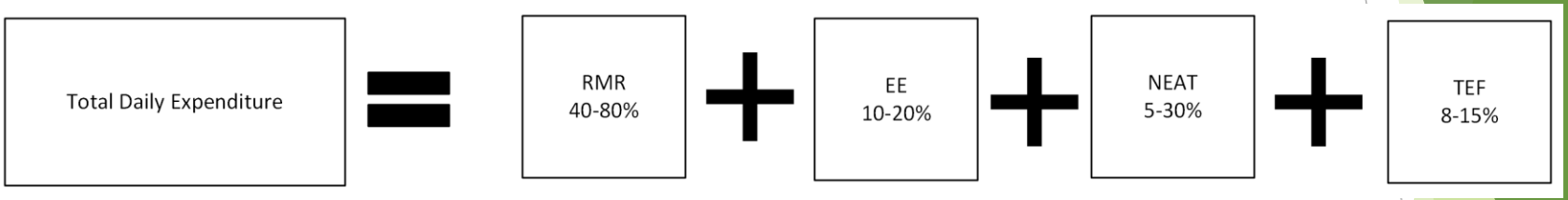
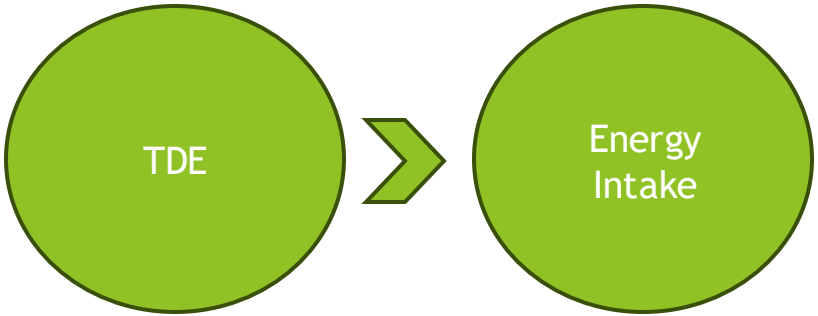
Obesity Medicine Approach

Part 2: Treatment

Nutrition, Physical Activity and Medications

Foundation of Energy Balance





Nutrition

What is a calorie

Amount of heat required to raise the temp of 1g of H2O by 1C (14.5 to 15.5)

Measure of energy

1C = kcal = 1000 cal

Macronutrients

Carbohydrates

- 4 kcal/gram
- RDA 130g

Protein

- 4kcal/gram
- RDA 56g-Males 46g-Females
- Wt Maint – 0.7-1gm/kg
- Wt loss – 1.2-1.5g/kg

Fats

- 9kcal/gram
- RDA omega6=7-17g
- RDA omega3 = 0.5-1.6g

Alcohol

- 7kcal/gram

Micronutrient def post surgery

- Thiamine (B1)
  - Wet and dry beriberi
- Cyanocobalamin (B12)
  - Pernicious anemia
  - Subacute combined degeneration of the spinal cord
- Iron
  - Check ferritin
  - All bariatric patients on a multivitamin with Iron
  - 20-30% will need parenteral
- Vitamin D
  - Osteomalacia, fatigue
  - So common because a fat soluble vitamin

Others to know about

- Vitamin A
- Vitamin C
- Copper
- Vitamin K
- Vitamin E
- Zinc
- *consider anatomy and where nutrients are absorbed based on the procedure done

Sites of nutrient absorption

- Duodenum
  - Iron
  - Calcium
  - Received food, bile and digestive enzymes, neutralizes stomach acid
- Jejunum
  - Carbs, amino acids, vitamins, K
  - Absorbs iron and Ca in upper portion
- Ileum
  - Water, K, minerals, salts, fats, remaining nutrients
- Colon
  - Vitamin K, Biotin, B12, thiamine, riboflavin, water, Na, Cl
  - Secretes K and Bicarb

Nutrition Plans

Nutrition Types

Calorie Restricted	Balanced deficit diet Meal replacements are a type of calorie restriction
Timing	Intermittent – 16-18h or longer (24-72+) ADF (5/2)
Macronutrient Driven	High protein, low carb and fat usually Restricting certain nutrients (Keto)
Glycemic Index	Limit foods with high glycemic index or high glycemic load Proven for weight maintenance

Balanced

- Calorie intake usually 800-1800 cal/day
- I use BMR * 0.8 and round to get calorie goal
- Then use height and ref weight to calculate protein intake (this is just a chart)
- Calculate rest of macronutrients from there
- Typically 35% protein, 30% fat, 30-35% carb
- Use DM exchange list for meal planning

4’11”	111-123	69-96
5’0	113-126	69-96
5’1	115-129	69-96
5’2	118-132	69-96
5’3	121-135	69-102
5’4	124-138	69-102
5’5	127-141	70-108
5’6	130-144	70-111
5’7	133-147	72-111
5’8	136-150	72-114
5’9	139-153	75-116
5’10	142-156	76-120
5’11	145-159	78-123
6’0	148-162	80-125

- Womens reference weight and protein goals by height
- Reference weight should not be a goal weight

5’2	131-140	69-108
5’3	133-143	70-110
5’4	135-145	72-111
5’5	137-148	74-112
5’6	139-151	74-115
5’7	142-154	75-118
5’8	145-157	78-122
5’9	148-160	80-123
5’10	151-163	81-125
5’11	154-166	83-129
6’0	157-170	86-132
6’1	160-174	87-134
6’2	164-178	89-136
6’3	167-182	91-138
6’4	171-187	93-140

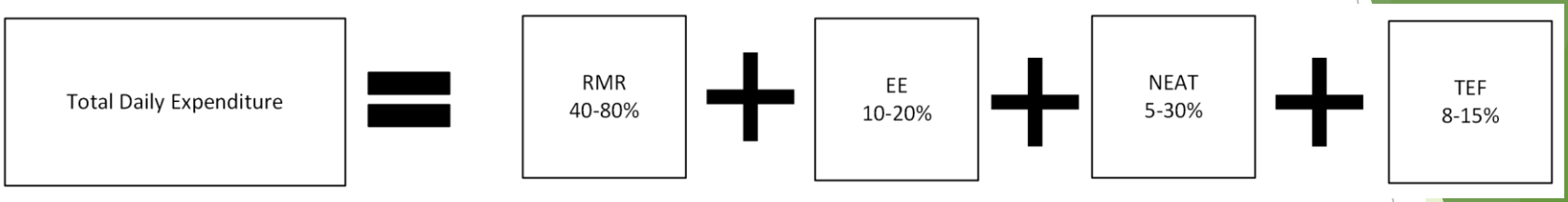
Mens reference weights and protein goals by height

Very Low Carb

- No evidence <30g better than <50g
- No external glucose load → use fat to make glucose (ketogenesis)
- Can follow plan (keto, atkins, etc) or just eat under 50g
- Watch drinks
- NET CARBS ARENT REAL – they are a calculated tool that can be used but know what they are tracking and goals

Meal Replacement

- Very low calorie diet - typically under 800 cal
- Protein 75-105g; carbs 50-100g; fat 10-20g
- “protein sparing modified fast”
- Have to watch electrolytes, gallstones
- Best evidence in studies → no human error



- Thermal Effect of Food – whole food takes more to digest
- Very low calorie will often cause a natural decline in NEAT (unconscious NEAT)
- Nutrition is impacting the other side of the equation (Energy Intake)

Nutrition Impacts

Physical Activity

Physical Activity

- Physical activity is any movement (EE+NEAT)
- Exercise is a planned activity
- Increases total blood volume, ventricular compliance, venous return, EF, stroke volume, cardiac output
- Reduces risk of CVD, cancers more than any other intervention (90mins/week)

Physical Activity Guidelines

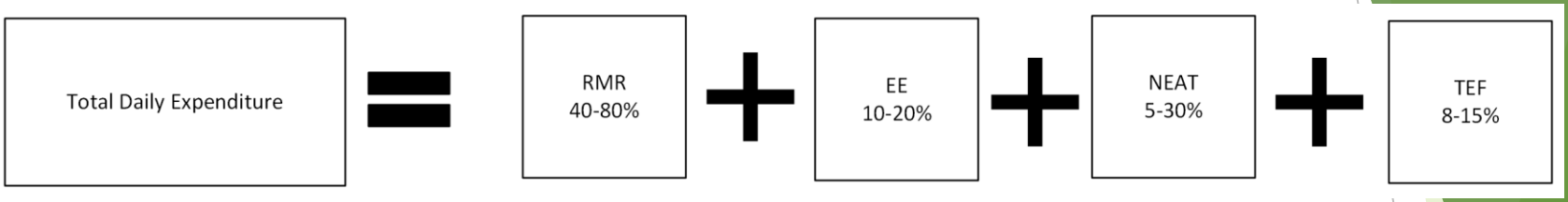
MUSCLE STRENGTHENING 2 OR MORE DAYS PER WEEK

ADULTS – AT LEAST 150 – 300 MINS A WEEK OF MODERATE INTENSITY, OR 75 -150 MINS A WEEK OF VIGOROUS INTENSITY AEROBIC PHYSICAL ACTIVITY

Physical Activity Rx

- (F)requency
- (I)ntensity
- (T)ime
- (T)ype
- (E)njoyment

- (S)pecific
- (M)easurable
- (A)ttainable
- (R)ealistic
- (T)ime oriented



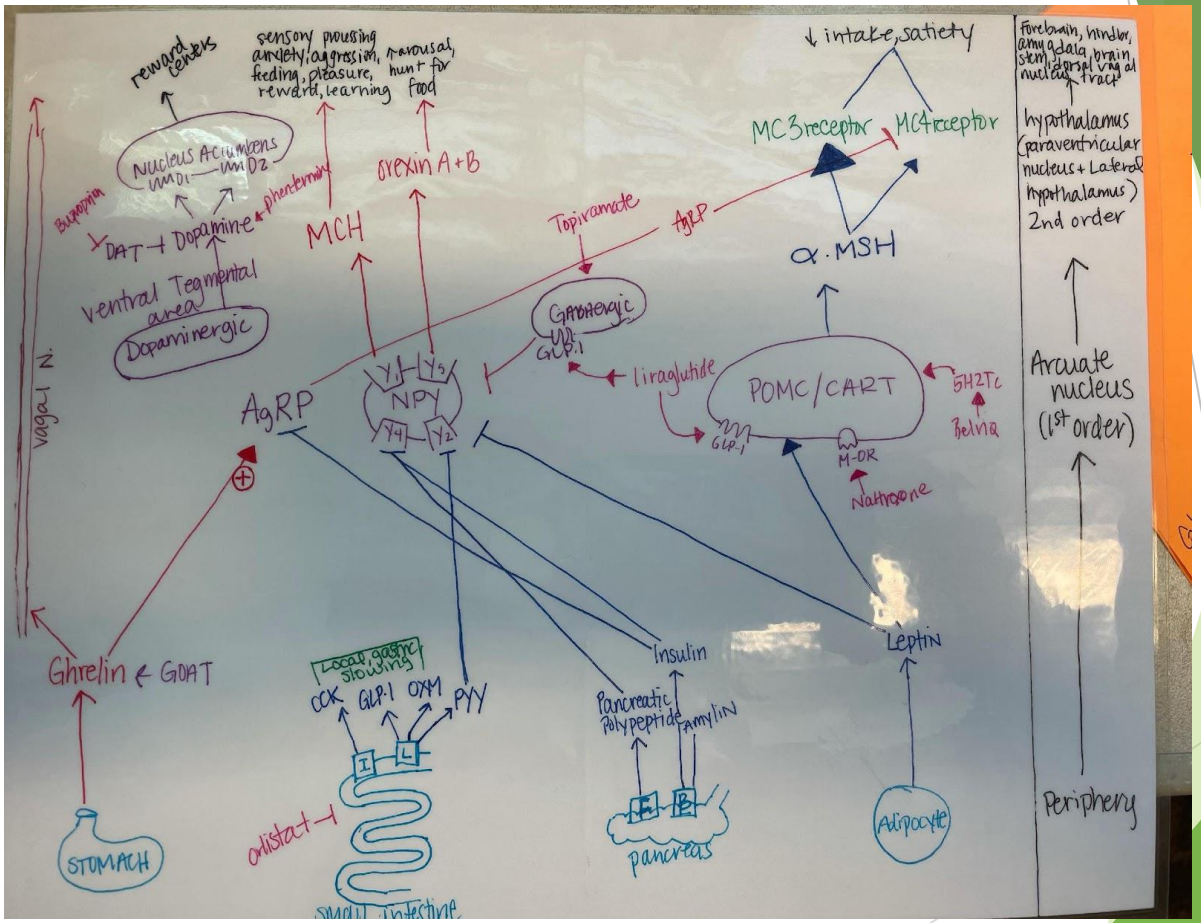
- EE – watch calorie trackers – overestimate by about 30%
- NEAT – trackers can be helpful (10,000 steps)
- RMR – indirectly affected by creation of muscle from exercise

Physical Activity Impacts

Medications

Why use medications?

- Weight loss causes a complex set of neuroendocrine adaptations that become more intense with greater weight loss. These work to slow, and eventually halt weight loss and may induce weight gain
- Pts who have lost weight find it very difficult to resist neuroendocrine physiology with diet and behavior modification alone
- Anti-obesity Medications (AOM) help offset the physiologic adaptations that resist weight loss and promote weight gain


reward centers
sensory processing anxiety, aggression, arousal, feeding, pleasure, reward, learning, hunt for food
↓ intake, satiety
Nucleus Accumbens
D1
D2
Bupropion
DAT
Dopamine
Phentermine
MCH
Orexin A+B
MC3receptor
MC4receptor
Topiramate
AgRP
α-MSH
Ventral Tegmental area
Dopaminergic
GABAergic
GLP-1
Liraglutide
Y1
Y5
NPY
Y4
Y2
POMC/CART
5HT2C
Belviq
GLP-1
M-OR
Naltrexone
Vagal N.
AgRP
Ghrelin ← GOAT
Local gastric slowing
CCK
GLP-1
OXM
PYY
I
L
Orlistat
Insulin
Pancreatic Polypeptide
Amylin
A
B
pancreas
Leptin
Adipocyte
STOMACH
small intestine
Forebrain, midbrain, amygdala, brain stem, dorsal vagal nucleus, tract
hypothalamus (paraventricular nucleus + Lateral hypothalamus)
2nd order
Arcuate nucleus (1st order)
Periphery

- Short Term – phentermine (12w), diethylpropion, phendimetrazine
- Long Term – Orlistat, Qsymia, Contrave, Saxenda, Wegovy, Zepbound

FDA approvals

Barriers to the use of AOM

- Perception that obesity is a disorder of willpower
- Failure to perceive obesity as a chronic incurable disease that requires lifelong intervention has resulted in perception that weight regain after stopping meds is due to failure of the med
- Regulatory bodies (FDA, etc)
- Inadequate funding for clinical work in obesity
- Lack of medication coverage by health plans

Meds FDA approved short term

- Sympathomimetics
  - Phentermine
  - Diethylpropion
  - Phendimetrazine

Phentermine

+	• Increased hunger • Low BMR	**Mechanism of Action:** -inhibits Na-dependent NE transporter, reduces NE uptake -inhibits serotonin and dopamine reuptake
CI	• Active CVD • Poorly controlled HTN • Hyperthyroidism • glaucoma	**Dosing** -15-30mg caps, 37.5mg tab QD-BID -8mg TID
AE	• Dry mouth • Constipation • Insomnia • Palpitations • HA • irritability	**Advice/precautions** -schedule IV controlled subtance -monitor BP, be aware of caffeine intake -NO evidence of addiction, withdrawal -NO established relationship to cardiac valvulopathy or pHTN

FDA approved for long term use

Orlistat

- Xenical (1999)
- Alli (2007)

Bupropion/Naltrexone ER

- Contrave (2014)

Phentermine/Topirimate ER

- Qsymia (2012)

GLP1s

- Saxenda (liragutide- 2014)
- Wegovy (semaeglutide – 2021)
- Zepbound (tirzepatide –2024)

Orlistat

+	• Hyperlipidemia • Low risk med	**Mechanism of Action:** -pancreatic lipase inhibitor – blocks about 30% of fat intake
CI	• Cholestasis • Chronic malabsorption syndrome	**Dosing** -start: 120mg daily Range – 120mg/d - 120mg TID Alli is OTC and 60mg
AE	• Flatulence • Diarrhea • Bloating • Cramping • Abdominal pain • Inc urinary oxalate • Fat soluble vitamin deficiency	**Advice/precautions** -advise daily multivitamin -monitor fat-soluble vitamins (ADEK) -decrease levels of cyclosporine if co-administered -no casual relationshup with liver failure

Phentermine/Topirimate ER - QSYMIA

+	• Increased hunger • Mile SE with phentermine • Non child bearing	**Mechanism of Action:** -inhibits Na-dependent NE transporter, reduces NE uptake -inhibits serotonin and dopamine reuptake -TOP: AMPA, GABA receptor – decreases cravings
CI	• Active CVD • Poorly controlled HTN • Hyperthyroidism • Glaucoma • Kidney stones • During or within 1d of MAOI	**Dosing** -start 3.75/23mg x14d then 7.5/46mg Range: 3.75/23mg - 15/92mg/d
AE	• Dry mouth, constipation, HA, palps, insomnia • Paresthesias, dysgeusia, somnolence, cognitive impairement	**Advice/precautions** -schedule IV controlled subtance -monitor BP, be aware of caffeine intake -rule out pregnancy before starting -increase hydration -1/4c lemon/lime juice for paresthesias

Bupropion/Naltrexone ER (Contrave)

+	• Increased hunger and cravings • Patients who smoke • On bup already	**Mechanism of Action:** -reuptake inhibitor DA and NE activity increases POMC -Naltrexone blocks B-endorphin, POMC autoinhibitor
CI	• seizures • Poorly controlled HTN • bulimia • Chronic opioid use	**Dosing** -90mg/8mg caps -I cap x1w, 1 BID x1w, 2qAM, 1PM x1w then 2 BID
AE	• Neuropsychiatric rxns, suicidal thoughts and behavior • Nausea • HA • Insomnia • Dizziness • Dry mouth	**Advice/precautions** -avoid opioids – ask about surgery -results of LIGHT trial (2017) do not show reduction in CV events -avoid in high fat diet (increases bioavailability)

Liraglutide (Saxenda)

+	• DM or preDM • Pts wit insurance coverage	**Mechanism of Action:** -GLP1 receptor agonist -increases satiety, decreases gastric emptying -97% homologous to human GLP1
CI	• Medullary thyroid Ca (incl fam hx) • MEN type II • Hx pancreatitis	**Dosing** -start 0.6mg subq daily, titrate to 3mg daily
AE	• Nausea • HA • Pancreatitis • Hypoglycemia if used with other DM agents	**Advice/precautions** -nausea may improve with time -NO data to support increased risk of pancreatic cancer -generic liraglutide now available

Semaglutide (Wegovy)

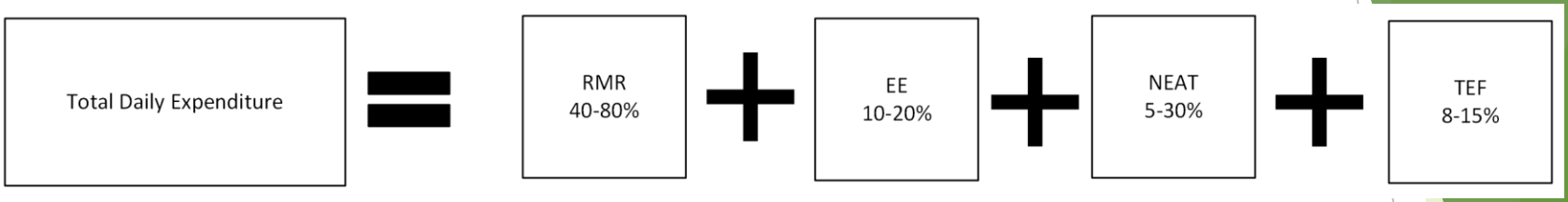
+	• DM or preDM • CVD/PAD • CKD • Pts wit insurance coverage	**Mechanism of Action:** -GLP1 receptor agonist once weekly -increases satiety, decreases gastric emptying -97% homologous to human GLP1
CI	• Medullary thyroid Ca (incl fam hx) • MEN type II • Hx pancreatitis	**Dosing** -start 0.25mg weekly, titrate up after at least 4 doses
AE	• Nausea • HA • GERD • Pancreatitis • Hypoglycemia if used with other DM agents	**Advice/precautions** -nausea may improve with time -discuss smaller meal portions

Wegovy at dose 2.4mg/week (packet insert)

	Study 1 (Obesity or overweight with comorbidity)		Study 2 (Type 2 diabetes with obesity or overweight)		Study 3 (Obesity or overweight with comorbidity undergoing intensive lifestyle therapy)	
Intention-to-Treat[a]	PLACEBO N = 655	WEGOVY N = 1306	PLACEBO N = 403	WEGOVY N = 404	PLACEBO N = 204	WEGOVY N = 407
Body Weight						
Baseline mean (kg)	105.2	105.4	100.5	99.9	103.7	106.9
% change from baseline (LSMean)	-2.4	-14.9	-3.4	-9.6	-5.7	-16.0
% difference from placebo (LSMean) (95% CI)		-12.4 (-13.3; -11.6)*		-6.2 (-7.3; -5.2)*		-10.3 (-11.8; -8.7)*
% of Patients losing greater than or equal to 5% body weight	31.1	83.5	30.2	67.4	47.8	84.8
% difference from placebo (LSMean) (95% CI)		52.4 (48.1; 56.7)*		37.2 (30.7; 43.8)*		37.0 (28.9; 45.2)*
% of Patients losing greater than or equal to 10% body weight	12.0	66.1	10.2	44.5	27.1	73.0
% difference from placebo (LSMean) (95% CI)		54.1 (50.4; 57.9)*		34.3 (28.4; 40.2)*		45.9 (38.0; 53.7)*
% of Patients losing greater than or equal to 15% body weight	4.8	47.9	4.3	25.1	13.2	53.4
% difference from placebo (LSMean) (95% CI)		43.1 (39.8; 46.3)*		20.7 (15.7; 25.8)*		40.2 (33.1; 47.3)*

Tirzepatide (Zepbound)

+	• DM or preDM • OSA • Pts wit insurance coverage	**Mechanism of Action:** -GLP1 and GIP receptor agonist -increases satiety, slows gastric emptying
CI	• Medullary thyroid Ca (incl fam hx) • MEN type II • Hx pancreatitis • Suicide attempt	**Dosing** -start 2.5mg weekly, titrate after 4w at each dose
AE	• Nausea • HA • Pancreatitis • Hypoglycemia if used with other DM agents	**Advice/precautions** -nausea may improve with time



- Energy Intake decrease

Medication Impacts

Other things that affect the equation

- RMR: MUSCLE!!!! When muscle mass in controlled for, RMR does not change drastically with age or gender
- RMR: caffeine, supplements (fish oil) can increase but often give you acute increase and if you don't use that energy it will compensate and decrease
- RMR: SLEEP!!!! Huge chronic part of the equation
- TEF: The way you prepare food