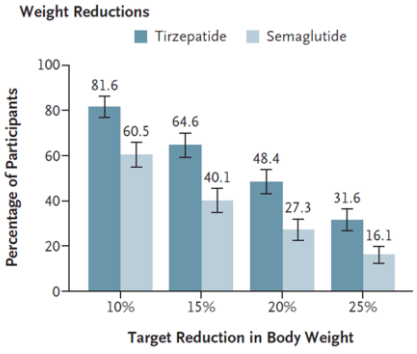
SURMOUNT-5
Greater Body Weight Reduction and Target Weight Loss Achievement with Tirzepatide Vs Semaglutide





Weight reduction ≥30% in 20% vs 7% of tirzepatide vs semaglutide-treated participants, respectively

P<0.001 for all primary and key secondary end points

Once-weekly tirzepatide (maximum tolerated dose, 10 mg or 15 mg) as compared with once-weekly semaglutide (maximum tolerated dose, 1.7 mg or 2.4 mg) on body weight (% change and categorical endpoints) at Week 72

Aronne LJ, Horn DB, le Roux CW, et al. N Engl J Med. 2025 May 11. Epub ahead of print.

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Metformin

Off-Label

+

Diabetes, Pre-diabetes

PCOS, Insulin resistance

Atypical antipsychotic medication-induced weight gain

HIV Lipodystrophy (Protease inhibit)

CI

Renal impairment

AE

WARNING: lactic acidosis

Nausea, Vomiting,

Diarrhea, abdominal pain

Altered taste

Mechanism/Action:

Activates AMPK; Decreases Hepatic Glucose Production, Increases Muscle Glucose Uptake

Dosing:

- Start 500mg QD (Range: 500mg – 2000mg)

Advice/Precautions:

- Monitor for Vitamin B12 deficiency
- Interaction with topiramate
- Reports *Lactic Acidosis* in the presence of renal insufficiency

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CLEVELAND CLINIC JOURNAL OF MEDICINE VOLUME 90 • NUMBER 9 SEPTEMBER 2023

1-MINUTE CONSULT

Paloma Rodriguez, MD
Marcio L. Griebeler, MD
Kevin M. Pantalone, DO, ECNU, FA
Bartolome Burguera, MD, PhD

ONE MINUTE CONSULT
BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Should I consider metformin therapy for weight loss in patients with obesity but without diabetes?

A: Yes. Evidence supports the weight-loss effects of metformin in adults with obesity and without type 2 diabetes.

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- Reduction in body weight (3%–5%) is associated with improvements in blood pressure, and lipids, and is a strong predictor of type 2 diabetes prevention
- Metformin as an initial and adjunct weight-loss medication, especially in the presence of prediabetes, severe obesity (BMI ≥ 35), use of antipsychotic medications, or PCOS
- Consider a long-term treatment, particularly in patients who demonstrate a good response
- Dosage of 1,500 mg/day or more (or adjusted according to renal function)

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JAMA Network

Cleveland Clinic - Pragmatic Trial

INTERVENTION

200 Participants randomized

AOMs
- Liraglutide
- Lorcaserin
- Phentermine & Topiramate
- Wellbutrin & Naltrexone

100 Weight management program (WMP)
Monthly visits focused on accomplishing a healthier lifestyle including focus on nutrition and physical activity

100 Weight management program and Anti-Obesity Medication (AOM)
WMP plus an anti-obesity medication

PRIMARY OUTCOME

Percent change in body weight at month 12 from baseline

Pragmatic study designs can bridge the gap between clinical trials and clinical practice

Provide real-world evidence of effectiveness, with the rigor of randomized clinical trials, to inform the treatment decisions of insurance, physicians, companies and patients

Pantalone et al. **Effectiveness of Combining Antiobesity Medication With an Employer-Based Weight Management Program for Treatment of Obesity: A Randomized Clinical Trial**JAMA Netw Open. 2021;4(7):e2116595. doi:10.1001/jamanetworkopen.2021.16595

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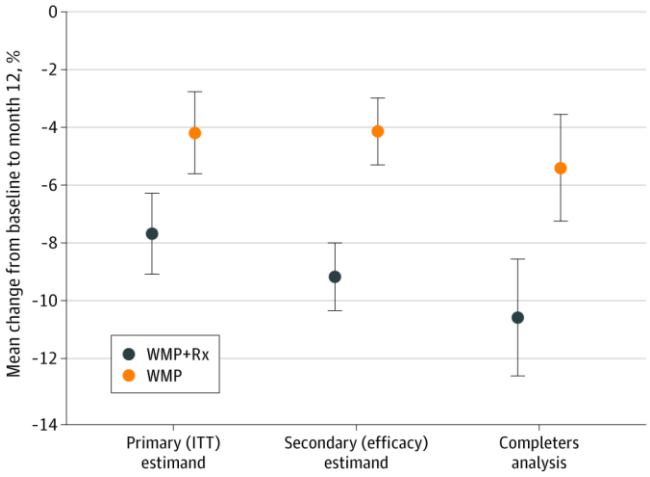
JAMA Network



Change in Percentage Body Weight From Baseline to 12 Months, Primary End PointITT indicates intention to treat; WMP, weight management program; and WMP+Rx, WMP plus antiobesity medication. Mean baseline indicates mean body weight at baseline, and error bars indicate 95% CI. All comparisons are significantly different at P < .001.

Pantalone et al. **Effectiveness of Combining Antiobesity Medication With an Employer-Based Weight Management Program for Treatment of Obesity: A Randomized Clinical Trial**JAMA Netw Open. 2021;4(7):e2116595. doi:10.1001/jamanetworkopen.2021.16595

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Contents lists available at ScienceDirect
Obesity Research & Clinical Practice
journal homepage: www.elsevier.com/locate/orcp

Weight gain following an employer-based randomized trial evaluating the treatment of obesity with and without anti-obesity medication

Noura Nachawi [a], Marcio L. Griebeler [b], Huijun Xiao [c], James Bena [c], Kevin M. Pantalone [b], Bartolome Burguera [b,*]

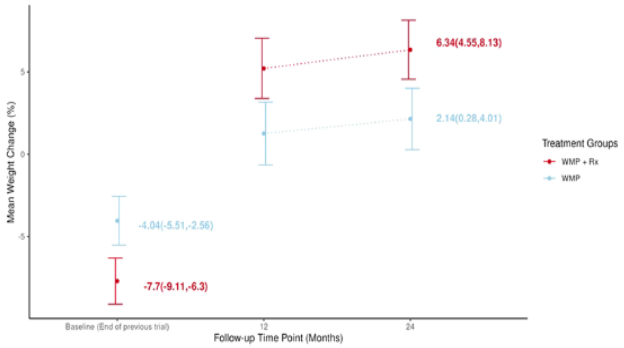

Fig. 1.

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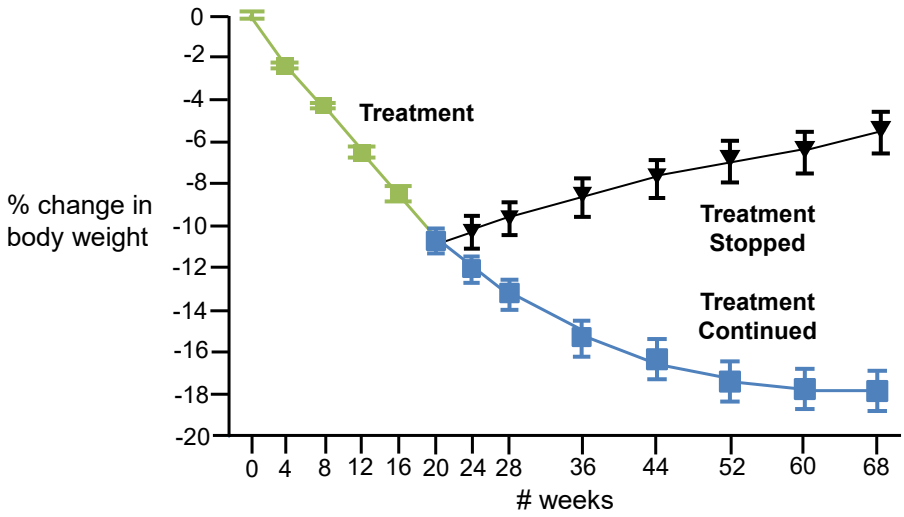
Anti-Obesity Medications Required Long-Term



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CLEVELAND CLINIC JOURNAL OF MEDICINE VOLUME 91 • NUMBER 11 NOVEMBER 2024

COMMENTARY

Bartolome Burguera, MD, PhD Marcio L. Griebeler, MD W. Timothy Garvey, MD, MACE

Effective but inaccessible antiobesity medications: A call for sharing responsibility for improving access to evidence-based care

TABLE 1
US list prices (monthly cost) of second-generation antiobesity medication compared with selected other countries

	United States	Spain	Denmark	Netherlands	United Kingdom	Japan	Canada	Dubai
Semaglutide 2.4 mg	$1,349	$314	$343	$296	$233	$69	$388	$326
Tirzepatide 10–15 mg	$1,069	$400	$632	$444	$162	$319	$104	$472

Information based on web searches, direct pharmacy pricing information, and reference 22.

India

200

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Received: 13 February 2025 | Revised: 1 May 2025 | Accepted: 2 May 2025
DOI: 10.1002/oby.24331

ORIGINAL ARTICLE
Clinical Trials and Investigations

Obesity WILEY

Changes in weight and glycemic control following obesity treatment with semaglutide or tirzepatide by discontinuation status

Hamlet Gasoyan[1,2] | W. Scott Butsch[3,4] | Rebecca Schulte[5] | Nicholas J. Casacchia[1] | Phuc Le[1,2] | Christopher B. Boyer[5] | Marcio L. Griebeler[2,6] | Bartolome Burguera[2,6] | Michael B. Rothberg[1,2]

Weight loss after 1 year with semaglutide or tirzepatide:

11.9% Patients who continued the drug

6.8% Adults discontinuing the drug between 3 months and 1 year

3.6% Those discontinuing the drug in less than 3 months

Healio

Treatment	Early Discontinuation	Later Discontinuation	Did Not Discontinue
Semaglutide	21.6% (1318)	31.4% (1917)	47.0% (2874)
Tirzepatide	16.4% (291)	34.1% (605)	49.4% (876)

Conclusions: The average weight reduction in this cohort was lower than that observed in the main phase 3 trials, likely because of higher rates of discontinuation and lower maintenance dosages.

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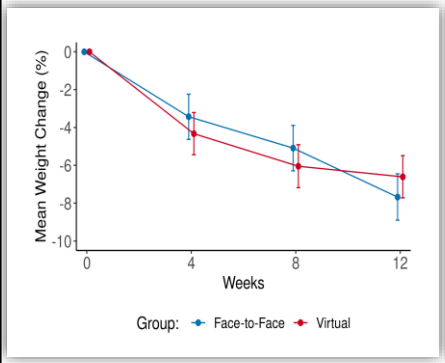
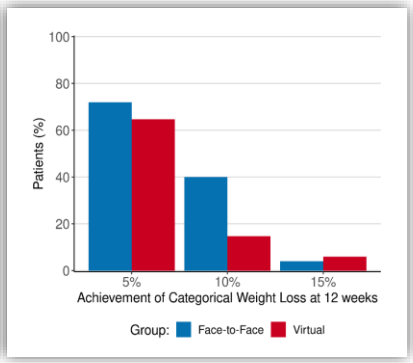
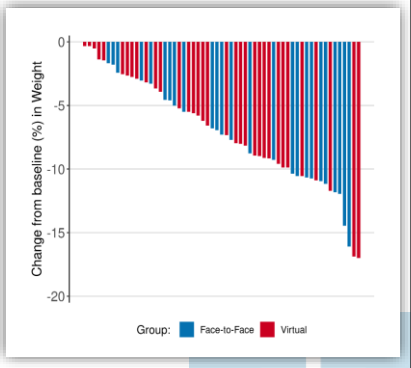
Comparation of Virtual Vs. In-Person Encounters In Patients with Obesity







Griebeler ML, Butsch WS, Rodriguez P, Lomeli L, Kampert M, Makin V, Bena J, Pantalone KM, Burguera B. The use of virtual visits for obesity pharmacotherapy in patients with overweight or obesity compared with in-person encounters. Obesity (Silver Spring). 2022 Nov;30(11):2194-2203. doi: 10.1002/oby.23548. Epub 2022 Sep 25. PMID: 36156456; PMCID: PMC9826334.

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nature medicine

Article https://doi.org/10.1038/s41591-025-03893-3

Macrovascular and microvascular outcomes of metabolic surgery versus GLP-1 receptor agonists in patients with diabetes and obesity

Bariatric surgery is STILL superior to GLP-1 therapies for major health outcomes

At the end of the study, patients who underwent surgery had:

- 32% lower risk of death
- 35% lower risk of adverse cardiovascular events such as heart attack, heart failure, or stroke
- 47% lower risk of chronic kidney disease
- 54% lower risk of retinopathy

Future studies should compare the cardiometabolic outcomes of metabolic surgery with newer GLP-1 RAs that are more effective for weight reduction

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In Summary:

- Obesity is a major health and socio-economic problem
- Majority of your patients will suffer obesity
- Respect and try understand what is behind their disease
- Need to maximize novel care delivery initiatives:
  - Interdisciplinary care
  - Shared medical appointments
  - Technology and digital care

Medications, in addition to Nutrition, Phys activity, Sleep, and Psycho-Social aspects

Liraglutide, Naltrexone/Bupropion, Phentermine/Topiramate (5–10% wt loss)

Consider Metformin and other combinations

Semaglutide and Tirzepatide (15–25% weight loss, ~ surgical outcomes)

Chronic condition → long term therapeutic plan

Cleveland Clinic

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