Optimizing diabetes control with lifestyle and weight reduction techniques

UW MEDICINE

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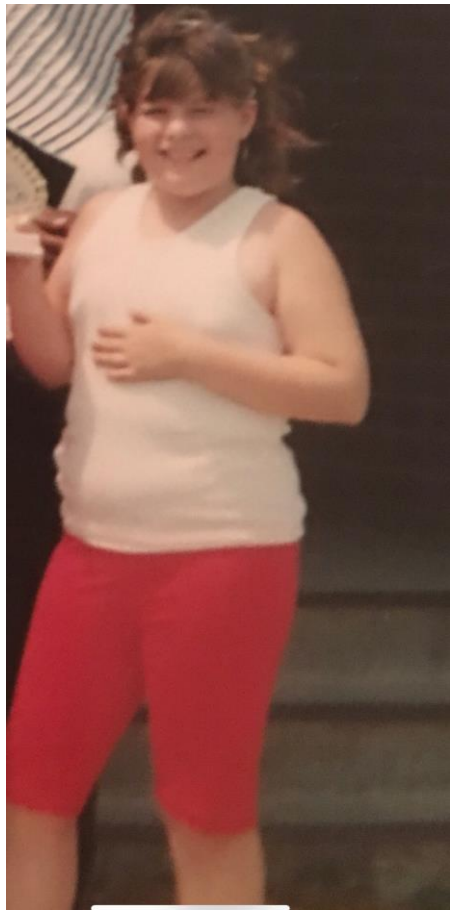
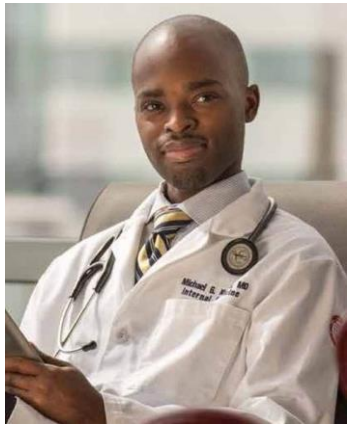
Disclosures



- No financial disclosures
- I grew up as a child with obesity
- This presentation was a collaborative effort with **Michael G. Knight, MD, MSHP, FACP, Dipl. ABOM,** Assistant Professor of Medicine, the George Washington University



Introductions

About me…

- Canadian/Native American
- Family Physician Board certified in Canada and USA
- I practiced 5 years in Ontario Canada and 6 years in the USA
- Diplomate of the American Board of Obesity Medicine 2019
- Started working full-time at the UW Center for Weight Loss and Metabolic Surgery in Oct/19- My dream job!!

UW Medicine

CENTER FOR WEIGHT LOSS & METABOLIC SURGERY

Objectives

- Be able to optimize diabetes control with lifestyle and weight reduction techniques
- Understand which diabetes medications cause weight loss, weight gain or are weight neutral

Diabesity: Diabetes related to Obesity

- The risk of type 2 diabetes (T2DM) rises with increasing body weight.
- It is estimated that 90% of T2DM is associated with overweight and obesity
- The prevalence T2DM is three to seven times higher in those who are affected by obesity than in normal weight adults
- T2DM 20 times more likely in those with a body mass index (BMI) greater than 35

Hossain P, Kawar B, El Nahas M. Obesity and diabetes in the developing world – a growing challenge.

N Engl J Med. 2007;356(3):213–5.

Obesity: Adiposity-Based Chronic Disease/ABCD

- In June 2013 the American Medical Association voted to recognize Obesity as a chronic disease
- adipose tissue is a major endocrine organ (adipokines) that cause immune and metabolic dysfunction (elevated blood glucose, elevated blood pressure, dyslipidemia, cancer)

- Physical forces cause stress to other body tissue- DJD, reflux, sleep apnea, intertrigo

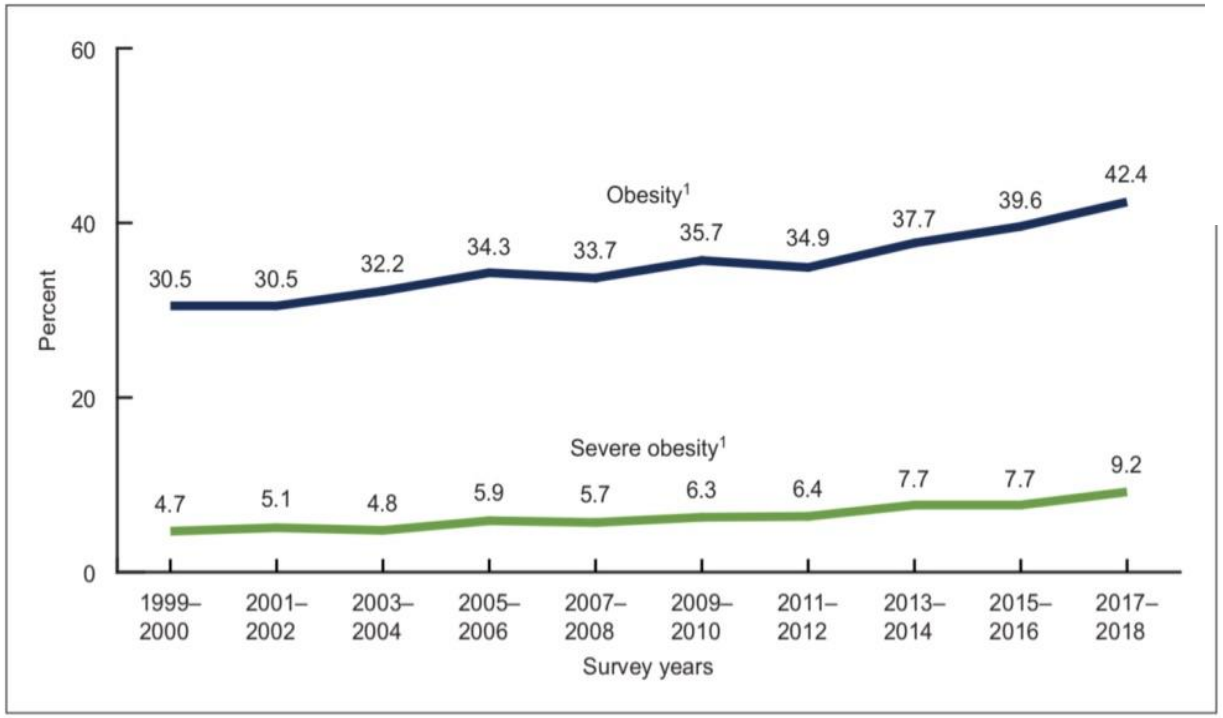
- 2016 AACE/ACE gives new term ABCD to Obesity so people better understand the adiposopathy (?? **Adiposity)**

Conside
r

Obesity: Adiposity-Based Chronic Disease/ABCD

Epidemiology:

Figure 4. Trends in age-adjusted obesity and severe obesity prevalence among adults aged 20 and over: United States, 1999–2000 through 2017–2018

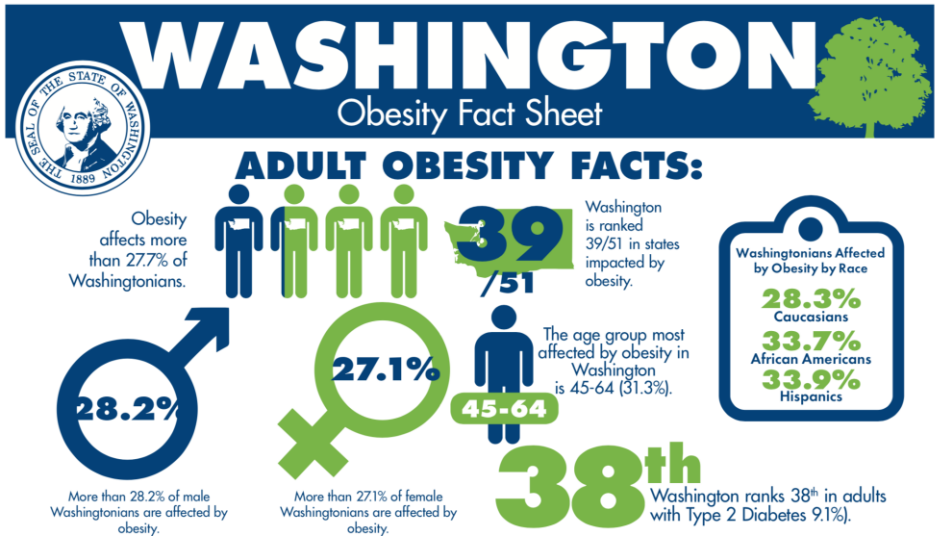


[1]Significant linear trend.
NOTES: Estimates were age adjusted by the direct method to the 2000 U.S. Census population using the age groups 20–39, 40–59, and 60 and over. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db360_tables-508.pdf#4.
SOURCE: NCHS, National Health and Nutrition Examination Survey, 1999–2018.

Key findings NCHS Data Brief No.360, February 2020

Data from the National Health and Nutrition Examination Survey

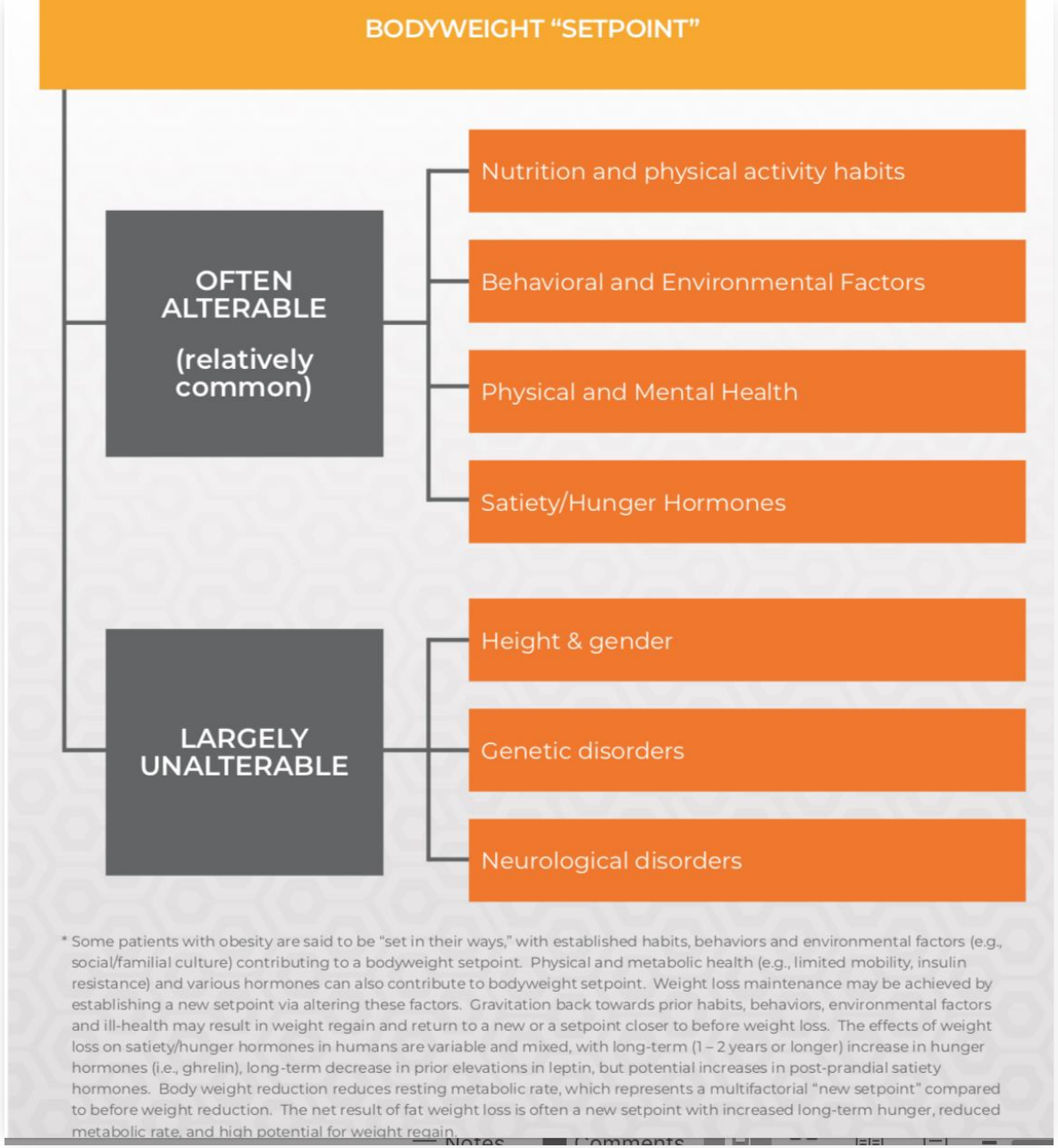
- In 2017–2018, the age-adjusted prevalence of obesity in adults was 42.4%, and there were no significant differences between men and women among all adults or by age group.
- The age-adjusted prevalence of severe obesity in adults was 9.2% and was higher in women than in men.
- Among adults, the prevalence of both obesity and severe obesity was highest in non-Hispanic black adults compared with other race and Hispanic-origin groups.
- The prevalence of severe obesity was highest among adults aged 40–59 compared with other age groups.
- From 1999–2000 through 2017–2018, the prevalence of both obesity and severe obesity increased among adults.



Obesity Action Coalition

Obesity: Adiposity-Based Chronic Disease/ABCD

- Not just calories in and calories out!!!
- treatment (lifestyle, surgical and pharmaceutical) can help patients adhere to calorie restriction by assisting in suppression the hormonal changes that are occurring in the body to keep our patients at a “set-point”
- METABOLIC ADAPTATION



Obesity Algorithm 2021-OMA

Obesity: Adiposity-Based Chronic Disease/ABCD

- Weight loss in patients with diabetes and Adiposity-Based Chronic Disease Improves A1c

Overweight or Obesity	BMI ≥25 (≥23 in certain ethnicities)	Metabolic syndrome		10%	Prevention of T2DM
		Prediabetes		10%	Prevention of T2DM
		T2DM		5% to ≥15%	• Reduction in A1C • Reduction in number and/or doses of glucose lowering medications
		Dyslipidemia		5% to ≥15%	• Lower triglycerides • Higher HDL-c • Lower non-HDL-c
		Hypertension		5% to ≥15%	• Lower systolic and diastolic BP • Reductions in number and/or doses of antihypertensive medications
		Nonalcoholic fatty liver disease	Steatosis	5% or more	Reduction in intrahepatocellular lipid
			Steatohepatitis	10% to 40%	Reduction in inflammation and fibrosis
		Polycystic ovary syndrome		5% to 15% or more	• Ovulation • Regularization of menses • Reduced hirsuitism • Enhanced insulin sensitivity • Reduced serum androgen levels
		Female infertility		10% or more	• Ovulation • Pregnancy
		Male hypogonadism		5% to 10% or more	Increase in serum testosterone
		Obstructive sleep apnea		7% to 11% or more	• Improved symptomatology • Decreased apnea-hypopnea index
		Asthma/reactive airway disease		7% to 8% or more	• Improvement in forced expiratory volume at 1 second • Improved symptomatology
		Osteoarthritis		• ≥10% • 5% to 10% or more when coupled with exercise	• Improvement in symptomatology • Increased function
		Urinary stress incontinence		5% to 10% or more	Reduced frequency of incontinence episodes
		Gastroesophageal reflux disease		10% or more	Reduced symptom frequency and severity
		Depression		Uncertain	• Reduction in depression symptomatology • Improvement in depression scores

AACE guidelines on Obesity

Obesity: Adiposity-Based Chronic Disease/ABCD

Diagnosis and Treatment:

Body Mass Index: Increased Body Fat (Adiposity)

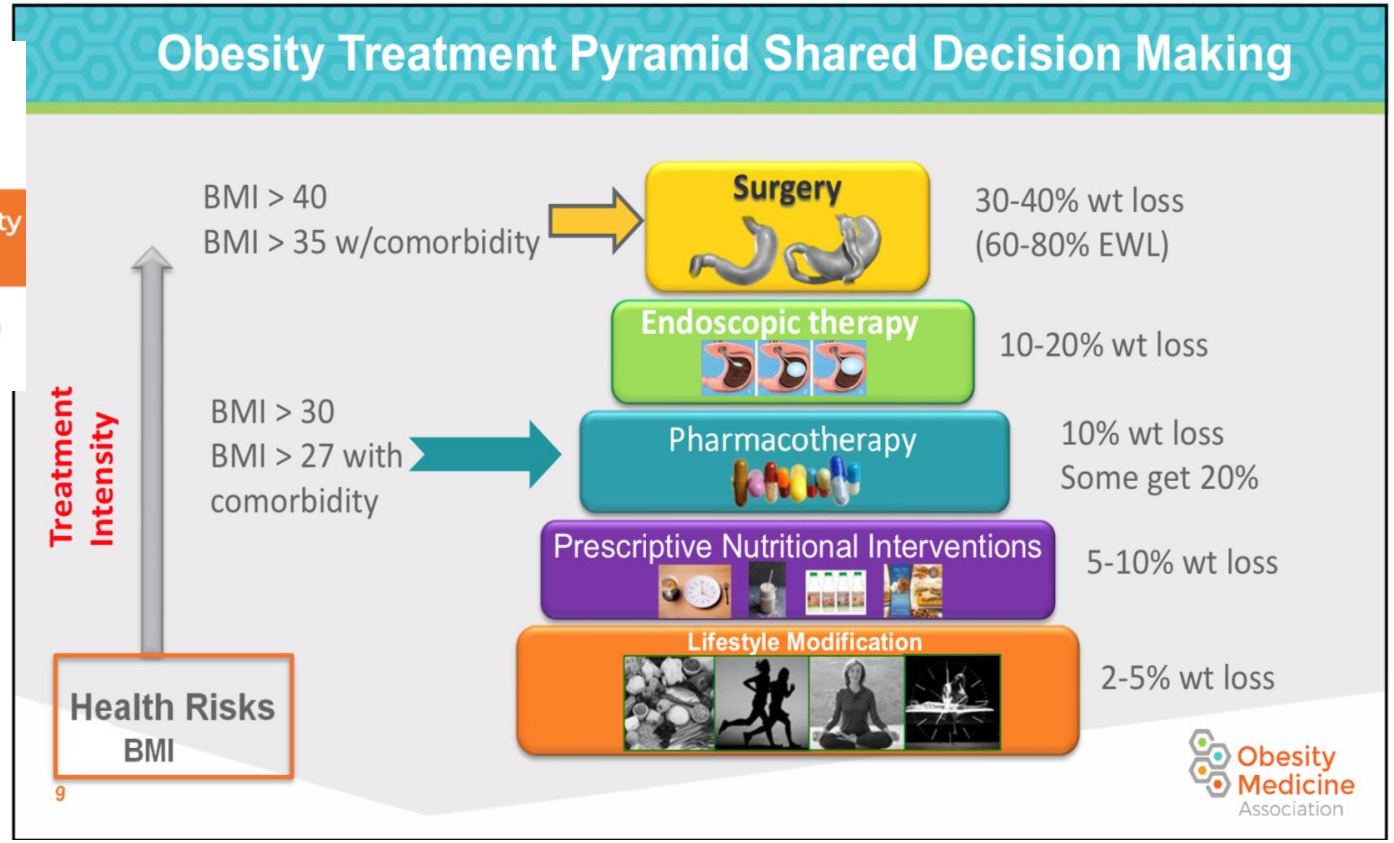
Body mass index (BMI) in kilograms per meters squared (kg/m²)*

Normal Weight	Overweight	Class I Obesity	Class II Obesity	Class III Obesity
18.5-24.9	25.0-29.9	30.0-34.9	35.0-39.9	≥ 40

*Different BMI cut-off points may be more appropriate based upon gender, race, ethnicity, and menopausal status. For example, among Asians, a BMI ≥23 kg/m² may be a more appropriate cut-off point to define overweight and to screen for type 2 diabetes mellitus. Among postmenopausal women, BMI may underestimate percent body fat.

Asian American:

- BMI 23 and over is overweight
- BMI 27 and over is obesity

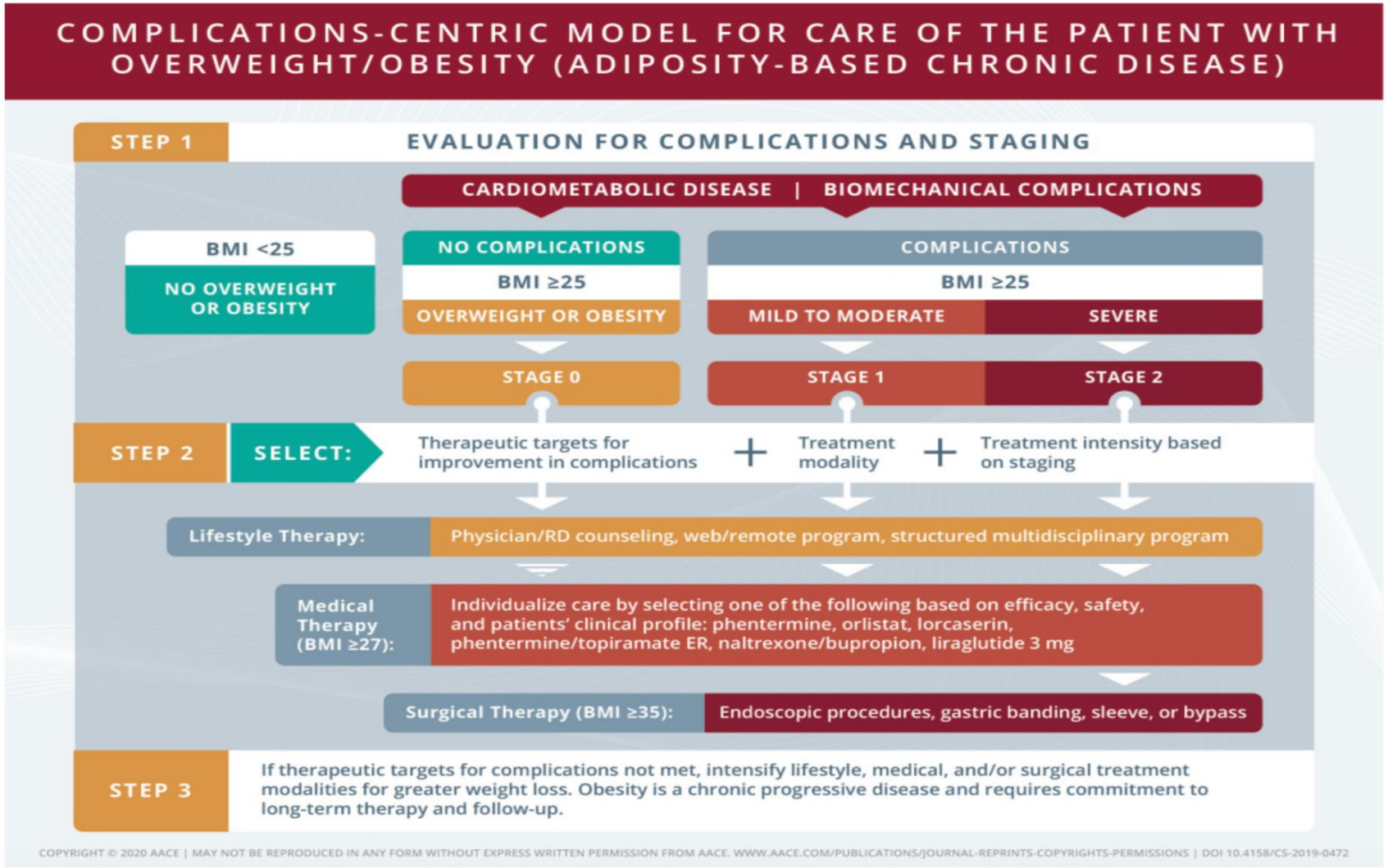


Obesity: Adiposity-Based Chronic Disease/ABCD and Diabetes

Diagnosis and Treatment:

Asian American:

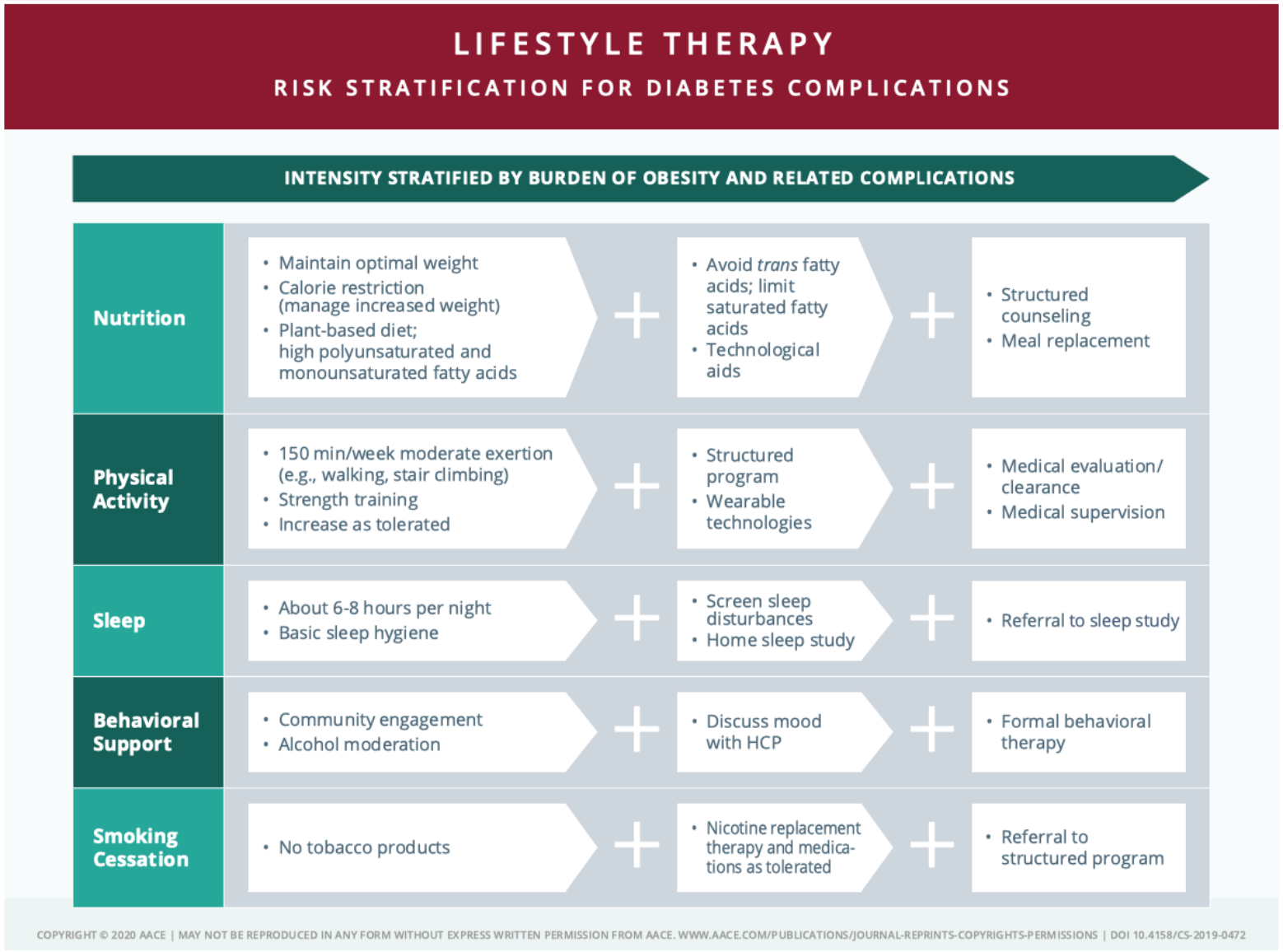
- BMI 23 and over is overweight
- BMI 27 and over is obesity



AACE T2DM management algorithm 2020

Lifestyle Therapy

- Essential part of treatment for patients with diabetes and obesity
- Multifaceted
- Multidisciplinary (pcp, RD, PT, psychologist, endocrinologist, sleep medicine, obesity specialist etc.)
- At least 5% or more weight loss with long-term support for maintenance of weight lost



AACE T2DM management algorithm 2020

Lifestyle Therapy

Nutrition

- "The best nutritional intervention is a plan that is evidence-based, quantitatively sound, qualitatively appropriate and one the patient prefers and is therefore most likely to adhere to over a lifetime" – 2021 Obesity Algorithm

AACE 2020

Lifestyle Therapy

Nutrition General Principles:

- Encourage foods that result in a negative caloric balance to achieve and maintain a healthy weight
- Consider the following:
  - Eating behaviors, and meal patterns
  - Cultural background, traditions, and food availability
  - Time constraints and financial issues
  - Nutritional knowledge and cooking skills
  - Medical conditions potentially affected by the nutrition plan
- Nutritional approaches for weight loss typically focus on the caloric manipulation of the three macronutrients: carbohydrate, fat, or protein
- Very low-calorie diets contain less than 800 kcal/day and require close medical supervision for safety reasons
- Low calorie diets range from 1,200-1,800 kcal/day (1,200-1,500 for women, 1,500-1,800 for men)
- Restricting dietary fat leads to a greater reduction in total and LDL cholesterol, whereas restricting dietary carbohydrate leads to a greater reduction in serum triglycerides and an increase in HDL-cholesterol
- Reduction of carbohydrates can lead to a greater reduction in serum glucose and hemoglobin A1C

Limit:

- **Unhealthful ultra-processed foods of minimum nutritional value such as:** "sweets", "junk foods," cakes, cookies, candy, pies, chips, and ultra-processed meats such as bacon, sausage, hot dogs, pastrami
- Energy-dense foods high in calories
- **Energy-dense beverages:** sugar-sweetened beverages, juice, cream
- Avoid trans fats and excessive sodium
- Among sweeteners, sucrose and saccharin may increase body weight compared to aspartame, rebaudioside A, and sucralose

Encourage:

- Consumption of healthful proteins and fats, vegetables, leafy greens, fruits, berries, nuts, legumes, whole grains
- Complex carbohydrates over simple sugars: Low glycemic index over high glycemic index foods
- High-fiber foods over low-fiber foods
- Many dairy products (while being mindful of caloric content)
- Reading labels rather than marketing claims

Obesity Algorithm 2021

Lifestyle Therapy

myfitnesspal

BARITASTIC

Nutrition

- Patients need to create an energy deficit to promote weight loss ~ 500-750 kcal deficit
- Technological aids- use food tracking apps!
- Patients with Obesity have higher resting/basal metabolic rates so patients should track and reduce total calorie intake by at least 500 kcal to lose ~ 1lb per week
- If you want specific accurate RMR/calorie goals→ Mifflin St Jeor is most reliable in patients with and without obesity and is recommended by the Academy of Nutrition and Dietetics (indirect calorimetry)

Mifflin St. Jeor, 1990	Male: REE = 9.99 × BW + 6.25 × H – 4.92 × A + 5 Female: REE = 9.99 × BW + 6.25 × Ht – 4.92 × A – 161

REE, resting energy expenditure in kcal/day. BW, body weight in kg, H, height in cm, and A, age in years. All equations use actual body weight.

INPUT DATA:

Actual Body Weight	**lb**	0 **kg**		
Height	**ft**	**in**	0 inches tall	0.0 cm tall
Age	**years**		BMI	#DIV/0! kg/m2

Activity Factor	1.1	*Activity Factor: Sedentary = 1.1* *Exercise 60 min 3x/wk = 1.3* *Exercise 60 min 5 or more x/wk = 1.5*

Calculated Basal Metabolic Rate:	
Basal Energy Expenditure (Mifflin)	
Male	5 kcal/day
Female	-161 kcal/day

INITIAL CALORIE TARGET (to achieve 500kcal/day energy deficit):		Carbs (g)	Protein (g)	Fats (g)
		45%	20%	35%
Male Daily Calorie Goal	-495 kcal/day	-56	-25	-19
Female Daily Calorie Goal	-677 kcal/day	-76	-34	-26

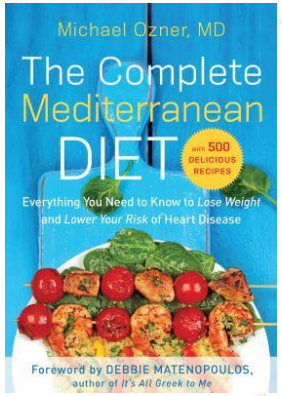
Lifestyle Therapy

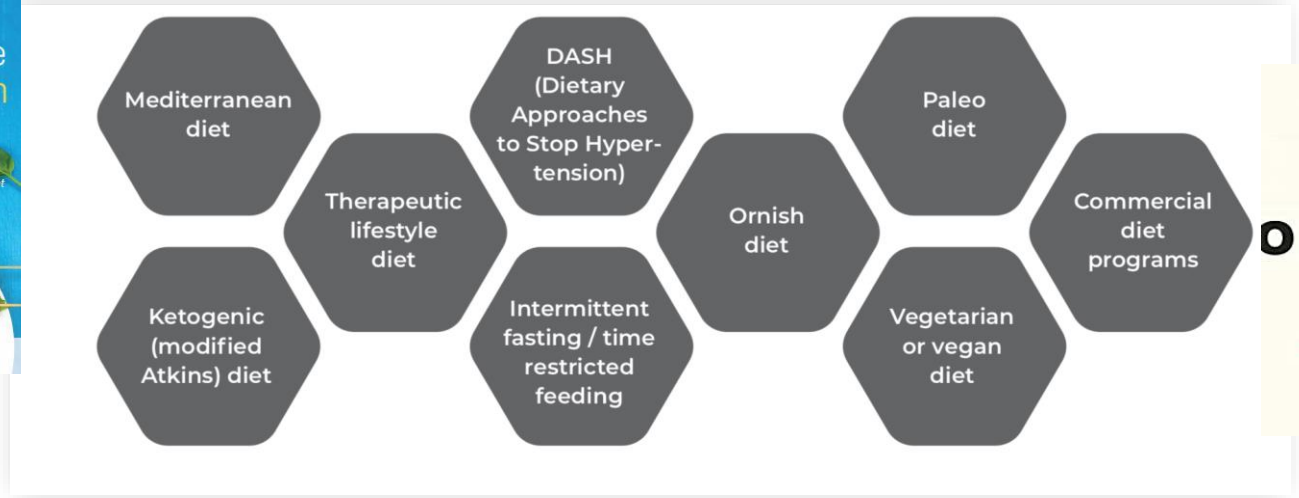
Nutrition: Macronutrients

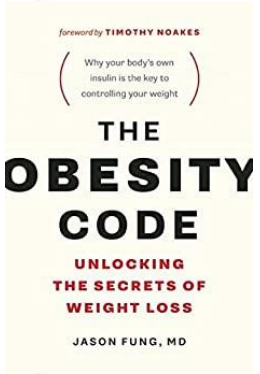
- Protein- satiating, important to preserve muscle mass during weight loss. I try to really maximize this and in general minimize carbs and proteins
  - Need to get at least 20% calories in diet from protein
  - USDA DRI for protein is 0.8-2.0 g/kg/day depending on age, gender and physical activity
- Fats
  - USDA DRI for fat is a least 30g/day
  - Limit saturated fats and avoid trans fat. Choose lean meats without skin
  - Omega 3 and omega 6 fatty acids are essential and cannot be made by our body→ importance of consuming cold water marine fish
- Carbohydrates
  - Includes sugars, starch and fiber
  - Fiber is also satiating so should be emphasized.
  - USDA DRI for carbohydrates is 130 g/day

Lifestyle Therapy

Nutrition







https://www. /a19518210/cures-for-bad-doctors-appoinmenshealth.com/healthtment/

Lifestyle Therapy

Nutrition: Keto diet considerations

- Keto flu
- LDL/ TC
- Hypoglycemia
- Aren’t saturated fats bad?

Lifestyle Therapy

Physical Activity:

AACE 2020

ACSM and CDC Recommendations

150 minutes of moderate-intensity aerobic activity every week

2X per week Muscle-strengthening activities on 2 or more days a week that work all major muscle groups

AMERICAN COLLEGE of SPORTS MEDICINE LEADING THE WAY

Lifestyle Therapy

Physical Activity: Intensity

- Talk test- subjective
- Heart rate
- Perceived effort- subjective, 0-10
- Motion sensors

https://getbackintofitness.com/2018/01/25/wahoo-tickr-x-heart-rate-monitor/

https://www.health.harvard.edu/mind-and-mood/more-evidence-that-exercise-can-boost-mood

- Moderate intensity exercise is a step rate of 100 steps per minute, or 1,000 per 10 minutes
- A common recommendation is to achieve 3,000 steps in 30 minutes
- Vigorous intensity is > 100 steps per minute.

- A percentage of maximal heart rate indicates intensity (%HRmax)
- Moderate intensity exercise is estimated at 65-75 %HRmax
- Vigorous exercise is 76-96 %HRmax
- Target HR = (220-age) x %HRmax

ACSM guidelines

Lifestyle Therapy

Physical Activity Guidelines for Patient's with Obesity

The study built on similar research at McMaster University that showed exercise snacks can lead to meaningful improvements in fitness. In that study, a dozen exercisers raced up three flights of stairs just three times a day for three days a week. After six weeks of these 20-second snacks of exercise, the exercisers had increased their aerobic fitness by about 5 percent. They also showed improvements in leg power and could generate more power while cycling.

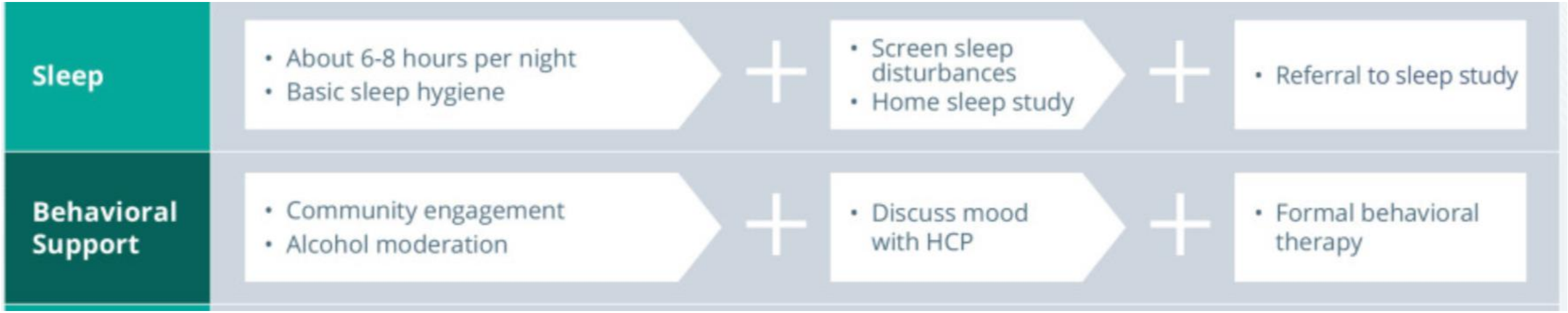
Exercise Snacking: https://www.nytimes.com/2021/01/04/well/move/for-an-exercise-snack-try-the-new-standing-7-minute-workout.html

Lifestyle Therapy

Physical Activity Guidelines for the Patient's with Obesity: Other Considerations

- Prevention of Weight Regain After Weight Loss --→200-300 minutes/week of moderate intensity physical activity
- METABOLIC ADAPTATION!

Lifestyle Therapy



AACE 2020

Medical Therapy: BMI

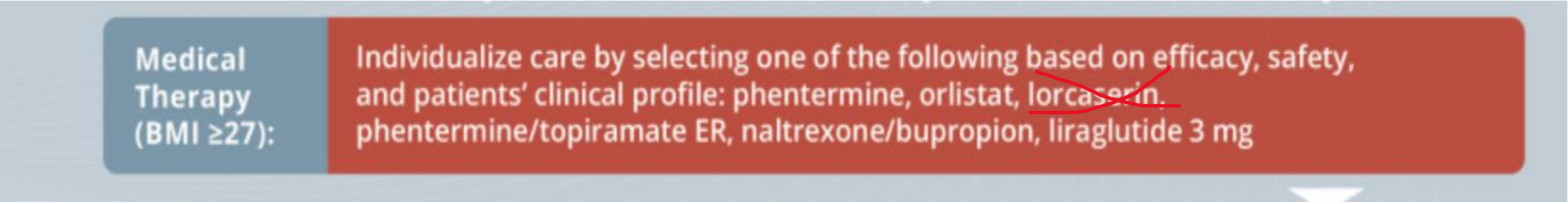
2 Major Components:

1

8.12 When choosing glucose-lowering medications for patients with type 2 diabetes and overweight or obesity, consider the medication's effect on weight. **B**

8.13 Whenever possible, minimize medications for comorbid conditions that are associated with weight gain. **E** ADA-2021

2



AACE 2020

Medical Therapy

Screen for Obesogenic Medications

CNS drugs	Endocrine agents	Miscellaneous
Atypical Antipsychotics eg. olanzipine	**Glucocorticoids** eg. prednisone	**Beta blockers** eg. metoprolol
Anti-epileptics eg.valproate	**Hormonal contraceptives** eg. medroxyprogesterone	**Antihistamines** eg. diphenhydramine
Lithium	**Diabetes agents**	**Sleep aids** eg. zolpidem
Anti-depressants	**Insulin**	
SSRIs eg. paroxetine	**Sulfonylureas** eg. glyburide	
Tricyclic agents eg. nortriptyline	**Thiazolidenediones** eg. pioglitazone,	
Others eg. venlafaxine,mirtazapine		

Leslie, et al. QJM. 2007;100:395-404

Anti-diabetes medications that most promote body weight gain include most insulins, sulfonylureas, thiazolidinediones, and meglitinides

OMA 2021

Medical Therapy: For patients with Diabetes consider starting at BMI of 27 and over

Important notes about Anti-Obesity Agents:

- Similar to SSRI, not every tx works for each person
- Need at least 5% weight loss after 3 months of tx to demonstrate efficacy and to justify ongoing use
- long term tx is required for weight loss maintenance---- >when patients stop their anti-obesity tx weight regain occurs (set-point/metabolic adaptation!!)
- Combining agents like blood pressure lowering or hba1c lowering---> more weight loss combine agents for greater weight loss!!!
- pts on pharmaceutical treatments should be evaluated every 3 months to assess efficacy and safety (JCEM)
- Hypoglycemia

Medical Therapy: Choose Diabetes Agents that are weight neutral or cause weight loss

- Weight loss:
  - Metformin
  - SGLT2i
  - GLP1-RA
  - Pramlintide
- Weight Neutral
  - DPP4i
  - Alpha-glucosidase inhibitors
  - Colesvelam
  - Bromocriptine-QR

PROFILES OF ANTIHYPERGLYCEMIC MEDICATIONS

	MET	GLP1-RA	SGLT2i	DPP4i	AGi	TZD (moderate dose)	SU / GLN	COLSVL	BCR-QR	INSULIN	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/Severe / Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Slight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL / GU	Contra-indicated if eGFR <30 mL/min/ 1.73 m²	Exenatide Not Indicated CrCl <30 Potential Benefit of LA GLP1-RA	Not Indicated for eGFR <45 mL/ min/1.73 m² See #1 Genital Mycotic Infections Potential CKD Benefit; See #1	Dose Adjustment Necessary (Except Linagliptin) Effective in Reducing Albuminuria	Neutral	Neutral	More Hypo Risk	Neutral	Neutral	More Hypo Risk	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CHF CARDIAC ASCVD	Neutral	Neutral Potential Benefit of LA GLP1-RA	Prevent HF Hospitalization Manage HFrEF; See #2 See #3	See #4	Neutral	Moderate May Reduce Stroke Risk	Neutral Possible ASCVD Risk	Neutral Lowers LDL-C	Neutral Safe	CHF Risk Neutral	Neutral
BONE	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate Fracture Risk	Neutral	Neutral	Neutral	Neutral	Neutral
KETOACIDOSIS	Neutral	Neutral	DKA Can Occur in Various Stress Settings	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral

Few adverse events or possible benefits
Use with caution
Likelihood of adverse effects

1. Canagliflozin indicated for eGFR ≥30 mL/min/1.73 m² in patients with CKD 3 + albuminuria.
2. Dapagliflozin—potential primary prevention of HF hospitalization & demonstrated efficacy in HFrEF.
3. Empagliflozin—FDA approved to reduce CV mortality. Canagliflozin—FDA approved to reduce MACE events.
4. Possible increased hospitalizations for heart failure with alogliptin and saxagliptin.

AACE 2020

Medical Therapy: Phentermine

'https://www.freepik.com/photos/people'>People photo created by nakaridore - www.freepik.com

- Sympathomimetic amine
- Controlled substance- state by state restrictions
- Anorexiant/ Central nervous system stimulant
- came out in 1959
- Short-term adjunct (a few weeks) to lifestyle modification- But Obesity is a Chronic disease!!!!
- Individualize tx to get response with lowest effective dose
- Tolerance usually develops within the first month of use
- tablet: 37.5 mg in 1-2 divided doses
- Capsule: 15mg, 30mg- Resin- Absorbed 3x slower rate- often back-ordered at pharmacy
- Tablet 8mg TID- more expensive
- Avoid in patients with any hx of substance abuse

Medical Therapy: Phentermine

- Administer before breakfast or 1-2 hours after, 8mg tabs- 30 min before meals, avoid late evening dosing
- Tablets are scored- typically I will prescribe 37.5mg tablet so patients can break tablet to save money. Pt's can take ½ tab daily in AM
- Dosing Hepatic Impairment: no dose adjustments/ has not been studied (Willson C et al- Toxicology reports 2019- no hepatotoxicity)
- Dosing Renal Impairment:
  - eGFR ≥30 mL/minute/1.73 m^2: There are no dosage adjustments provided in the manufacturer's labeling; systemic exposure may be increased; use with caution.
  - eGFR 15 to 29 mL/minute/1.73 m^2: Maximum dose: 15 mg/day.
  - eGFR <15 mL/minute/1.73 m^2: Avoid use (has not been studied).
  - End-stage renal disease (ESRD) requiring dialysis: Avoid use (has not been studied).

Medical Therapy: Phentermine

Contraindications:

- “Hypersensitivity or idiosyncrasy to phentermine, other sympathomimetic amines or any component of the formulation; history of cardiovascular disease (eg, arrhythmias, heart failure, coronary artery disease, stroke, uncontrolled hypertension); hyperthyroidism; glaucoma; agitated states; history of drug abuse; use during or within 14 days following MAO inhibitor therapy; pregnancy; breast-feeding” – UptoDate

Medical Therapy: Phentermine

- Long term use/ off-label use

Safety and Effectiveness of Longer-Term Phentermine Use: Clinical Outcomes from an Electronic Health Record Cohort

Kristina H. Lewis [1,2], Heidi Fischer[3], Jamy Ard [1], Lee Barton[3], Daniel H. Bessesen[4], Matthew F. Daley[5], Jay Desai[6], Stephanie L. Fitzpatrick[7], Michael Horberg[8], Corinna Koebnick[3], Caryn Oshiro[9], Ayae Yamamoto[3], Deborah R. Young[3], and David E. Arterburn[10]

Medical Therapy: Phentermine

- Retrospective study
- EHR- 13972 patients from 2010-2015 on phentermine 15-37.5mg
- On-label use (12 weeks) vs. off-label use
- Compared % wt loss and risk of CVD or death 3 years after being on phentermine
- Results:
  - Wt loss was higher in the off-label group vs. short term use
  - Rare CVD or death (41 events/ 13972= 0.3%)
  - Longer term phentermine group had lower SBP

Medical Therapy: Phentermine

- Studies using modified cocaine craving and amphetamine withdrawal questionnaires
- No abuse or psychological dependence
- No amphetamine-like withdrawal
- No phentermine drug cravings

Published: 17 May 2013

Addiction potential of phentermine prescribed during long-term treatment of obesity

E J Hendricks, M Srisurapanont, S L Schmidt, M Haggard, S Souter, C L Mitchell, D G De Marco, M J Hendricks, Y Istratiy & F L Greenway

International Journal of Obesity **38**, 292–298(2014)

A Study of Abrupt Phentermine Cessation in Patients in a Weight Management Program

Hendricks, Ed J MD[1*]; Greenway, Frank L MD[2]

American Journal of Therapeutics: July 2011 - Volume 18 - Issue 4 - p 292-299

Medical Therapy: Qsymia(phentermine/topiramate)

- Mechanism of Action:
  - stimulates the sympathetic nervous system (noradrenergic and dopaminergic)
  - topirmate is neurostablizer -? reduces appetite, Dopaminergic (reward), metabolic benefits

- Contraindications: Pregnancy (REMS), glaucoma, hyperthyroidism, use of MOAi within 14 days, similar to phentermine BUT--->ok in patients with CVD, T2DM with mild congestive cardiomyopathy
- Side effects: dry mouth, dysgeusia, constipation, insomnia,
- Other notes:
  - Controlled substance
  - paresthesia, hypokalemia with non-potassium-sparing diuretics

Doses = Once daily in the morning with or without food

– Starting dose = 3.75 mg/23 mg (phentermine/topiramate extended release)

– After 14-day intervals, and as clinically indicated, escalate doses to:

- Recommended dose = 7.5 mg/46 mg
- Titration dose = 11.25 mg/69 mg
- Top dose = 15 mg/92 mg

– Gradually wean dose from the top dose (15 mg/92 mg) to help avoid potential seizures

Obesity Algorithm 2021-OMA

Medical Therapy: Contrave (bupropion/naltrexone)

- Mechanism of action:
  - Bupropion is dopaminergic which stimulates fullness by acting on neurons that control appetite
  - Naltrexone- opioid receptor blocker: our hunger neurons attach to opioid receptors on our fullness neurons so basically naltrexone block these signals in order to potentiate fullness
- Contraindications: seizure, Aug 2020 pregnancy was removed as contraindication, use of MAOi within 14 days, chronic opioid use, uncontrolled HTN
- Side effects:
- constipation, h/a, nausea, dry mouth
- Other Notes:
  - I usually prescribed Bupropion prescribe separately with naltrexone (bupropron xl 150mg AM to titrate up to 300mg with naltrexone 50mg take ½ tab nighty) Or bupropion SR 150mg BID with naltrexone 25mg. Contrave the brand is 2 tabs BID- compliance is an issue!

Medical Therapy: Saxenda/liraglutide

- Mechanism of action:
  - GLP-1 agonists stimulate fullness neurons via vagus nerve to brain
  - slow gut motility-→ fullness
- Contraindications: personal or family hx of medullary thyroid carcinoma or MEN 2, pregnancy
- Side effects: NAUSEA, HYPOGLYEMIA WITH INSULIN

Dosing:

– Week 1 = 0.6 mg per day
– Week 2 = 1.2 mg per day
– Week 3 = 1.8 mg per day
– Week 4 = 2.4 mg per day
– Week 5 and onward = 3.0 mg per day

Slower dose titration may improve tolerability and gastrointestinal side effects

Novonordisk announced May 13/20 results from the first completed phase 3 trial:

"Semaglutide 2.4 mg demonstrates superior and sustained weight loss versus placebo and in addition a 17.4% weight loss after 68 weeks"

Medical Therapy: Orlisat

- Mechanism of action:
  - Blocks fat aborption
  - No appetite effect
- Contraindications: chronic malabsorption syndrome or cholestasis
- Side effects: oily discharge from rectum, flatus with discharge, increased defecation, fecal incontinence
- Other notes: increased risk of cholelithiasis, kidney stones, worse s/e with higher fat diet, need for MVI with fat-soluble vitamins

Dose = One 120-mg capsule three times a day with each main meal containing fat (during or up to 1 hour after the meal)

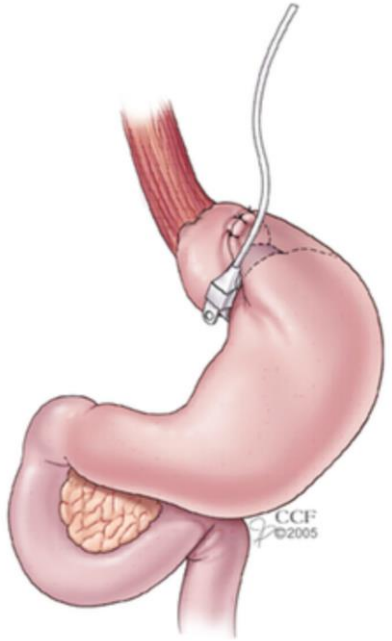
An over-the-counter formulation is available at 60 mg capsule with each meal containing fat

Obesity Algorithm 2021-OMA

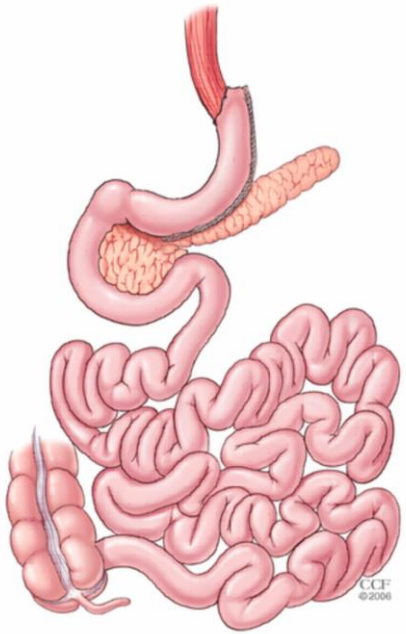
Surgical Therapy

Surgical Therapy (BMI ≥35):	Endoscopic procedures, gastric banding, sleeve, or bypass

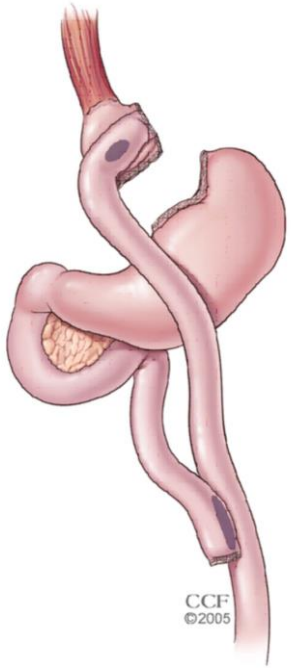
AACE 2020



Gastric banding



Gastric Sleeve



Gastric Bypass

https://asmbs.org/

ASMBS American Society for Metabolic and Bariatric Surgery

Surgical Therapy: Bariatric Surgery is a Metabolic Surgery!!!

Impact of Metabolic Surgery on Diabetes

- Meta-analysis of more than 135,000 metabolic surgery patients (mean BMI 47.9) in 621 studies (1990-2006) found 86.6% of those with type 2 diabetes experienced improvement or remission, and overall average excess weight loss (EWL) was 59.9% (American Journal of Medicine, 2009)[11]
- JAMA Surgery meta-analysis of nearly 162,000 patients with obesity (mean BMI 45.6) in 164 studies (2003-2012) shows of those with type 2 diabetes (26.2%) who had metabolic surgery, improvement or remission was achieved by:[12]
    - 92% of patients in randomized controlled trials (mean EWL 57%)
        - 95.1% gastric bypass; 73.8% gastric banding; N/A sleeve gastrectomy; 17.6% nonsurgical
    - 86% of patients in observational studies (mean EWL 46%)
        - 92.8% gastric bypass; 67.5% gastric banding; 85.5% sleeve gastrectomy; N/A nonsurgical

Surgical Therapy: Bariatric Surgery is a Metabolic Surgery!!!

Metabolic Surgery vs. Medical Therapy

- Randomized clinical trials have demonstrated that metabolic surgery is more effective than medical and/or lifestyle interventions including pharmacological therapy in producing diabetes remission, glycemic control, and weight loss
  - Final five-year results of the Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiency (STAMPEDE) Study show in patients with uncontrolled type 2 diabetes (mean BMI 37), metabolic surgery plus intensive medical therapy was more effective than intensive medical therapy alone for achieving and maintaining glycemic control, weight reduction, medication reduction, and improvements in lipid levels (NEJM, 2017)[13,14,15]
    - Diabetes remission rates at years one, three and five with metabolic surgery were about 40% (42% gastric bypass; 37% sleeve gastrectomy), 31% (38% gastric bypass; 24% sleeve gastrectomy), and 26% (29% gastric bypass; 23% sleeve gastrectomy), respectively; compared to 12%, 5% and 5% for medical therapy
  - Diabetes remained in remission for up to two years in 85% of patients with a BMI of 35 or greater randomized to metabolic surgery compared to no medical therapy patients (NEJM, 2012)[16] – 50% remission rates for metabolic surgery at 5 years and zero for medical therapy[17]

Surgical Therapy: Bariatric Surgery is a Metabolic Surgery!!!

Long-Term Results with Metabolic Surgery

- Among patients with type 2 diabetes who had metabolic surgery, 24% experienced complete, long-term remission – five years or more – of their diabetes; 26% experienced partial remission and 34% improved from baseline; mean excess weight loss was 55% (Annals of Surgery, 2013)[18]
- Six years after metabolic surgery, 62% of gastric bypass patients with severe obesity (mean BMI 45.9) experienced diabetes remission compared to only 6-8% in control groups (JAMA, 2012)[19]
  - Surgery patients lost an average of 27.7% of their initial body weight compared with 0.2% in controls
- Fifteen years after metabolic surgery, 30.4% of patients maintained remission of their diabetes, compared to 6.5% of control patients (JAMA, 2014)[20]

Summary: Take home

- Treatment of obesity and diabetes is multifaceted
- Consider the implications of weight gain with any medications you prescribe for these patients. PLEASE AVOID GABAPENTIN!
- Utilize your ”toolbox” of anti-obesity agents for patients with diabetes and BMI of 27 and over
- Avoid sugary beverages, refined CHO and trans-fats. Limit saturated fats. Maximize daily protein for satiety- protein with each meal and snack
- Exercise Snacking/ at least 5000 steps per day
- Screen for depression and sleep apnea
- Please consider metabolic surgery for patients with diabetes and BMI 35 and over!!!

THANK YOU!!

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QUESTIONS?