Expanding the Toolbox: Integrating Pharmacotherapy and Bariatric Surgery

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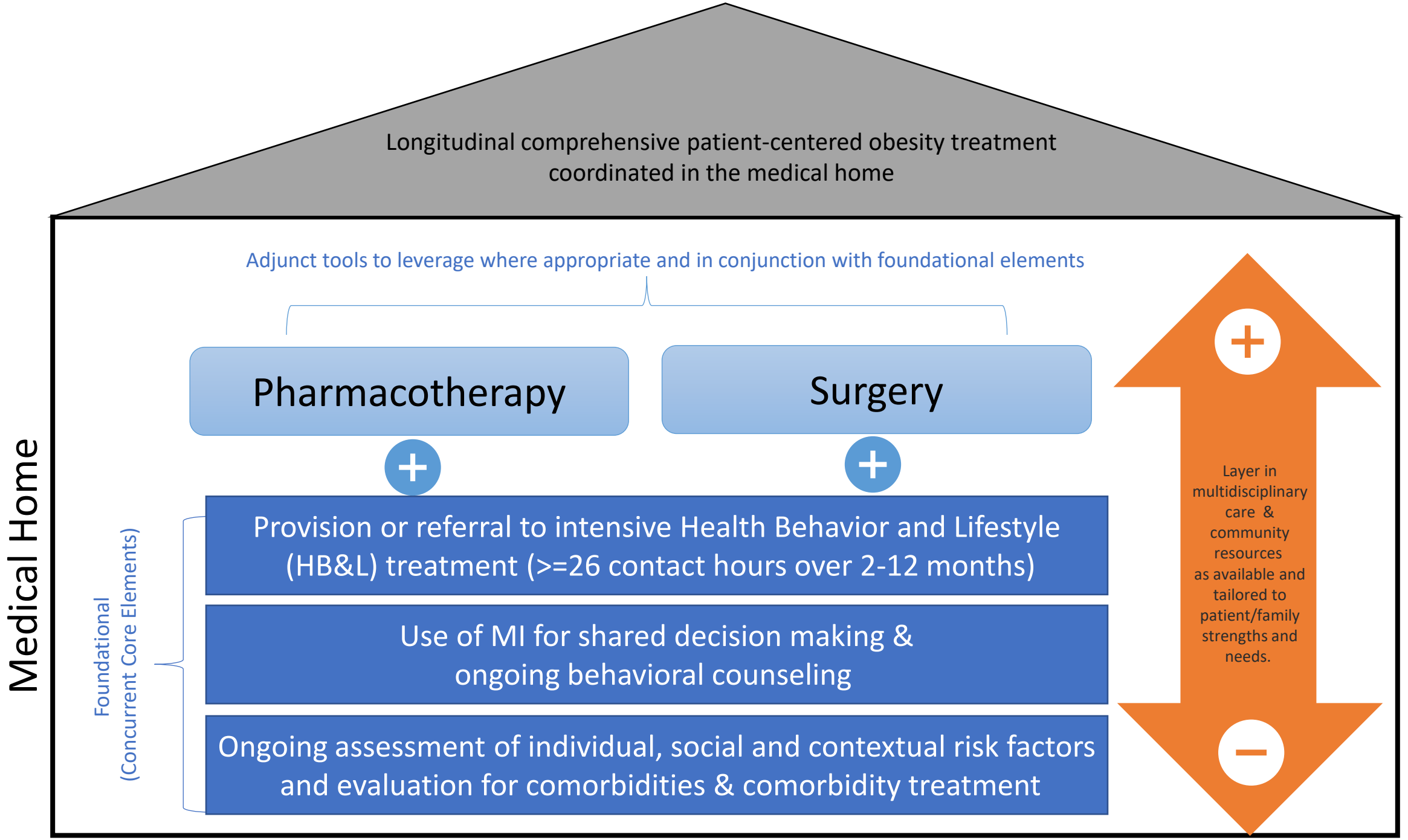
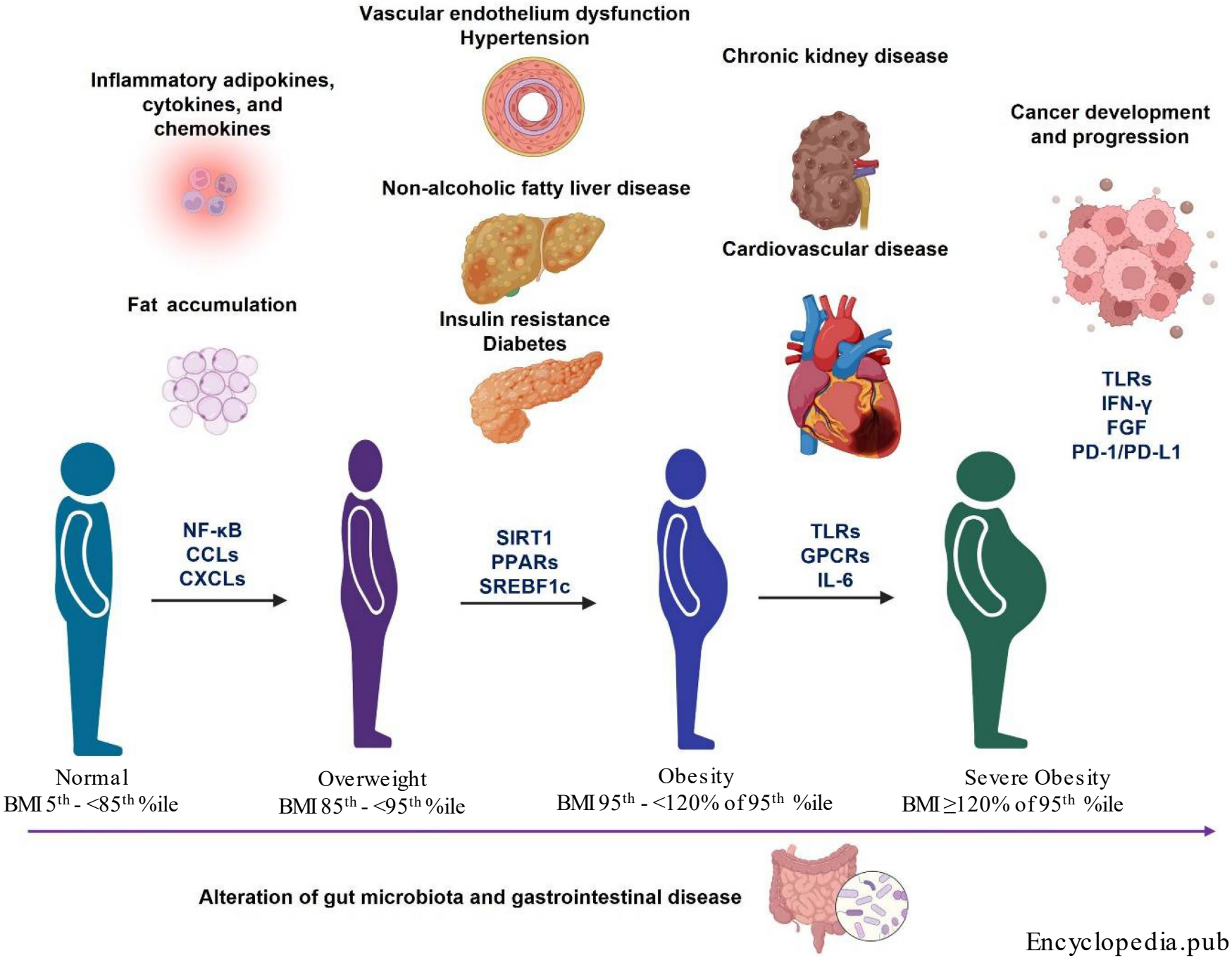
Objectives

- Identify medications that are FDA-approved for treatment of adolescents with obesity
  - Indications, prescribing, side effects, and outcomes
- Identify patients who may benefit from addition of medication to their lifestyle treatment
- Recognize indications for bariatric surgery in adolescents and refer to a pediatric program
  - Candidate selection, referral, preparation, and follow-up


Longitudinal comprehensive patient-centered obesity treatment coordinated in the medical home
Medical Home
Adjunct tools to leverage where appropriate and in conjunction with foundational elements
Pharmacotherapy
Surgery
+
+
Foundational (Concurrent Core Elements)
Provision or referral to intensive Health Behavior and Lifestyle (HB&L) treatment (>=26 contact hours over 2-12 months)
Use of MI for shared decision making & ongoing behavioral counseling
Ongoing assessment of individual, social and contextual risk factors and evaluation for comorbidities & comorbidity treatment
+
Layer in multidisciplinary care & community resources as available and tailored to patient/family strengths and needs.
−

Obesity is a metabolic disease that impacts dozens of tissues and organ systems

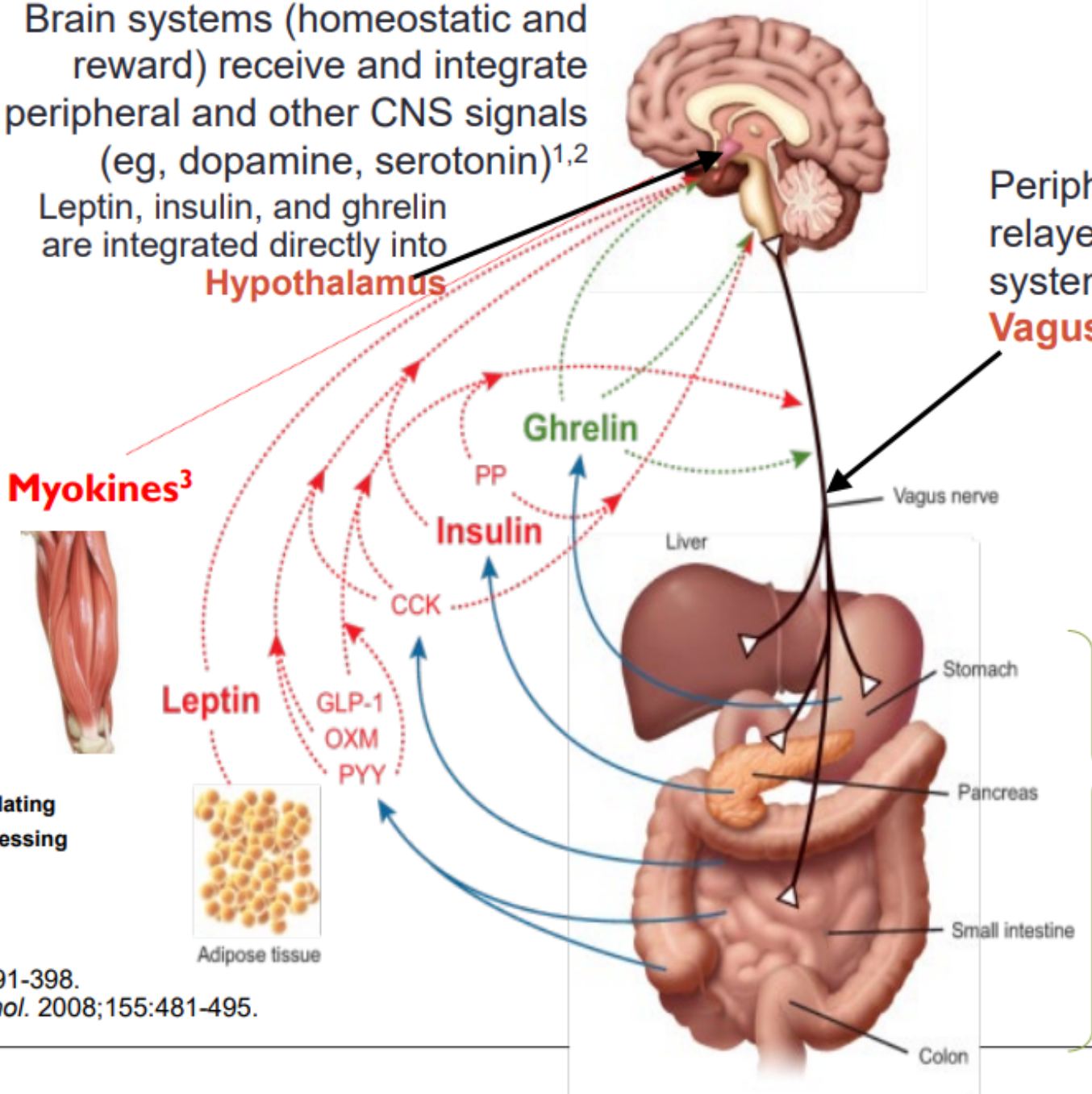


Complex Peripheral Signals are Integrated Into CNS Systems to Regulate Body Weight

Brain systems (homeostatic and reward) receive and integrate peripheral and other CNS signals (eg, dopamine, serotonin)[1,2]

Leptin, insulin, and ghrelin are integrated directly into **Hypothalamus**

Peripheral signals are relayed to brain systems via blood and **Vagus Nerve** [1,2]



Peripheral signals are released by pancreas, gastrointestinal system, and adipose tissue[1,2]

CNS, central nervous system
PfC, prefrontal cortex
NAc, nucleus accumbens
VTA, ventral tegmental area
PP, pancreatic polypeptide
CCK, cholecystokinin;
GLP-1, glucagon-like peptide 1
OXM, oxyntomodulin
PYY, peptide YY.
Primarily based on data from animal studies.

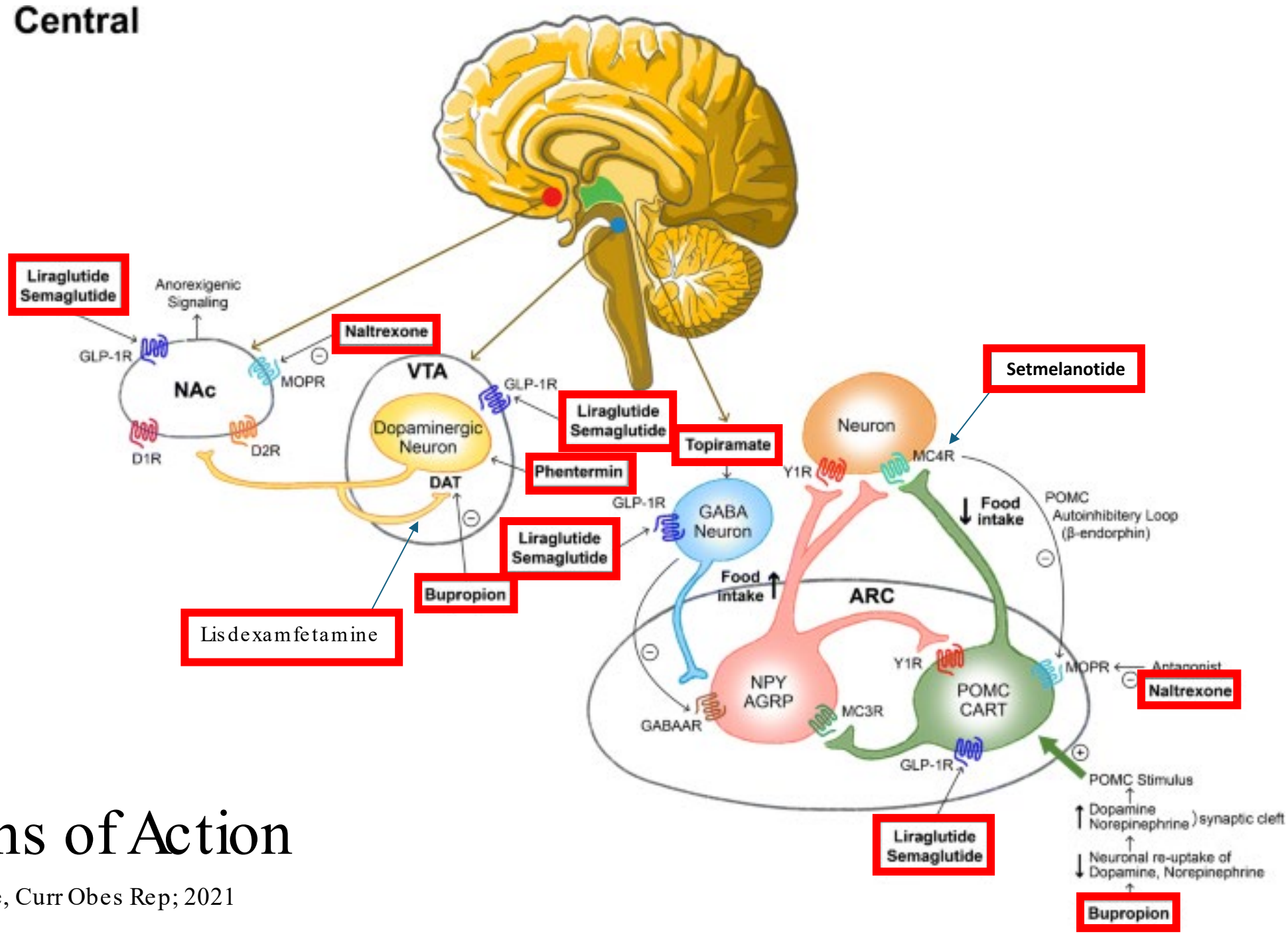
Appetite Stimulating
Appetite Suppressing

1. Yu JH et al. *Diabetes Metab J*. 2012;36(6):391-398.
2. Mendieta-Zerón H et al. *Gen Comp Endocrinol*. 2008;155:481-495.
3. Grannell A, et al. Muscles 2022, 1, 26–47.

Weight regulation occurs through a complex set of pathways

Many different opportunities for medicine and drug development

Overview:
Mechanisms of Action



Adapted from: Tak and Lee, Curr Obes Rep; 2021

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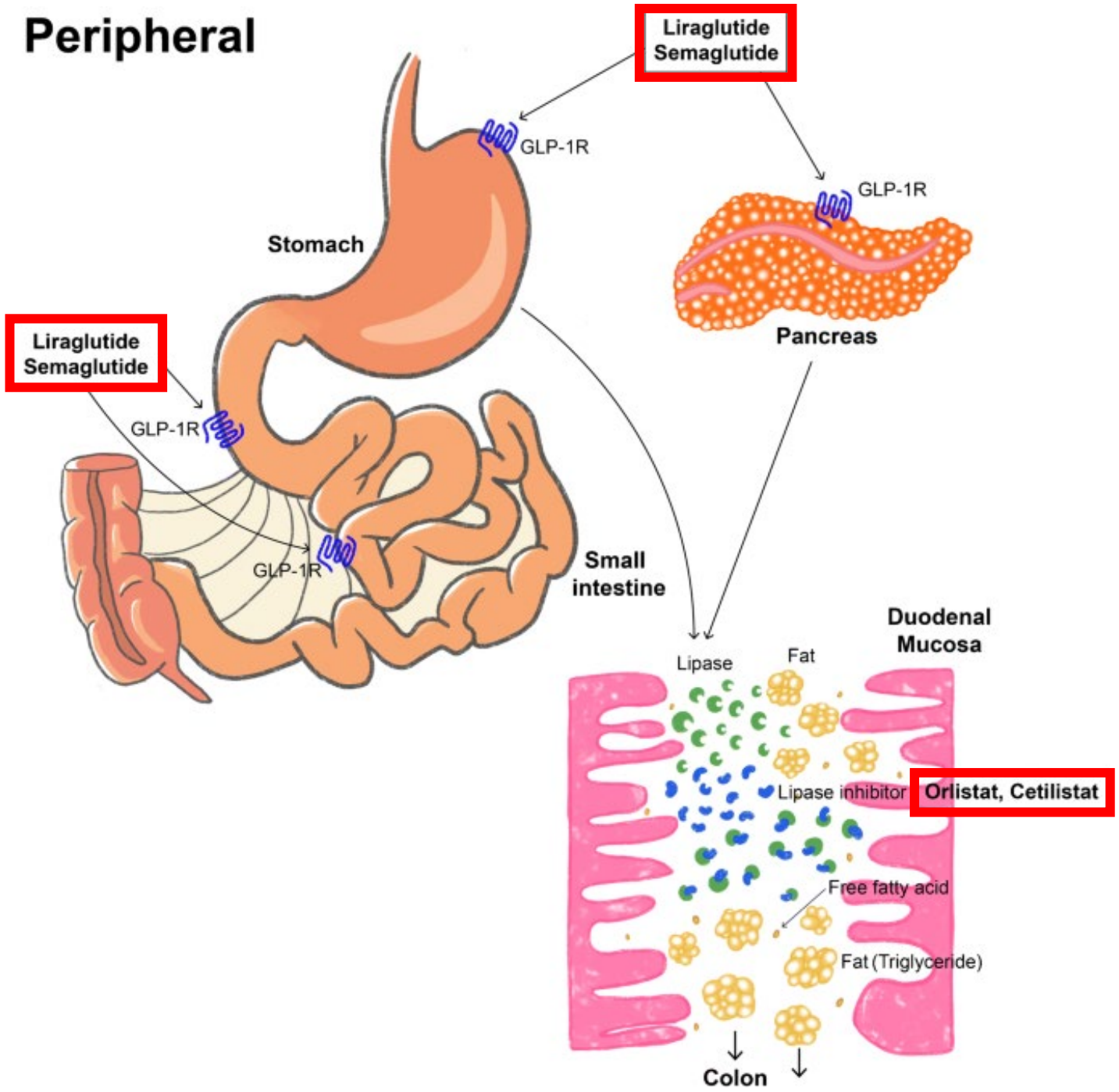
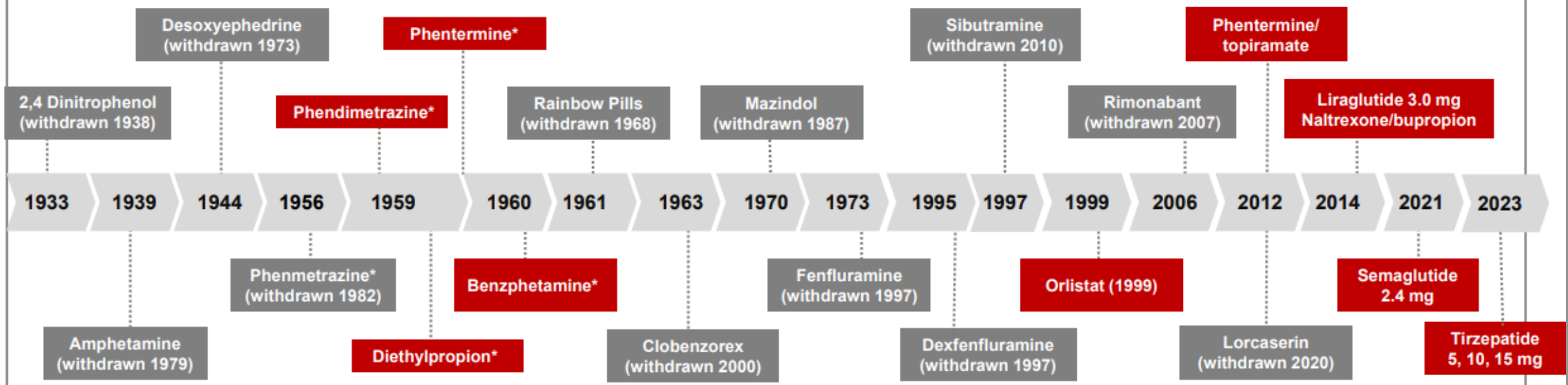


Adapted from: Tak and Lee, Curr Obes Rep; 2021

Progress in Anti-Obesity Pharmacotherapies[1-4]



*Approved for short term use in the US

Withdrawn AOMs

AOMs on market

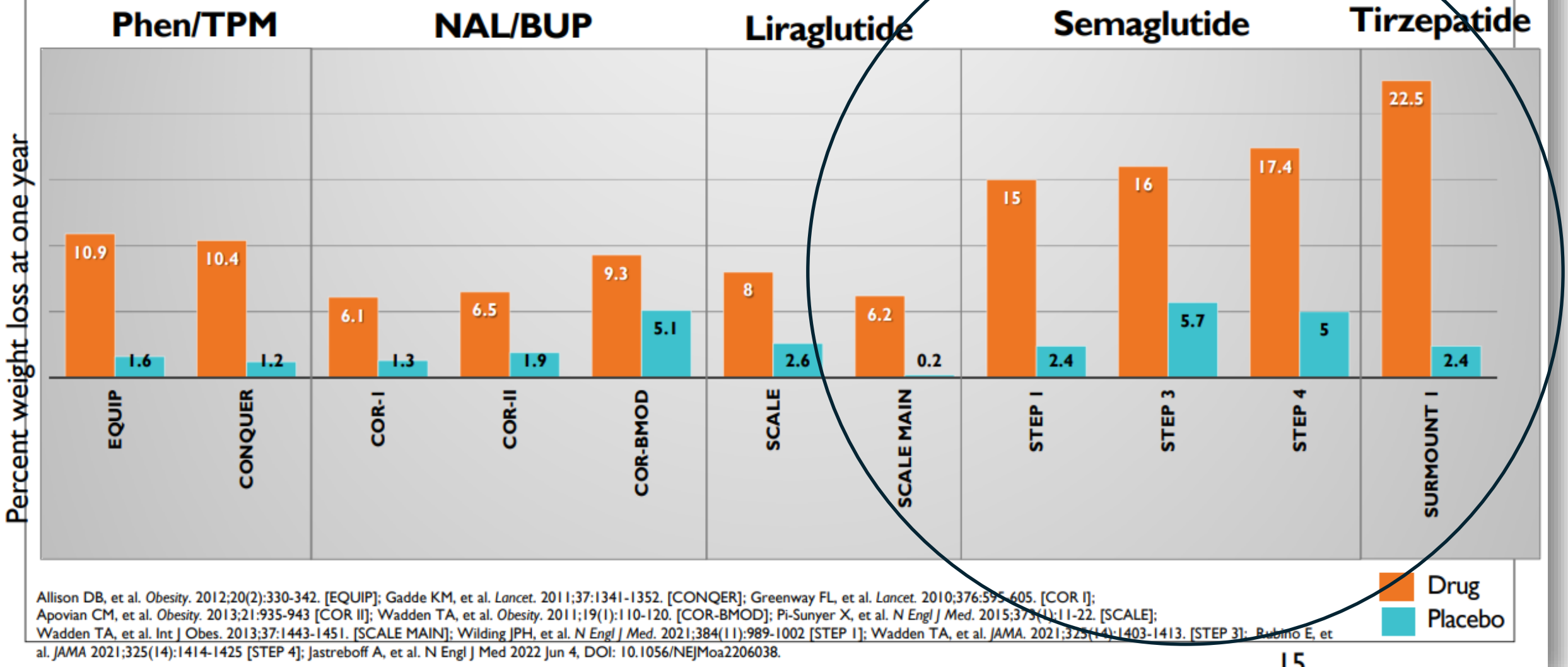
AOMs = Antiobesity medications

1. Pilitsi E, et al. *Metabolism*. 2019;92:170-192.
2. Müller TD, et al. *Nat Rev Drug Discov*. 2021;1-23.
3. Onakpoya IJ, et al. *BMC Med*. 2016;14:191.
4. https://www.ajmc.com/view/fda-approves-diabetes-drug-tirzepatide-for-chronic-weight-management

Slide courtesy Louis J. Aronne, M.D.

A Decade of Obesity Drug Discovery

Percent weight loss (drug vs placebo) for anti-obesity medications

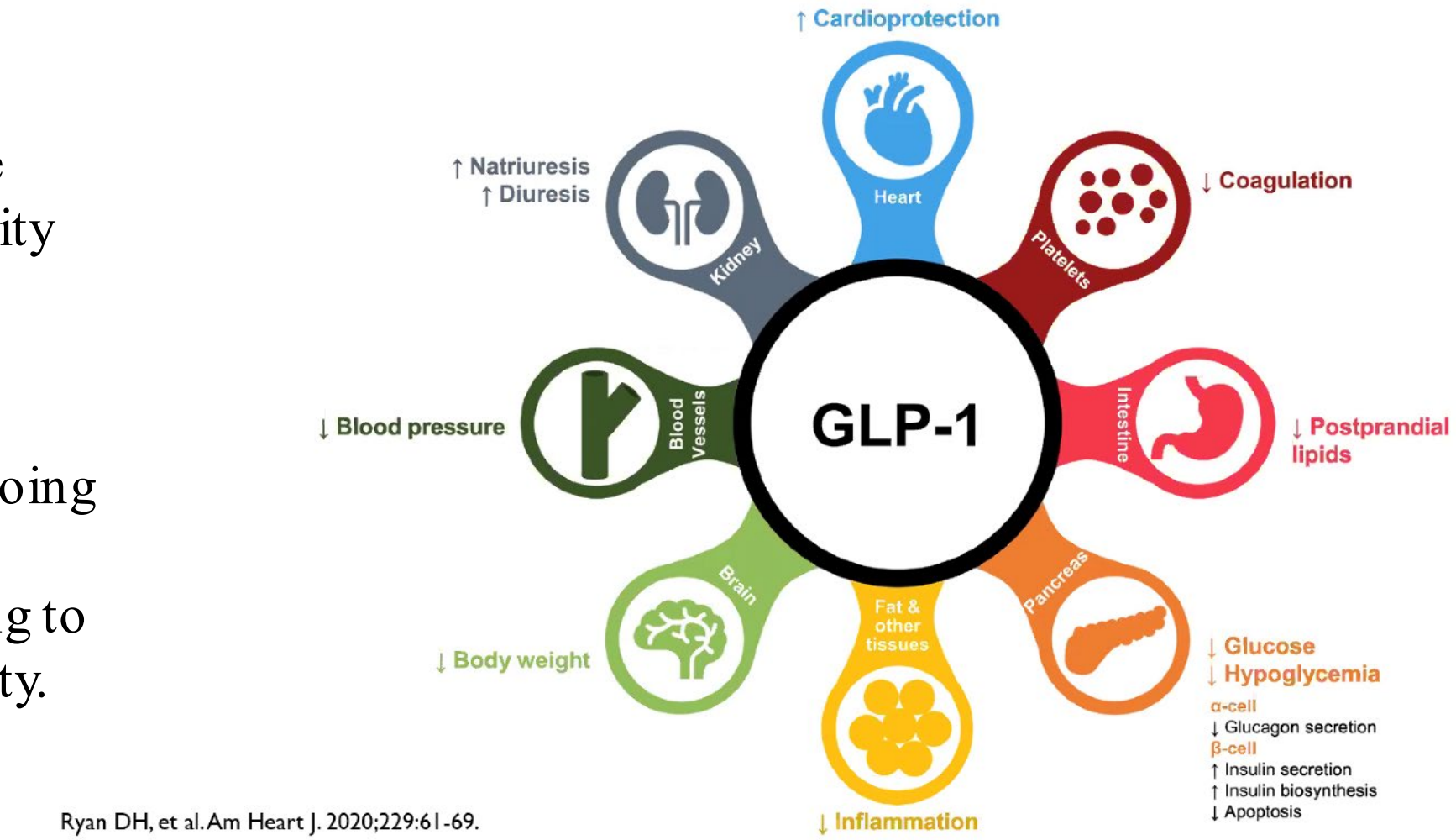


Allison DB, et al. *Obesity*. 2012;20(2):330-342. [EQUIP]; Gadde KM, et al. *Lancet*. 2011;37:1341-1352. [CONQER]; Greenway FL, et al. *Lancet*. 2010;376:595-605. [COR I]; Apovian CM, et al. *Obesity*. 2013;21:935-943 [COR II]; Wadden TA, et al. *Obesity*. 2011;19(1):110-120. [COR-BMOD]; Pi-Sunyer X, et al. *N Engl J Med*. 2015;373(1):11-22. [SCALE]; Wadden TA, et al. Int J Obes. 2013;37:1443-1451. [SCALE MAIN]; Wilding JPH, et al. *N Engl J Med*. 2021;384(11):989-1002 [STEP 1]; Wadden TA, et al. *JAMA*. 2021;325(14):1403-1413. [STEP 3]; Rubino F, et al. *JAMA* 2021;325(14):1414-1425 [STEP 4]; Jastreboff A, et al. N Engl J Med 2022 Jun 4, DOI: 10.1056/NEJMoa2206038.

Highly Effective GLP-1 Based Medications

Address underlying imbalances that drive the persistent nature of obesity

- Slow digestion
- Trigger insulin release
- Prevent glucose from going into the bloodstream
- Impact brain processing to improve enhance satiety.



Ryan DH, et al. Am Heart J. 2020;229:61-69.

2023 American Academy of Pediatrics
Clinical Practice Guideline for Child & Adolescent Obesity

P&PHCPs *should* treat overweight/obesity & comorbidities concurrently (KAS 4) following the principles of the **medical home** and the **chronic care model**, using a **family-centered** and **non-stigmatizing** approach that acknowledges obesity's **biologic, social, and structural drivers.**(KAS 9)

Components of Comprehensive Treatment	Overweight			Obesity		
	<6y	6 to <12y	≥12y	<6y	6 to <12y	≥12y
Motivational Interviewing[f] (KAS 10)	✓	✓	✓	✓	✓	✓
Intensive Health Behavior and Lifestyle Treatment[g] (KAS 11)	⚖	✓	✓	⚖	✓	✓
Weight Loss Pharmacotherapy[h] (KAS 12)						✓
Offer referral to Comprehensive Pediatric Metabolic & Bariatric Surgery programs[i] (KAS 13)						✓[i]

The Use of “Should” Within the KAS

The words "should" and "may" used in the KAS statements in the CPG:

-Are based on the level of associated evidence

-Reflect the action that is meant to be taken based on the evidence, under what circumstances to take that action and the level of obligation to follow the evidence-based recommendation

The use of “should” is meant to represent an intermediate level of obligation:

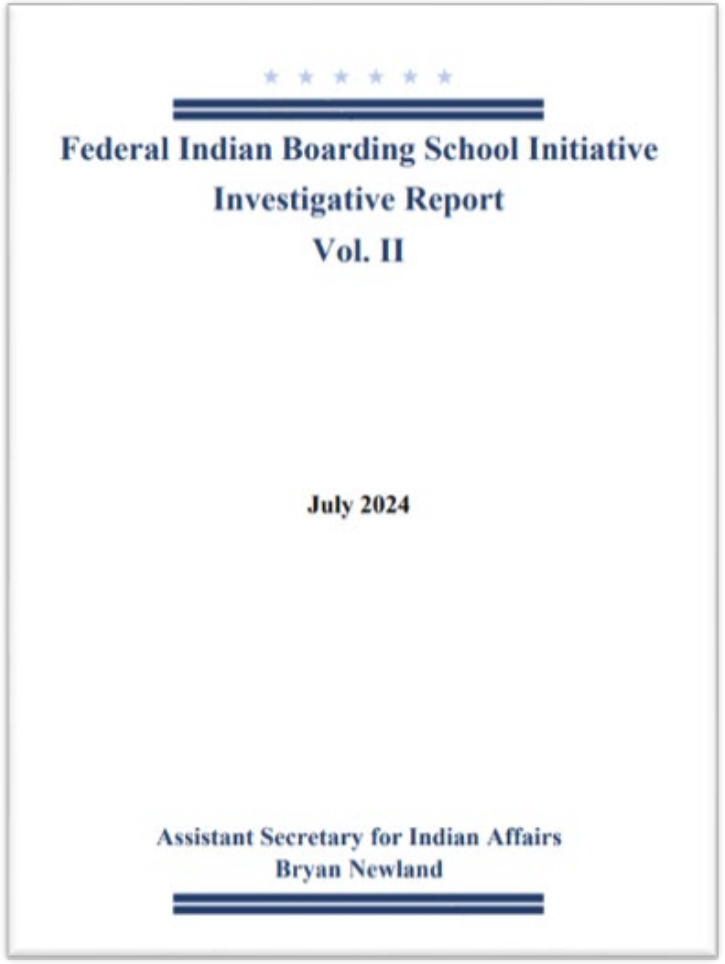
-NOT a required action

-An evidence-based recommendation that allows for some variation based on the circumstances

Clinical decision making is undertaken in partnership with the patient/family:

-Based on a comprehensive evaluation and understanding the components of evidence-based treatment to create an individualized and tailored treatment plan that includes longitudinal care are clinic-based, effective treatments for obesity

Recognition of importance of culture and holistic approaches



"Provide funding and support for culturally based, community-driven healing efforts…"

"In distributing these funds, U.S. Government agencies should be flexible when it comes to access and use of the funds…"

"The U.S. Government should, support holistic and innovative approaches, including those rooted in connections to homelands and culture…"

https://www.doi.gov/priorities/strengthening-indian-country/federal-indian-boarding-school-initiative

Cultural Considerations

Western Medicine

- Focus on pathology, intellect
- Reductionist, compartmentalized, concerned with individual and disease physiology
- Adversarial – oriented toward goal of disease conquest
- Physician is an authority

AI/AN Tradition

- Focus on general health, intuition
- Complex, holistic, looks at the "big picture", concerned with larger environmental context of disease
- Teleological – what can the disease teach the patient?
- Healer is an (spiritual) advisor

J Nurse Pract. 2010 Jun 1; 6(6): 477–478.
Urol Nurs. 2007 Apr;27(2):161-3, 173.

Providing Safe and High-Quality Care

- Discuss patient goals and expectations
  - Improving health vs. a “weight goal”
  - Benefits of early intervention vs. watchful waiting
  - Complications of rapid weight loss and/or inadequate energy intake
  - Long-term treatment and discontinuation; weight regain
- Discuss medication therapy as adjunct to lifestyle treatment
- Discuss compliance
  - Importance of regular visits to monitor overall health and magnitude/rate of weight/BMI change
- Evaluate for co-occurring mental health issues
  - Children with obesity (vs. normal or overweigh peers) report more psychosocial stress events and psychiatric disorders
- Evaluate for disordered eating/eating disorders
  - Importance of meal regulation and protein intake

Iwatate et al., 2023, J Adol HealthIwatate et al., 2023, J Adol Health
Forster et al., 2023; BMC Public Health; Rojo et al., 2021; Children;
Lindbergh et al., 2020; BMC Med
Mitchison et al., 2019, Psychol Med

General Approach to OMs

- Should be used adjunctively to behavior and lifestyle treatment.
- When prescribed, should consider comorbidities and pleiotropic effects.
- Do no harm → Maintain holistic focus

- Should not replace prevention strategies.
- Should not be used as monotherapy.

A number of OM options exist; the decision to initiate, continue, modify, or terminate treatment should be based on patient-specific factors and shared decision-making between the patient and provider.

Patient case

Picking up where we left off…

17-year-old male

For the last 6 months:

- Monthly visits/IHBLT
- Incorporated routine physical activity
- Improved nutritional habits
- Interested in initiating pharmacotherapy today

Vitals		
	May 2024	November 2024
Ht (cm)	178 (70 in)	178 (70 in)
Wt (kg)	116 (255 lb)	↓ 112 (246 lb)
BMI (kg/m^2)	36.5	↓ 35
Bmi %ile	130th of the 95th %ile	↓ 124th of the 95th %ile
BP (mmHg)	125/74	↓ 118/68
Body fat (%)	42	↓ 40
Fat mass (kg)	49	↓ 45
Muscle mass (kg)	38	↑ 39
Labs		
FG (mg/dL)	105	↓ 98
A1c (%)	5.5	↓ 5.4
ALT (U/L)	58	↓ 40
TC (mg/dL)	176	↓ 175
LDL (mg/dL)	139	↓ 114
HDL (mg/dL)	30	↑ 32
TG (mg/dL)	176	↓ 155

Classes of FDA-Approved Pediatric Obesity Medications

CNS Stimulants

- Phentermine
- Phentermine/ topiramate

Glucagon-Like Peptide Receptor Agonists

- Liraglutide
- Semaglutide

Lipase Inhibitors

- Orlistat

Melanocortin Receptor Agonist

- Setmelanotide

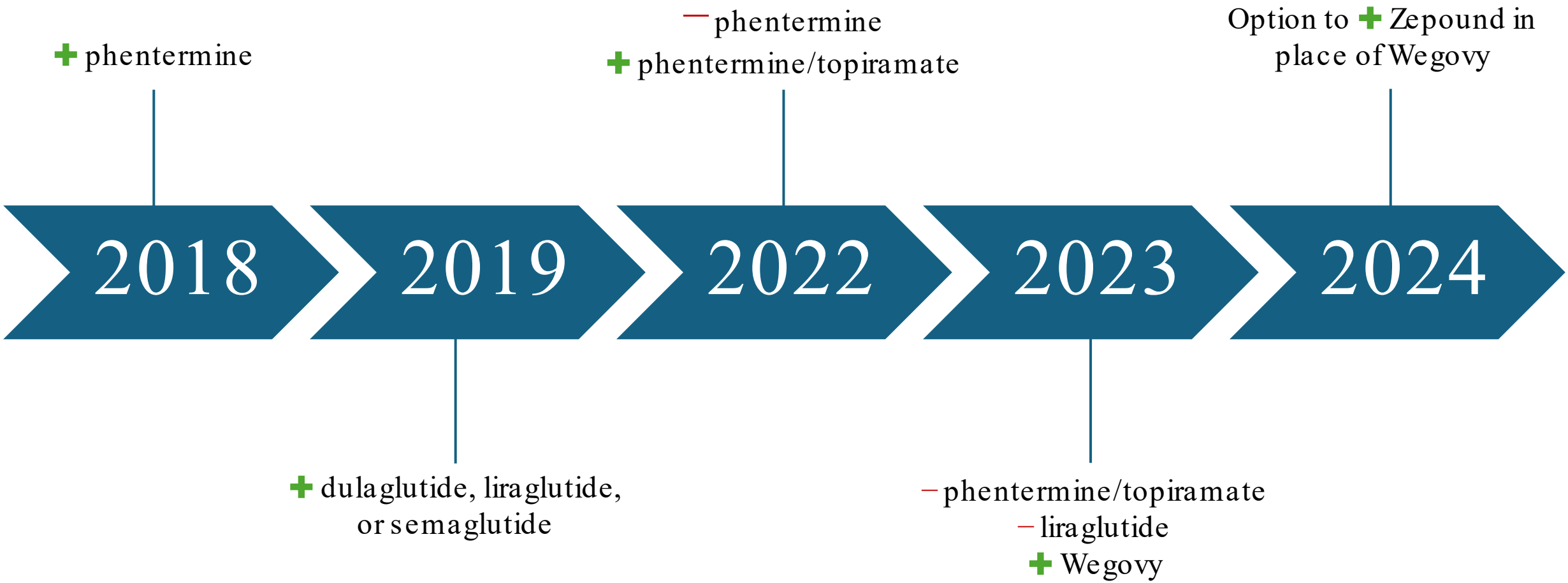
FDA-Approval Summary for Pediatric Obesity

Medication (year approved for peds)	Approved Indication	Age
Phentermine (1999)	Weight management, short term (up to 12 weeks), as adjunct to diet and exercise	≥17 yo
Orlistat (2003)	Obesity management, including weight loss and maintenance, as adjunct to reduced-calorie diet	≥12 yo
Liraglutide (2020)	Weight management, chronic, as adjunct to diet and increased physical activity	≥12 yo
Phentermine/topiramate (2022)	Weight management, chronic, as adjunct to diet and exercise	≥12 yo
Semaglutide (2022)	Weight management, chronic, as adjunct to diet and increased physical activity	≥12 yo
Setmelanotide (2020)	Weight management, chronic, with monogenic or syndromic obesity	≥6 yo

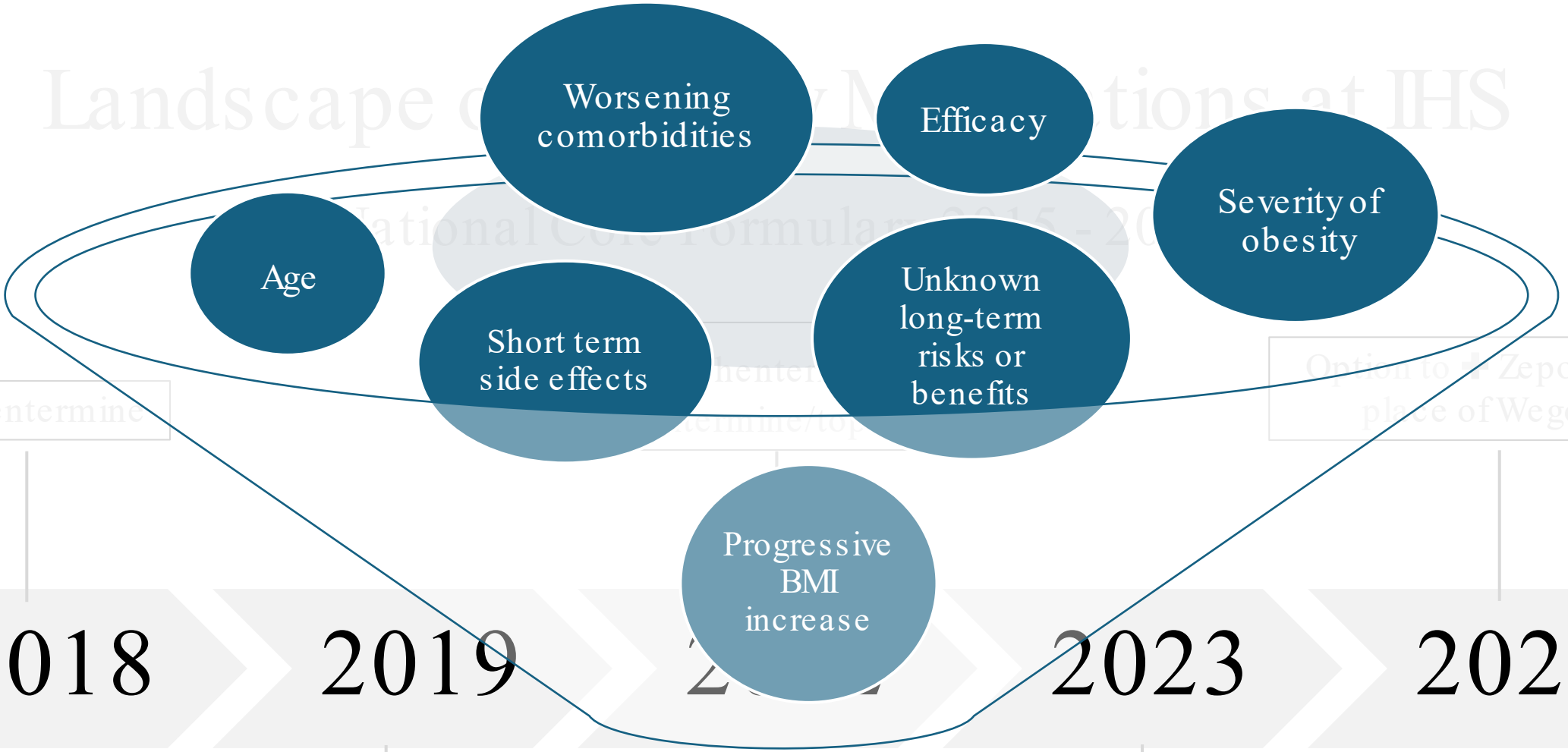
https://www.uptodate.com/contents/table-of-contents/drug-information/pediatric-drug-information

Landscape of Obesity Medications at IHS

National Core Formulary 2015 - 2025



https://www.ihs.gov/NPTC/formularysearch/



Work with local P&T Committee to adopt criteria for use
Discuss with patient and always take a holistic, health-focused approach

Pharmacotherapy Resource

Institute for Healthy Childhood Weight

https://downloads.aap.org/AAP/PDF/Obesity/Treatment%20Flow_12.19.22.pdf

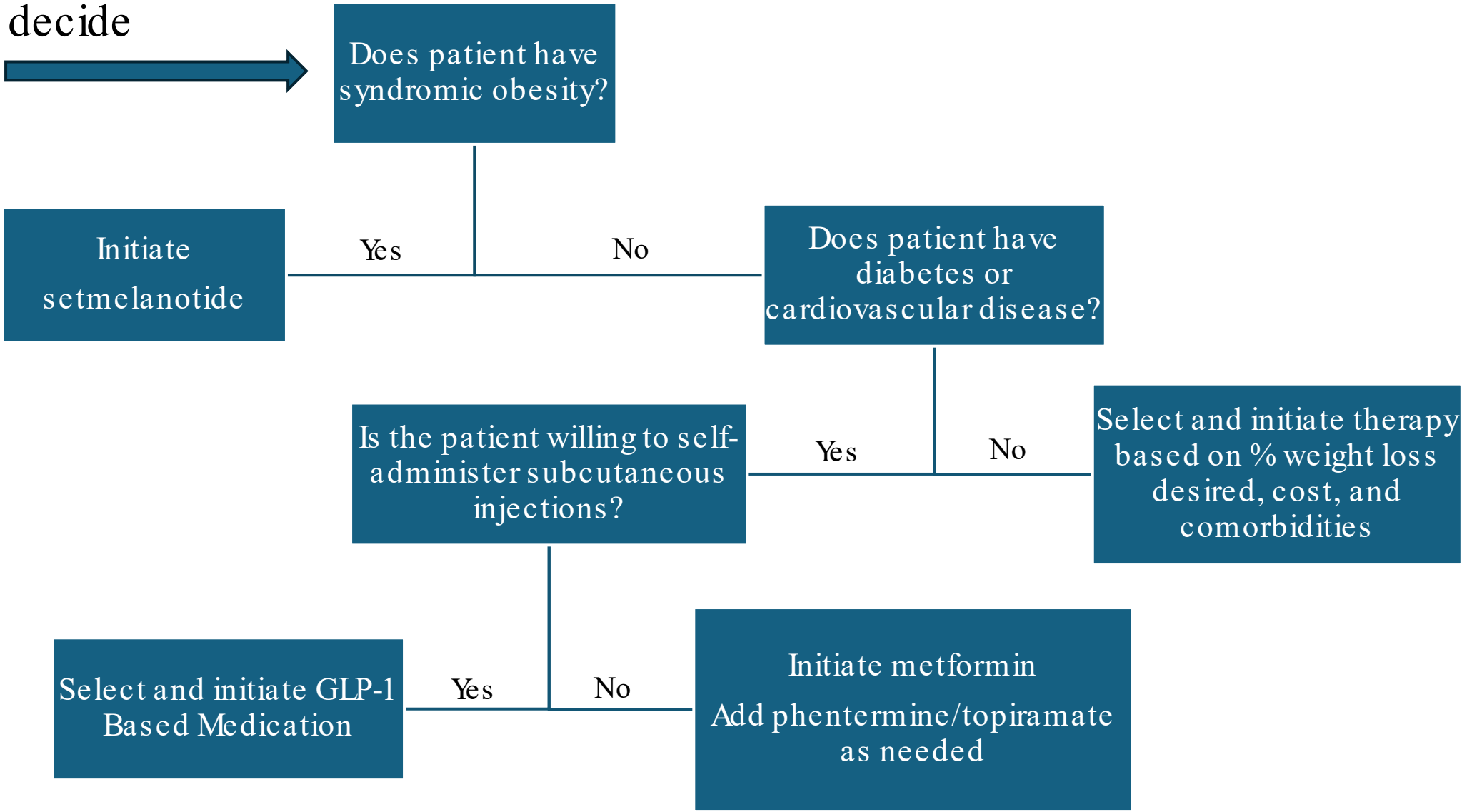
Weight Loss Medication Use & Mechanism#

PHCPs who prescribe weight loss medications should have knowledge of the patient selection criteria, medication efficacy, adverse effects, and follow-up monitoring guidelines. Injectables may require additional teaching. PHCPs may choose to refer to pediatric obesity experts or treatment centers for prescribing weight loss medication. There is no evidence to support the use of weight loss medications alone. Medication should be used in conjunction with IHBLT.

Drug	Function/Background	Age Approved	Dosage/Type	Impact	Side Effects
Metformin	• Originally to treat T2DM • Mechanism is to improve insulin sensitivity by increasing peripheral tissue uptake of glucose and by inhibiting hepatic glycogenesis	• 10 and older • Some safety info down to age 8	• Recommended starting dose is 500 mg 1 or 2x daily • Gradual increase up to 2500mg • Extended release recommended for fewer side effects	• 2/3 of studies show BMI reduction • 1/3 of studies show no benefit • Successful BMI reduction is more common in older children and adolescents	• Lactic acidosis is a rare but serious side effect • Side effects are dose dependent and include bloating, nausea, flatulence, & diarrhea
Orlistat	• Intestinal lipase inhibitor that blocks fat absorption through inhibition of pancreatic and gastric lipase	• Age 12 and older	• 120 mg 3X per day	• 2-3% BMI reduction	• Steatorrhea • Fecal urgency • Flatulence
Liraglutide & exenatide	• Glucagon-like peptide-1 (GLP-1) receptor agonists • Decrease hunger by slowing gastric emptying as well as through targets in CNS	• Age 12 and older	• Starting dose is 0.6 mg/day up to a maximum dose of 3.0 mg/day	• About 1/2 of patients will achieve a 5% BMI reduction • About 20% will achieve a 10% BMI reduction	• Nausea • Vomiting • Increased risk of medullary thyroid cancer among patients with family history of multiple endocrine neoplasia
Phentermine	• A central norepinephrine inhibitor • Nonselectively inhibits serotonin and dopamine • Suppresses appetite	• 16 and older • Short term use only (3 months)	• 7.5 mg, 15 mg, 30 mg or 37.5 mg	• Effectiveness does not always increase with increased dosage	Side effects are dose dependent • Elevated BP • Dizziness • Headache • Tremor • Dry mouth • Stomach ache
Lisdexamphetamine	• Stimulant • Approved for ADHD	• 6 and older with ADHD	• Dose increments of 10mg, no clear effective dose for BMI reduction	• Limited evidence of effectiveness	• Elevated blood pressure • Insomnia • Irritability
Topiramate	• Carbonic anhydrase inhibitor • Suppresses appetite	• 2 and older for epilepsy • 12 and older for headache	• Start 25mg qam/50mg qhs • Max dose 100mg/day	• Limited evidence of effectiveness	• Cognitive slowing
Setmelanotide	• Recently approved for obesity caused by mutations in the MC4R pathway & leptin deficiency or leptin receptor deficiency	• >= 6 years of age with POMC deficiency, PSK1 deficiency, LEPR deficiency confirmed by genetic testing	• 1-3 mg/day given subcutaneously	• Weight loss of 12-25%	• Injection site reaction • Nausea
Phentermine and Topiramate	• See above for mechanisms of action	• Combination medication is approved for weight loss in adults. • Recent data support BMI reduction in adolescents 12-17 years of age with documented history of failure to lose sufficient weight or maintain weight loss in a lifestyle modification program. (mean age = 14 years; mean BMI=37.8 kg/m2)	• Starting dose; 3.75mg/23mg • Mid-dose; 7.5mg/46mg • High dose; 15 mg/92mg	• BMI percent change at 56 weeks was -10.44 (high dose; 15mg/92mg) and -8.11 (mid-dose; 7.5 mg/46 mg) as compared with placebo • Treatment also improved HDL and TG cholesterol profiles	• Adverse event reports in the high- to mid-dose range were no more common than placebo.

OM Selection

Patient and provider have discussed and engaged in lifestyle interventions and decide to initiate OM

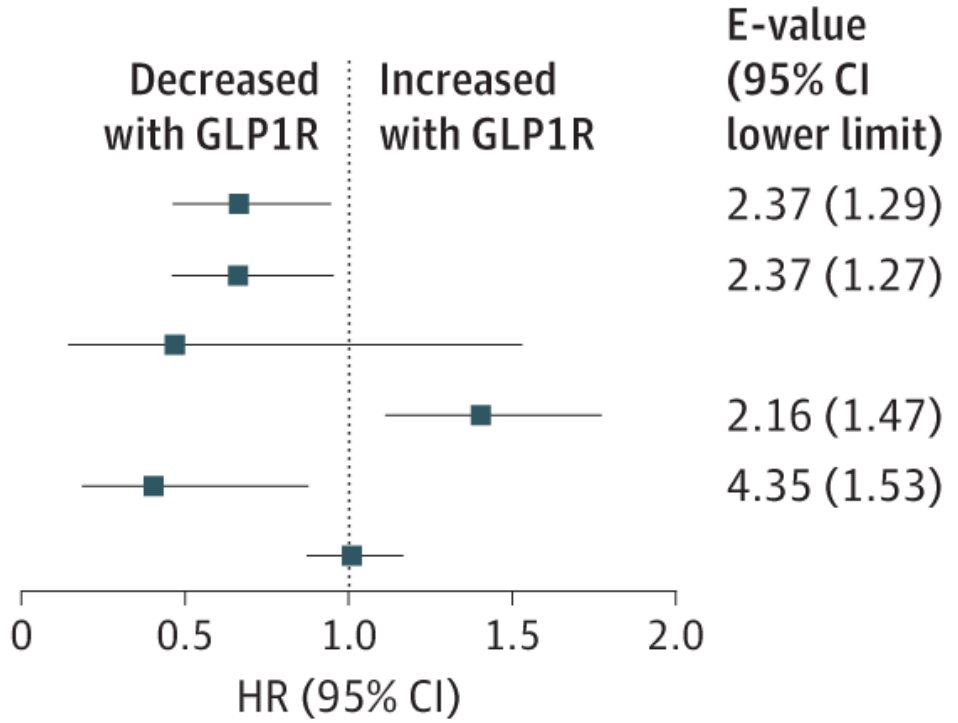


OM	Route of Administration	% Weight Loss Expected	~Cost/Month (target maintenance dose)	IHS ~Cost/Month	Comorbidities OM May Also Treat
Phentermine	Oral tablet or capsule	5%	$5.70	$1.20	
Orlistat	Oral tablet	5-10%	$53.10 (Alli) $520.20 (Xenical)	$37.50 (Alli) $305.1 (Xenical)	
Liraglutide	Subcutaneous inj.	5-10%	$1408.80	$675.60	Diabetes, Cardiovascular Disease
Phentermine/ topiramate	Oral capsule	5-10%	$9.15 (ind. generics) $269.10 (Qsymia)	$3.90 (ind. generics) Qsymia not available	Headache, Migraine
Semaglutide	Subcutaneous inj.	5-15%	$1618.84 (Wegovy)	$588.32 (Wegovy)	Diabetes, Cardiovascular Disease
Setmelanotide	Subcutaenous inj.	10-20%	$6424.71 – $38,548.26 (based on age and weight)	Not available	

OM	Adverse Reactions (significant or >10%) →	Monitoring
Phentermine	CV (increased blood pressure, tachycardia, arrhythmias, acute MI, cardiomyopathy, pulmonary hypertension); CNS (psychosis, insomnia, irritability, anxiety)	CV - BP, HR, lower extremity edema, chest pain Labs - creatinine and bicarb CNS effects - sleep and behavior changes
Orlistat	GI (flatulence, oily stool, urgency); vitamin deficiency (A, D, E); infection (influenza, URI, LRI); back pain; headache	Diet, and vitamin levels if concerned Labs - glucose, hepatic and renal function
Liraglutide	GI (nausea, vomiting, diarrhea, constipation); acute kidney injury; gallbladder disease; increased heart rate; hypoglycemia; antibody development	GI (low and slow until tolerable) Labs - glucose, renal function, triglycerides Signs of pancreatitis or gallbladder disease
Phentermine/ topiramate	CV (tachycardia); acidosis (decreased sodium bicarb); GI (constipation, xerostomia); headache; insomnia, decreased bone mineral density; increased serum creatinine; upper respiratory infection	CV - BP, HR Labs - bicarb, potassium, creatinine, pregnancy CNS effects - sleep and behavior changes Glaucoma
Semaglutide	GI symptoms (nausea, vomiting, diarrhea, constipation); acute kidney injury; gallbladder disease; pancreatitis	GI (low and slow until tolerable) Labs - glucose, renal function, triglycerides Signs of pancreatitis or gallbladder disease
Setmelanotide	Depression suicidal ideation; disturbance in sexual arousal; dermatologic (skin hyperpigmentation, alopecia); GI symptoms (abdominal pain, constipation, diarrhea, nausea, vomiting), back pain; headache; URI	GI Sexual adverse reactions Derm - hyperpigmentation Psych - depression

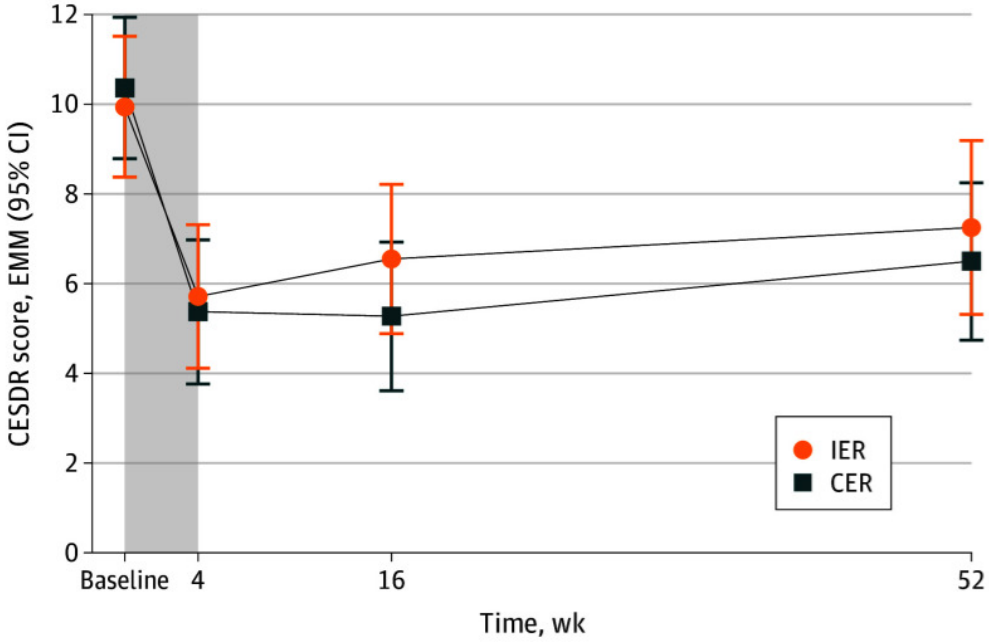
GLP-1 RA's do not increase risk of suicidal ideation and attempt in adolescents

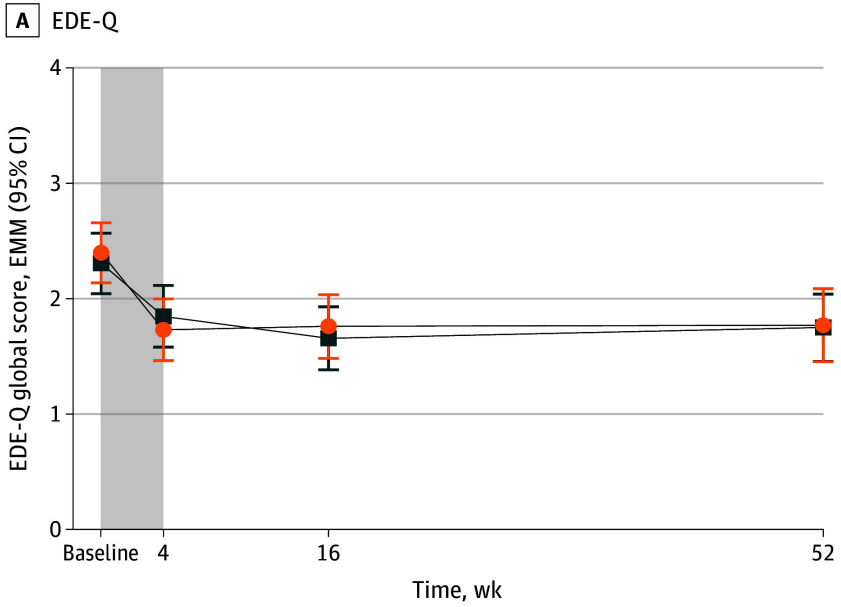
Outcome	No. (%) GLP1R	Control	HR (95% CI)	E-value (95% CI lower limit)
Suicidal ideation or attempt	50 (1.4)	78 (2.3)	0.67 (0.47-0.95)	2.37 (1.29)
Suicidal ideation	48 (1.4)	75 (2.2)	0.66 (0.46-0.96)	2.37 (1.27)
Suicidal attempt	2 (0.0)	3 (0.0)	0.47 (0.14-1.53)	
GI symptoms	166 (6.9)	125 (5.4)	1.41 (1.12-1.78)	2.16 (1.47)
Pancreatitis	10 (0.3)	23 (0.7)	0.41 (0.19-0.88)	4.35 (1.53)
URTI	357 (10.3)	376 (10.9)	1.01 (0.88-1.17)	

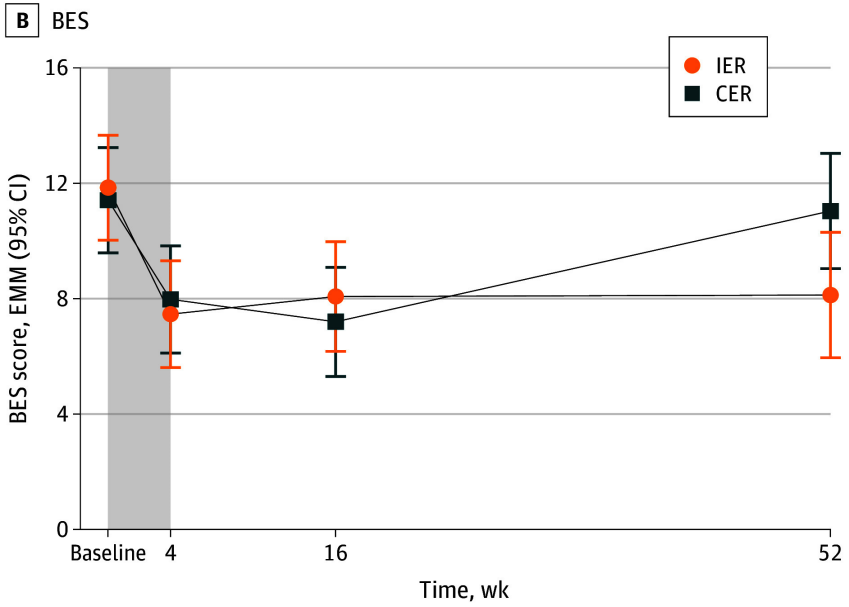


Risk of Suicidal Ideation or Attempts in Adolescents With Obesity Treated With GLP1 Receptor Agonists. JAMA Pediatr. Published online October 14, 2024. doi:10.1001/jamapediatrics.2024.3812

Lifestyle treatment in teens reduces symptoms of depression, eating disorders, and subjective size/weight/eating concerns







Jebeile H, Baur LA, Kwok C, Alexander S, Brown J, Collins CE, Cowell CT, Day K, Garnett SP, Gow ML, Grunseit AM, Henderson M, House ET, Inkster MK, Lang S, Paxton SJ, Truby H, Varady KA, Lister NB. Symptoms of Depression, Eating Disorders, and Binge Eating in Adolescents With Obesity: The Fast Track to Health Randomized Clinical Trial. JAMA Pediatr. 2024 Oct

What about compounded GLP-1 based medications? The Rules…

Federal Food, Drug and Cosmetic Act - Sections 503A&503B

"If a **compounded drug product is identical or nearly identical to an approved drug** that is **not on FDA's drug shortage list** at the time of compounding, distribution, and dispensing, the compounded product is essentially a copy, and an outsourcing **facility may not produce it** under section 503B."

Identical or nearly identical:

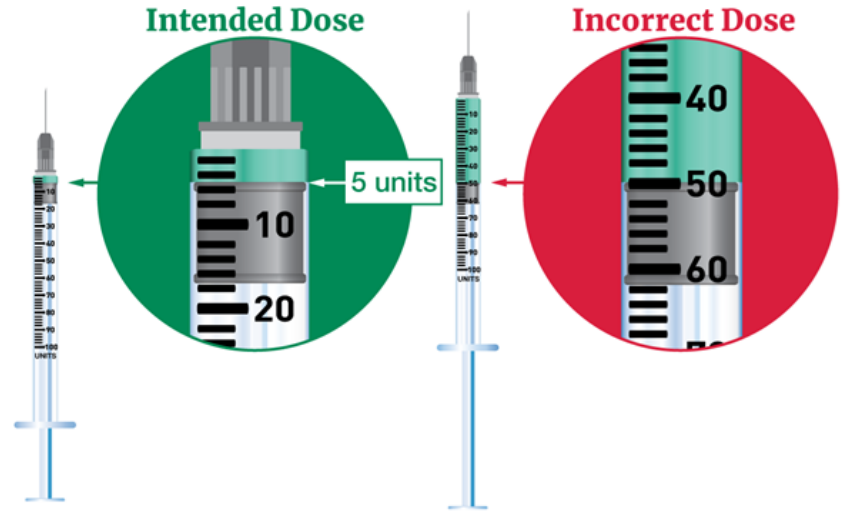
- ✓ active ingredient(s),
- ✓ route of administration,
- ✓ dosage form,
- ✓ dosage strength, and
- ✓ excipients

https://www.fda.gov/media/98964/download?attachment
https://www.fda.gov/drugs/human-drug-compounding/section-503a-federal-food-drug-and-cosmetic-act

Concerns with Compounded GLP-1 Based Medications

- Administration/dosing errors
- Quality
- Unapproved salt forms
- Use of additional ingredients
- Counterfeit products
- Injectable medications
- Research products or those not for human consumption

Figure 1. **U-100 insulin syringe with fill volume of 5 units and 50 units**



https://www.fda.gov/drugs/human-drug-compounding/fda-alerts-health-care-providers-compounders-and-patients-dosing-errors-associated-compounded

https://www.tga.gov.au/news/safety-alerts/counterfeit-ozempic-pens-detected-and-adverse-event-reported

https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss

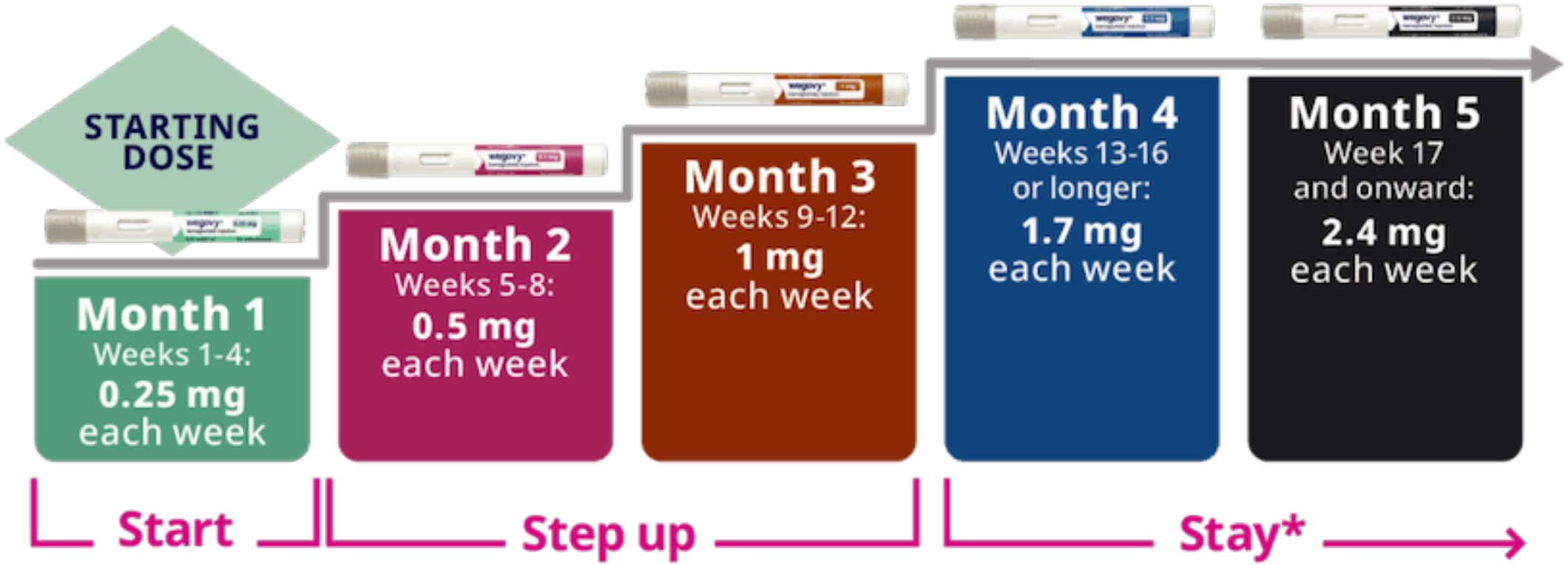
Other Considerations

- Injectables
  - Injection of a foreign body
  - Safe needle disposal
- Storage in the absence of refrigeration
- Lacking necessities

	US Population (%)	AI/AN On Reservation (%)	AI/AN Alaska Native Village (%)
Lack complete plumbing	0.5	8.6	24.8
Lack complete kitchen	0.8	7.5	20.5
No telephone	3.7	18.9	7.3

Am J Public Health. 2014 June; 104(Suppl 3): S263–S267.
IHS Profile

How to prescribe semaglutide (as Wegovy for obesity)



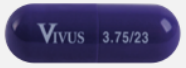
*At month 5 and on, you may either stay at 1.7 mg or increase to 2.4 mg. Work with your health care provider to determine which dose is right for you.

https://www.novomedlink.com/obesity/products/treatments/wegovy/dosing-administration/wegovy-dosing.html

How to prescribe phentermine/topiramate (as Qysmia for obesity)

GET STARTED

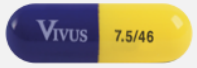
WEEKS 1-2



Take one Qsymia 3.75 mg/23 mg capsule each morning for the first 2 weeks (Starter Dose).

You may or may not lose weight during this period. If not, don't be discouraged. Move onto the prescribed recommended dose for weight-loss results.

WEEKS 3-12

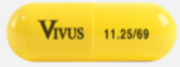


On the first day of week 3, start taking one Qsymia 7.5 mg/46 mg capsule daily (Recommended Dose).

After 12 weeks of therapy, evaluate your weight loss with your doctor. They may increase your dose of Qsymia if you have not lost a certain amount of weight.

OPTIMIZE PLAN

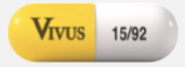
WEEKS 13-14



On the first day of week 13, start taking Qsymia 11.25 mg/69 mg daily (Titration Dose).

If your doctor has escalated your dose, you will be on this dose for 2 weeks before moving on to the top dose.

WEEKS 15+

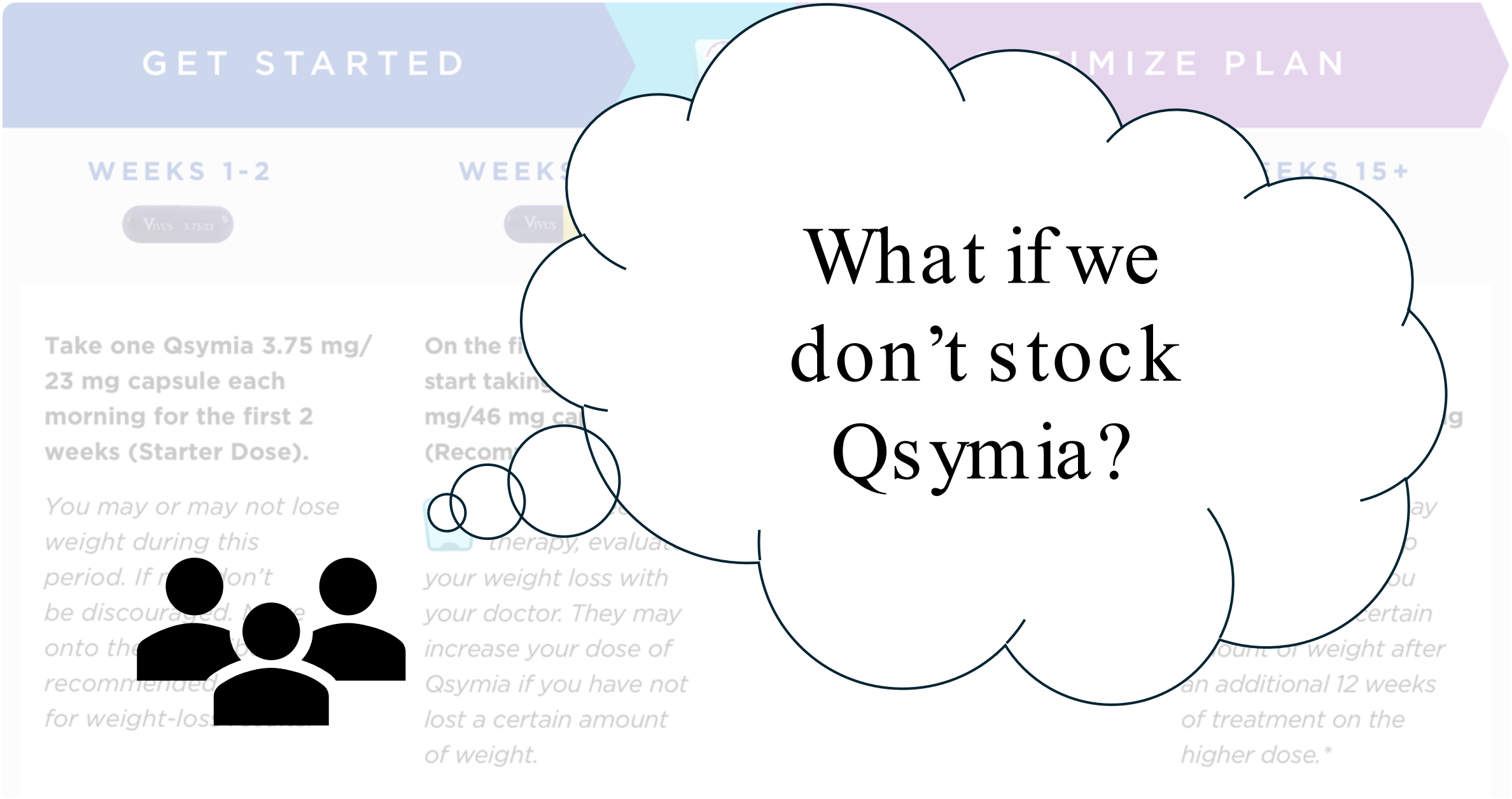


Follow with ongoing monthly prescriptions of Qsymia 15 mg/92 mg (Top Dose).

*Your doctor may tell you to stop taking Qsymia if you have not lost a certain amount of weight after an additional 12 weeks of treatment on the higher dose.**

https://qsymia.com/caregiver/support-and-resources/taking-qsymia

How to prescribe phentermine/topiramate (as Qysmia for obesity)



Options!

- Generics
  - Phentermine
  - Topiramate – extended release available

- Week 1: phentermine 15mg qam / topiramate 25mg qpm
- Week 2: phentermine 15mg qam / topiramate 50mg qpm
- Target = phentermine 15mg / topiramate 50mg

  - May start phentermine at 7.5mg qam
  - May add topiramate 25 qam (total daily dose 75mg)
  - Topiramate ok up to 200mg/day, but expect sleepiness

Gaps, Barriers, and Unknowns

- Lifestyle and obesity medications administered together
- Prescribing nuances
  - E.g., tapering protocols
- Long-term cost (vs. benefit)
- Population-specific considerations
  - E.g., differences in pharmacokinetics/pharmacodynamics, nutrition and physical needs for elderly vs. adult vs. pediatric patients
- Adverse event monitoring strategies and safety signals with chronic use
- Future of environmental factors
  - E.g., food policy and systems

Novel nutrient-stimulated hormone-based therapies in the pipeline

GLP-1 receptor agonists approved for obesity treatment		
Semaglutide	Weekly SC	STEP trials
Liraglutide	Daily SC	SCALE trials

MONOTHERAPY

ENDO-PANCREATIC receptor agonists				
Cagrilintide	AMY RA	Phase II	Novo Nordisk	NCT03856047
ZP8396	AMY RA	Phase I	Zealand Pharma	NCT05096598
Amylin agonist LA	AMY RA	Phase I	Eli Lilly	Not available
DACRA QW II	AMY/CAL RA	Phase I	Eli Lilly	Not available

ORAL MONOTHERAPY

ORAL GLP-1 receptor agonists				
Semaglutide	GLP-1 RA	Phase III	Novo Nordisk	NCT05035095
Danuglipron	sm GLP-1 RA	Phase II	Pfizer	NCT04707313
LY3502970	GLP-1R NPA	Phase II	Eli Lilly	NCT05051579

DUAL RA combinations

ENTERO-ENDOCRINE receptor agonists/antagonists				
Tirzepatide	GIP/GLP-1 dual RA	Phase III	Eli Lilly	NCT04184622
CT388	GIP/GLP-1 dual RA	Phase I	Carmot Therapeutics	NCT04838405
Dapiglutide	GIP/GLP-2 dual RA	Phase I	Zealand Pharma	NCT04838405
AMG133	GIP Receptor Antagonist/ GLP-1 RA	Phase I	Amgen	NCT04478708

DUAL RA combinations

PANCREATIC-ENTERO-ENDOCRINE receptor agonists				
Cagri-Sema	AMY/GLP-1 dual RA	Phase III	Novo Nordisk	NCT03600480
Pemvidutide	GCG/GLP-1 dual RA	Phase II	Altimmune	NCT05295875
BI456906	GCG/GLP-1 dual RA	Phase II	Boehringer Ingelheim	NCT04667377
NN9277	GCG/GLP-1 dual RA	Phase I	Novo Nordisk	NCT03308721

TRIPLE RA combinations

PANCREATIC-ENTERO-ENDOCRINE receptor				
Retatrutide	GIP/GCG/GLP-1 triple RA	Phase II	Eli Lilly	NCT04881760

Jastreboff AM, Kushner RF. New Frontiers in Obesity Treatment: GLP-1 and Nascent Nutrient-Stimulated Hormone-Based Therapeutics. Annu Rev Med. 2023 Jan 27;74:125-139.

Key Message #1

Individuals taking OMs need lifestyle interventions as foundational and complimentary treatment

- OMs do not replace the need for:
  - ✓Chronic disease prevention and self-management
  - ✓Efforts at the policy, system, and environmental level
- Peer/family support systems
  - ✓Screen for food insecurity, transportation, housing instability
  - ✓Assess quality of life, adjustment issues, peer relationships, body self-image
  - ✓Use accessible resources to address positive screens
- GET CREATIVE AND TAP INTO THE RESOURCES YOU HAVE

Key Message #2

Patient AND family education is imperative

- Medications
  - ✓Administration, side effect management, monitoring and storage
- Nutrition
  - ✓Adequate protein and nutrient intake
- Physical activity
  - ✓ Strength training to retain lean mass
- Realistic explanations
  - ✓ Titration/taper schedules, rebound/cycling, plateaus/maintenance

Key Message #3

Co-manage obesity and mental health/eating disorders

- Eating disorders are more common in teens with obesity
  - ✓ Screen at baseline and routinely (EDE-Q, SCOFF)
- Depression is more common in teens with obesity
  - ✓ Screen at baseline and routinely (PHQ2/9)
- Language matters!
  - ✓Reduce weight stigma and bias

Patient Case – 6 month follow up

Initiate Wegovy – start at 0.25mg weekly and titrate to target dose of 1.7mg weekly

Follow-up:

- ❑ Monthly visits with team
- ❑ Lifestyle treatment
  - Continued physical activity and nutrition support
- ❑ Monitoring
  - Labs – CMP, HbA1c, fasting lipid panel
  - Vitals – BP, Wt, Ht, BMI, BMI percentile
  - ROS and PE – neuro, cardiorespiratory, musculoskeletal, derm, GI, GU, growth/development
- ❑ Treat co-morbidities
  - Dyslipidemia, NAFLD/MASLD, prediabetes, sleep, physical limitations, etc.
- ❑ Psych
  - Disordered eating or concerning patterns?
  - Anxiety, depression?
  - Other behavioral support needs? Quality of life!

Vitals			
	May 2024	November 2024	May 2025
Ht (cm)	178 (70 in)	178 (70 in)	178 (70 in)
Wt (kg)	116 (255 lb)	↓ 112 (246 lb)	↓ 96 (211 lb)
BMI (kg/m^2)	36.5	↓ 35	↓ 30
Bmi %ile	130th of the 95th %ile	↓ 124th of the 95th %ile	↓ 97th %ile
BP (mmHg)	125/74	↓ 118/68	↓ 115/68
Body fat (%)	42	↓ 40	↓ 37
Fat mass (kg)	49	↓ 45	↓ 35
Muscle mass (kg)	38	↑ 39	↓ 37
Labs			
FG (mg/dL)	105	↓ 98	↓ 86
A1c (%)	5.5	↓ 5.4	↓ 4.9
ALT (U/L)	58	↓ 40	↓ 23
TC (mg/dL)	176	↓ 175	= 175
LDL (mg/dL)	139	↓ 114	↓ 112
HDL (mg/dL)	30	↑ 32	↑ 34
TG (mg/dL)	176	↓ 155	↓ 132

2023 American Academy of Pediatrics Clinical Practice Guideline for Child & Adolescent Obesity

P&PHCPs *should* treat overweight/obesity & comorbidities concurrently (KAS 4) following the principles of the **medical home** and the **chronic care model**, using a **family-centered** and **non-stigmatizing** approach that acknowledges obesity's **biologic, social, and structural drivers.**(KAS 9)

Components of Comprehensive Treatment	Overweight			Obesity		
	<6y	6 to <12y	≥12y	<6y	6 to <12y	≥12y
Motivational Interviewing[f] (KAS 10)	✓	✓	✓	✓	✓	✓
Intensive Health Behavior and Lifestyle Treatment[g] (KAS 11)	⚖	✓	✓	⚖	✓	✓
Weight Loss Pharmacotherapy[h] (KAS 12)						✓
Offer referral to Comprehensive Pediatric Metabolic & Bariatric Surgery programs[i] (KAS 13)						✓[i]

Candidate Selection

KAS 13: **Offer referral for adolescents 13 y and older with severe obesity** (BMI ≥ 120% of the 95th percentile for age and sex) for evaluation for metabolic and bariatric surgery to local or regional comprehensive multidisciplinary pediatric metabolic and bariatric surgery centers

Criteria for Pediatric Metabolic and Bariatric Surgery[733]

Weight Criteria	Criteria for Comorbid Conditions
Class 2 obesity, BMI ≥ 35 kg/m^2 or 120% of the 95th percentile for age and sex, whichever is lower	Clinically significant disease; examples include but are not limited to T2DM, IIH, NASH, Blount disease, SCFE, GERD, obstructive sleep apnea (AHI >5), cardiovascular disease risks (HTN, hyperlipidemia, insulin resistance), depressed health-related quality of life.
Class 3 obesity, BMI ≥ 40 kg/m^2 or 140% of the 95th percentile for age and sex, whichever is lower	Not required but commonly present.

AHI, apnea-hypopnea index.

Note: Additional research is needed before broad recommendations can be made for children ≤12 years

Pediatrics (2023) 151 (2): e2022060640.

Referral

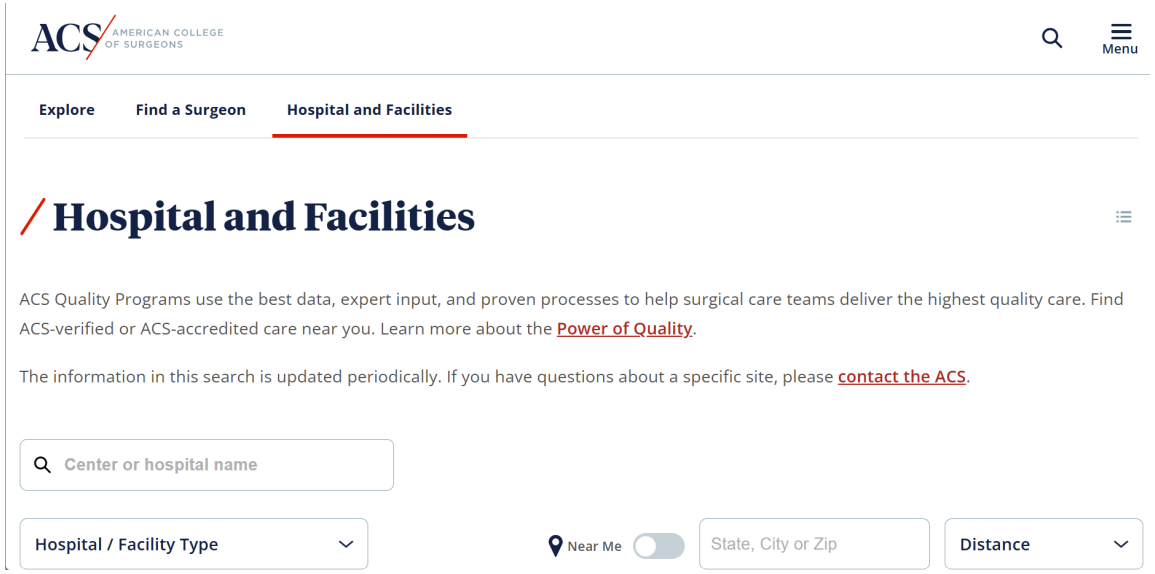
- ❑ Begins within medical home
  - Patient + family + pediatrician or primary care provider
- ❑ Comprehensive assessment
  - Longitudinal BMI
  - Comorbidities
  - Physiological and psychosocial factors
- ❑ Shared decision making with ongoing communication
  - Patient/family + PCP + surgery team
  - Risks, harms and costs vs. benefits

Note: a referral/assessment does not guarantee surgery

Pediatrics (2019) 144 (6): e20193224.

Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program Adolescent Center

- Safe and effective surgical care
- Continuous quality improvement
- Public and private payer coverage



AMBSAQIP Adolescent Center:

✓Has access to child- and adolescent-specific clinical care resources

✓ Incorporates pediatric health care experts
- General pediatric medicine
- Nutrition
- Anesthesia
- Behavioral disciplines

https://www.facs.org/quality-programs/accreditation-and-verification/metabolic-and-bariatric-surgery-accreditation-and-quality-improvement-program/
https://www.obesityaction.org/resources/bariatric-surgery-centers-of-excellence-why-they-are-important-when-selecting-your-surgeon-and-hospital/

Preparation*

Informed Consent

Step 1 — Realistic discussion of available options and likely outcomes

- Document weight-loss attempts (e.g., IHBLT, Rxs)
- Screen for and document necessary social and emotional supports for postoperative lifestyle modifications

Step 2 — Comprehensive evaluation by PCP, surgical team, or collaboratively

- Screen for and document management of comorbid conditions
- Assessment by a behavioral clinician

Step 3 — Pre- and post-surgical care planning

- Counseling, support and education
- Lifestyle modifications
- Follow-up, monitoring and routine, long-term care

*Be familiar, but typically led by the surgical team or done at the site

Semin Pediatr Surg. 2020 Jan 20;29(1):150890.
Surg Obes Relat Dis. 2018 Mar 23;14(7):882–901.
Pediatrics (2019) 144 (6): e20193224.

Follow Up

Early Post-Operative

- Complications: 15% minor (e.g., nausea, dehydration)

Perioperative

- Monitor progress and report symptoms to surgical program
  - Complications: 8% major

Long-term; routine

- Nutritional status and micronutrient deficiencies
- Hydration status
- Weight regain
- Bone mineral density
- Family planning for adolescent females
- Ongoing/additional behavioral evaluation and treatment

Pediatrics (2019) 144 (6): e20193223.

Gaps, Barriers, and Unknowns

- Optimal timing to maximize long-term health benefits
  - “Ceiling effect”
- Gold standard procedure for pediatrics
- Access and coverage
- Obesity medications after surgery

Key Message #1

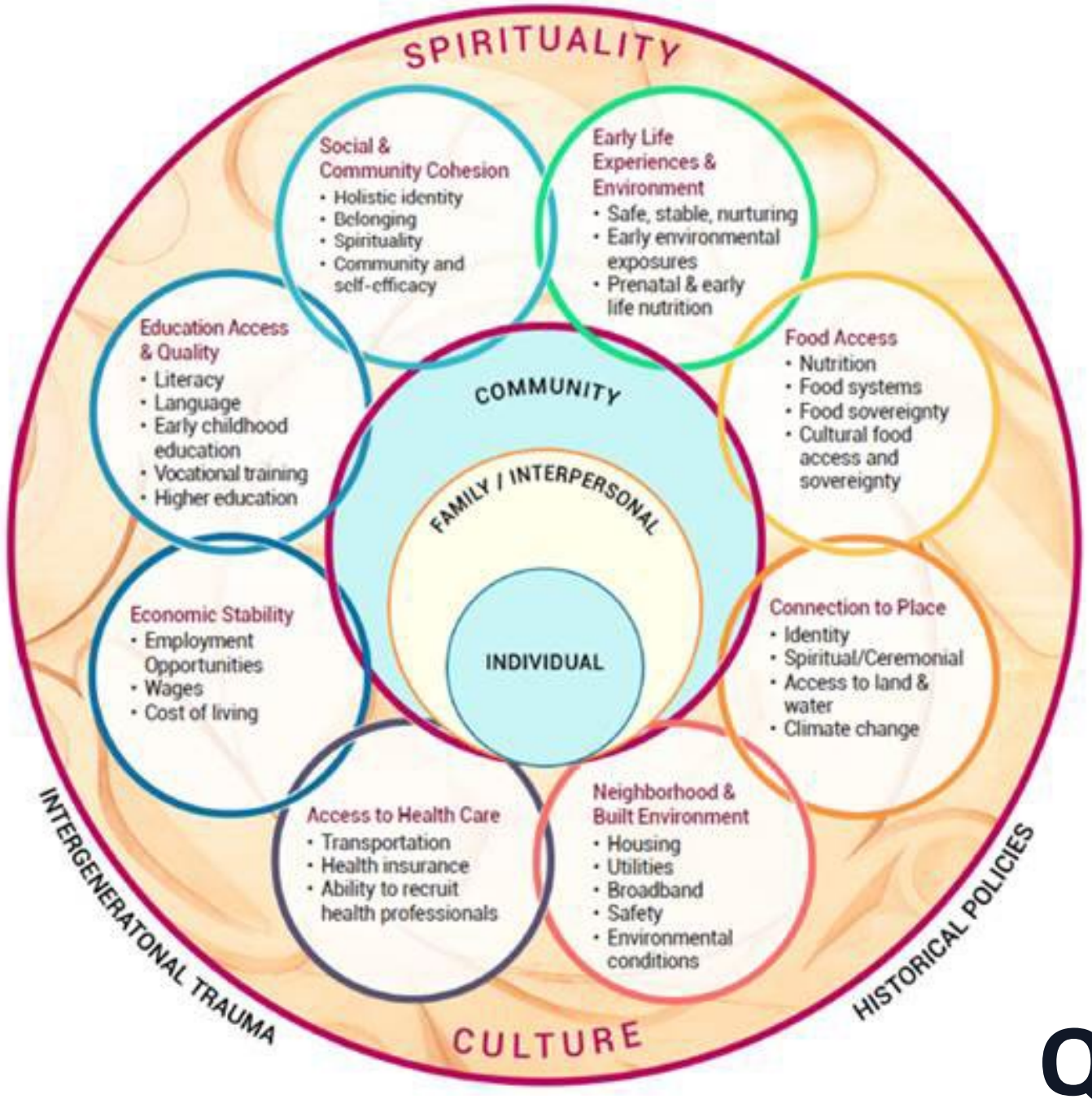
Surgery as adjunct treatment to foundational, comprehensive care starts within the medical home

- Coordinate and communicate
  - ✓ Early, honest and comprehensive discussions
  - ✓ Bi-directional communication with patient/family and multidisciplinary surgical team
  - ✓ You don't have to be the expert but expect to play a role!

Key Message #2

Family matters

- Adolescents WILL REQUIRE family support
  - ✓ Evaluate family readiness and support for treatment and follow-up compliance
  - ✓ Unique opportunity to lean on community health workers and public health nurses
- Share resources



Ahéhee'!

Questions?