Roundtable on Obesity Solutions
Medications and Obesity: Exploring the Landscape and Advancing Comprehensive Care
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Mental Health Considerations

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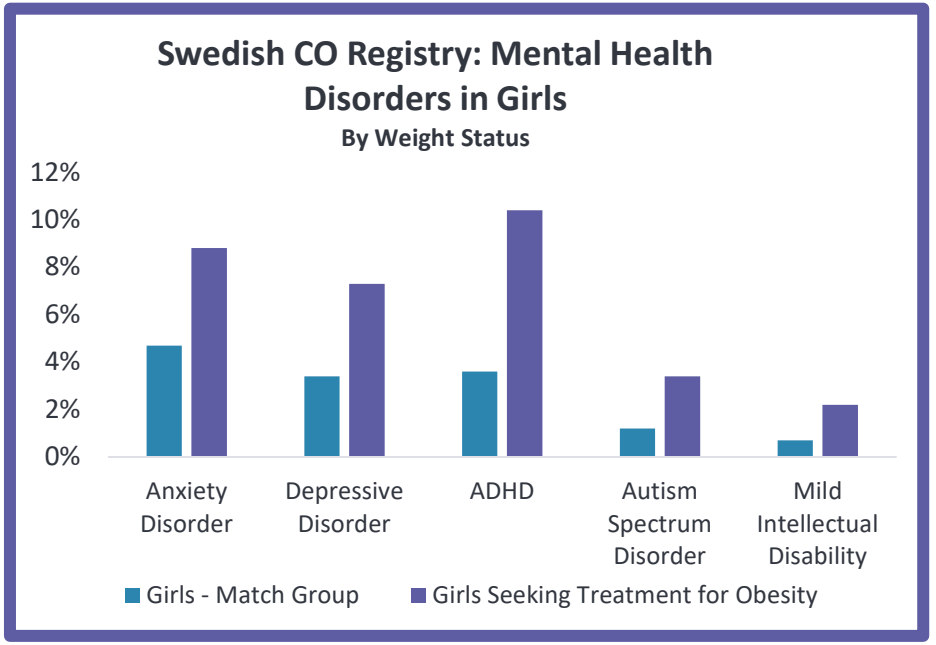
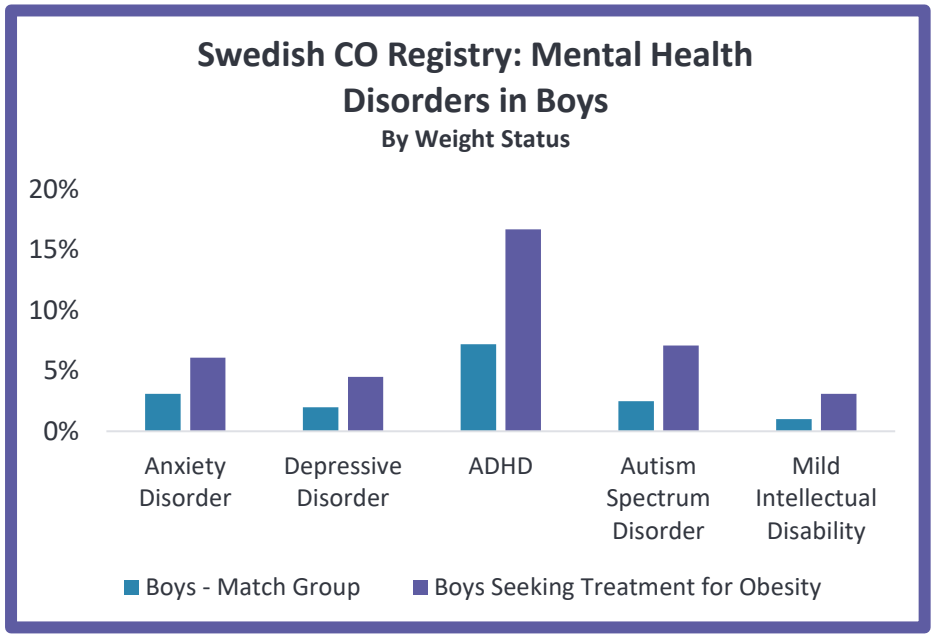
Co-Occurrence of Psychiatric Disorders and Obesity

Mental Health in Children/Adolescents with Obesity

- Mental health problems are associated with obesity in youth (e.g. QOL; conduct, peer, and emotional problems)
- Children with obesity, as compared to OW and NW peers, report more psychosocial stress events and psychiatric disorders





In Swedish study, there was a 43% and 33% higher risk ($p>.0001$) of anxiety and depression, in girls and boys respectively, as compared to girls and boys in the matched sample

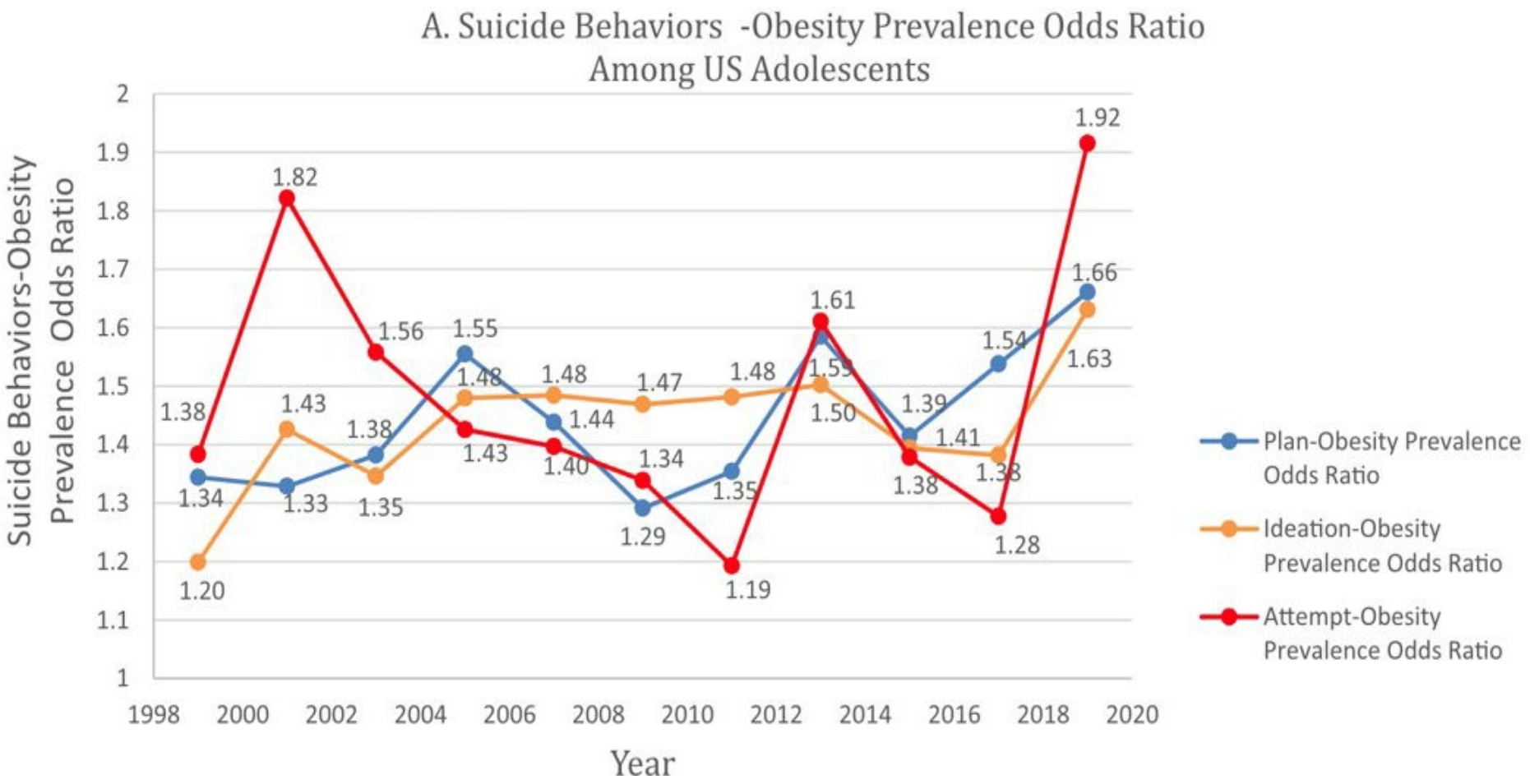
Forster et al., 2023; *BMC Public Health;* Rojo et al., 2021; *Children;* Lindbergh et al., 2020; *BMC Med*

Obesity in Adolescents is Associated with Increased Suicide Behaviors

- Adolescents in the Unites States, sampled from 2019 Youth Behavior Survey Data (N=13,871)
- After controlling for psychosocial confounding factors (i.e., sexual identity, depressed mood, alcohol and drug use, and other traumatic events), obesity was associated with increased odds of:
  - Suicide Attempts: 1.65 (95%CI, 1.30 – 2.11); $p < .001$
  - Suicidal Ideation: 1.31 (95%CI, 0.89-1.61); $p = .06$
  - Suicide Planning: 1.27 (95%, CI, 1.02 – 1.57); $p = .03$

Iwatate et al., 2023, *J Adol Health*

Obesity in Adolescents is Associated with Increased Suicide Behaviors



Iwatate *et al.*, 2024; *Eur Child Adolesc Psychiatry*

Adjusted Odds Ratios for Underweight, Overweight and Obesity Relative to Healthy Weight in Adolescents with Eating Disorders

Higher Rates of Eating Disorders in the Obesity Range

	AN	BN	BED	AAN	SBN %, AOR (95% CI)	SBED	PD	NES	UFED
Underweight	**21.6 (9.9–47.1)**	**0.2 (0.1–0.7)**	0.3 (0.0–2.4)	[a]	0.5 (0.1–1.5)	[a]	0.5 (0.2–1.2)	1.4 (0.8–2.4)	[a]
Overweight	[b]	1.3 (0.9–2.0)	1.3 (0.6–3.1)	**1.6 (1.0–2.6)**	1.5 (0.9–2.7)	1.7 (0.5–6.1)	**1.7 (1.1–2.7)**	1.0 (0.6–1.6)	**2.2 (1.5–3.3)**
Obese	[b]	**2.3 (1.5–3.6)**	**2.7 (1.2–6.1)**	**2.4 (1.4–3.9)**	**3.2 (1.9–5.6)**	[b]	1.5 (0.8–2.6)	1.6 (0.9–2.5)	**2.5 (1.5–4.2)**

Significant effects indicated in bold text. AOR, adjusted odds ratio; AN, anorexia nervosa; BN, probable bulimia nervosa; BED, probable binge eating disorder; AAN, atypical anorexia nervosa; SBN, subthreshold bulimia nervosa; SBED, subthreshold binge eating disorder; PD, purging disorder; NES, night eating syndrome; UFED, unspecified feeding or eating disorder.

All AORs are adjusted for gender, school grade and migrant status. Weight definitions are from the Center for Disease Control: <5th % = underweight, 5 to <85th % = healthy weight, 85th to <95th % = overweight, ≥95% percentile = obese.

[a]No cases of underweight.

[b]No cases of overweight or obese. Based on weighted data (findings unchanged with un-weighted data).

Mitchison et al., 2019, *Psychol Med*

Why the Comorbidity?

The high level of comorbidity between obesity and mental health disorders may be explained by numerous factors:

- Influence of overeating or underactivity on MH symptoms and vice versa
- Shared risk factors (e.g., experience of toxic stress in early years, resulting in executive functioning deficits which might increase risk for both obesity and MH disorders, and low SES)
- Stigma of obesity and MH problems can affect quality of life and increase each problem independently and in combination
- Treatment using antipsychotics, which affects adiposity and glucose regulation, and other psychotropic medications may lead to weight gain as well

Scott et al., *2008, Int J Obesity*; Scott et al., 2008, *Psychosomatic Res*; Halfon et al., 2013, *Academic Pediatr;* Nicol et al., 2016, *Child Obes*; Simon et al. 2006, *Arch Gen Psychiatr;* Avila et al., 2015, *Curr Obes Rep*

Mental Health Considerations in RCTs of AOMs

FDA Approved Pharmacotherapy Treatments for Children and Adolescents – Mental Health Exclusion Criteria

Across the AOM RCTs, stringent exclusion criteria were used for mental health conditions.

In clinical practice, practitioners routinely prescribe to youth not represented in the trials.

Chanoine et al., 2005, *JAMA;* Kelly et al., 2020, *N Engl J Med;* Kelly et al., 2022, *NEJM Evid*; Weghuber et al., 2022, *N Engl J Med;* Maahs et al., 2006. *Endocrine Practice*

FDA Approved Pharmacotherapy Treatments for Children and Adolescents – Mental Health Measures

Limited data were collected for psychosocial outcomes.

The limited evidence suggests that the AOMs evaluated were not associated with adverse psychosocial outcomes.

*Clinical trial included a lifestyle intervention

Risk for Suicidal Thoughts and Behaviors

Semaglutide-Associated Depression: A Report of Two Cases

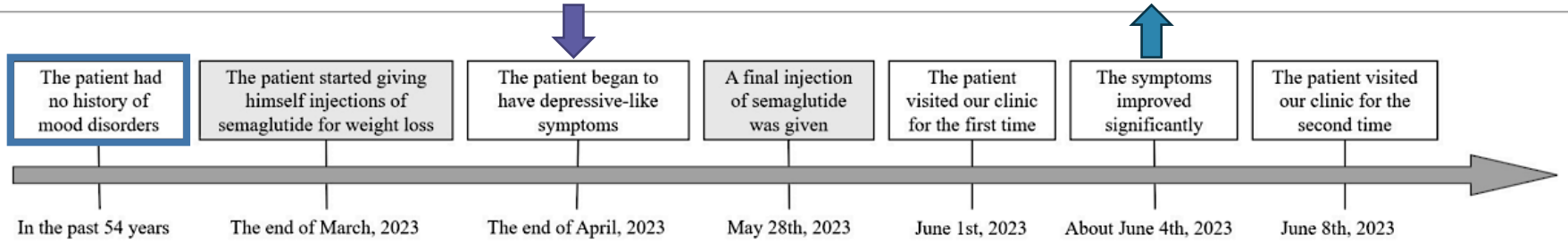


FIGURE 1
The timeline of case 1.

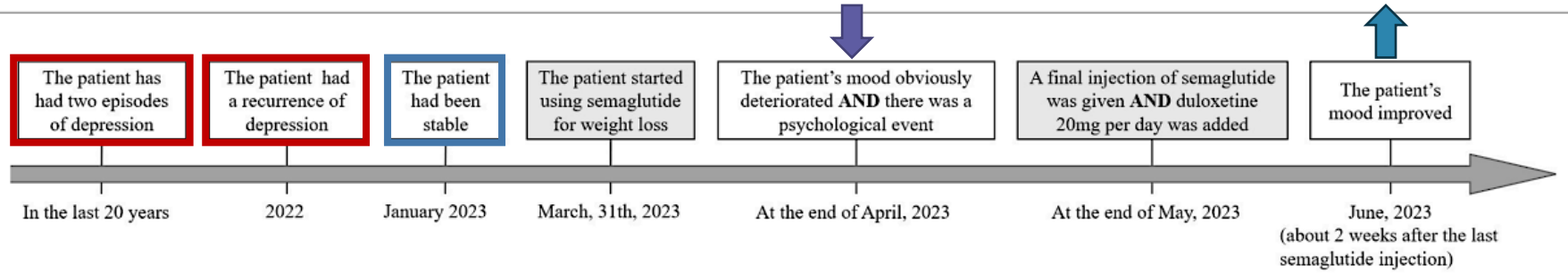


FIGURE 2
The timeline of case 2.

Li et al., 2023, *Front in Psychiatr*

Medical Complications and Consequences of Rapid Weight Loss

Current Understanding of Eating Disorders

Increased Understanding

- Unique medical complications of starvation (impaired growth, bone development, and brain maturation) in children and adolescents
- Medical complications of starvation may be present in children and adolescents with weight loss **despite presenting at normal or above normal weights**

Increased Recognition

- Failure of adequate energy intake or failure of adequate weight gain in a growing child or adolescent may have the same medical complications as overt weight loss
- Children and adolescents with **inadequate energy intake may be at risk for serious medical complications including medical instability and refeeding syndrome**

Tanner et al., 2023, *J Eat Disord*

Refeeding Risk

- Need for monitoring during nutritional rehabilitation due to risk of refeeding syndrome with weight suppression
    - Refeeding hypophosphatemia
    - Hypokalemia, hypomagnesemia, and thiamine deficiency
- Refeeding risk may be present in child and adolescent patients at any presentation weight in the setting of inadequate energy intake
- New criteria from ASPEN (American Society for Parenteral and Enteral Nutrition) on refeeding risk in children and adolescents
    - Weight loss defined as failure to gain weight as expected
    - Energy insufficiency is defined as consecutive days of inadequate protein or energy intake (e.g., significant risk – only 1 risk criteria needed - consider growing patients to have inadequate energy intake if they have *7 of more consecutive days* with protein or energy intake less than *75% of estimated needs*)

Tanner et al., 2023, *J Eat Disord*

SAHM (Society for Adolescent Health and Medicine) 2022 Classification of Malnutrition

Table 3
Proposed classification of the degree of malnutrition for adolescents and young adults with eating disorders

	Mild	Moderate	Severe
% mBMI[a]	80%–90%	70%–79%	<70%
BMI Z-score[b]	−1 to −1.9	−2 to −2.9	−3 or greater
Magnitude of weight loss[c]	5%	7.5%	10%
Rapidity of weight loss[d]		5% in 1 month 7.5% in 3 months 10% in 6 months 20% in 1 year	>5% in 1 month >7.5% in 3 months >10% in 6 months >20% in 1 year

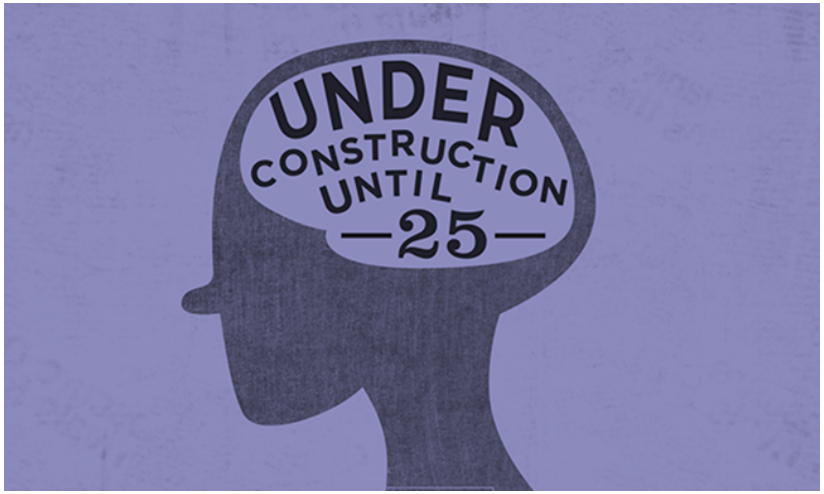
One or more of the following would suggest mild, moderate, or severe malnutrition.

[a] Percent median BMI.
[b] Mehta et al. [6].
[c] When two or more data points are available to calculate percent of body mass lost [8].
[d] When two or more data points are available and timeframe is known [10].

Golden et al., 2022, *J Adolesc Health*

Impact on Growth and Development

- Potentially irreversible medical complications that include negative impact on
  - Linear growth
  - Bone deposition
  - Brain maturation
    - Neuronal myelination



Tanner et al., 2023, *J of Eat Disord*

UC Irvine Researchers Issue Warning that GLP-1RAs May be Harmful for Children

*"Our major concern is the **unbalance** and **inappropriate reductions** in **calorie or energy intake** associated with these weight loss drugs…Unlike in adults, children and adolescents need energy and sufficient calories not only for physical activity but for growth and development."*
-Dr. Dan M. Cooper, UC Irvine School of Medicine

"*With the increase in social media, young people are already exposed to a diet culture and body images which may not be attainable and, ultimately, unhealthy. These **drugs** administered without proper supervision **could cause a minefield of health** and **emotional problems for children as they age."***
-Dean Jan D. Hirsch, UC Irvine School of Pharmacy and Pharmaceutical Sciences

Cooper et al., 2023, *J Clin and Translat Sci*
https://news.uci.edu/2023/08/28/uc-irvine-researchers-issue-warning-that-glp-1ras-may-be-harmful-for-children/

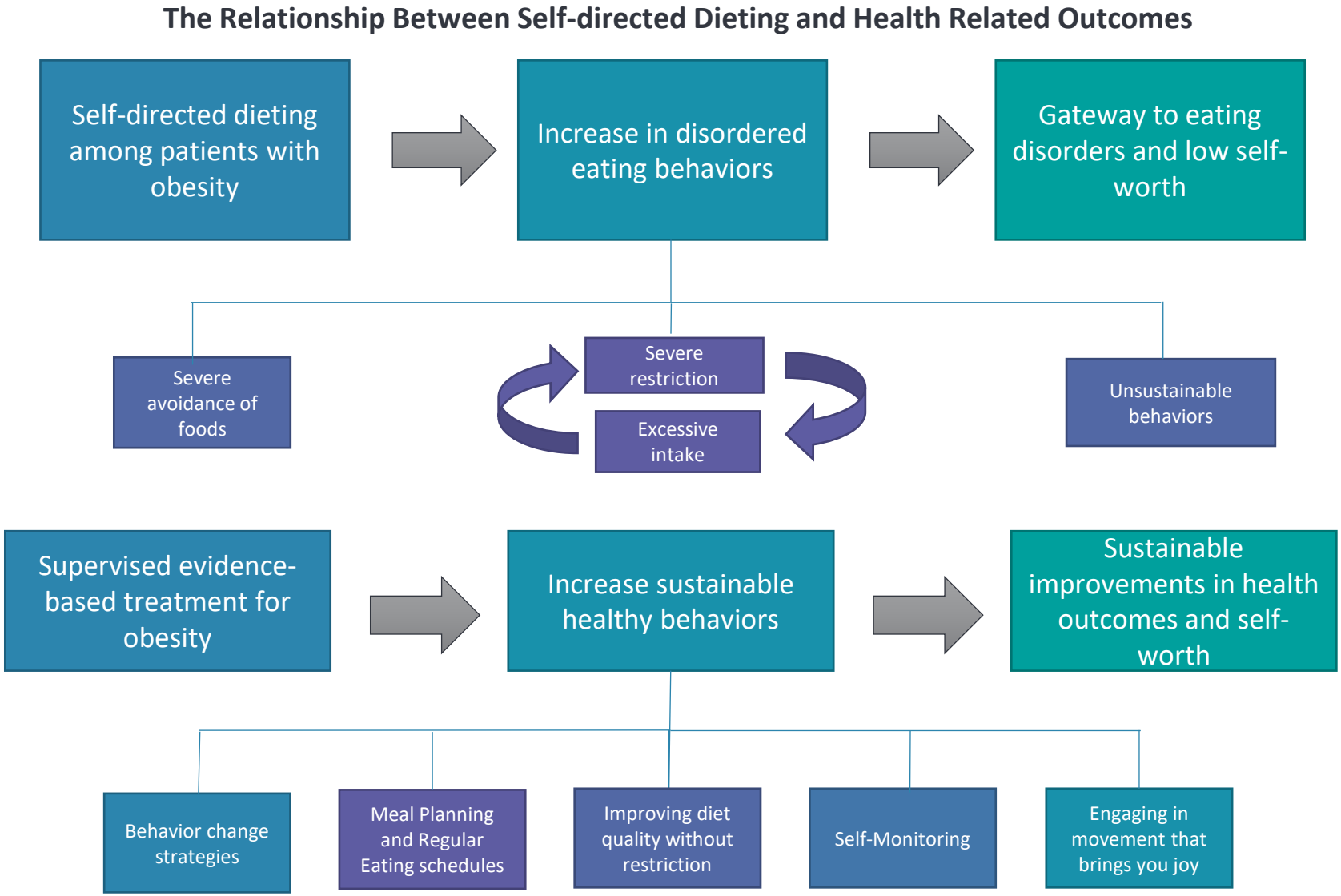
Mental and Physical Health Concerns following Bariatric Surgery Among Adolescents

- Bariatric surgery is an effective treatment option for many adolescents with severe obesity, and positively impacts weight-related QOL, particularly physical aspects
- Ongoing monitoring and assessment prior to and following surgery is **critical** for MH outcomes, as has been shown to:
  - Increased risk of alcohol use disorder and associated diseases
  - Lower percent BMI change at follow-ups in individuals with post-operative loss of control eating
  - Increase suicide risk (ideation and attempts) in adults

Goldschmidt et. al, 2018*, Pediatrics*; Beamish et. al, 2023, *J Clin Endocrinol Metab*; Williams et al., 2020*, Clinical Obesity*; White et. al, 2023, *Ann Surg*; Alvarado-Tapias et. al, 2023 *Obes Surgery*; Decker et. al, 2022, *Obes Sci Pract*.

IHBLT and Mental Health Outcomes

Evidence-based Treatment is not Dieting



Cardel et al., 2022, *J Acad Nutri and Diet*

Impact of Family-based Treatment (FBT)

- FBT is a robust, IHBLT that improves psychosocial function, particularly ED attitudes/behaviors, given its focus on:
  - Developing healthy energy-balance behaviors and routines
  - Increasing positive parenting and a positive shared home environment
  - Promoting positive body image and self-esteem
  - Increasing supportive family and peer networks
  - Creating and choosing environmental and community contexts to promote overall physical and mental well-being

FBT can serve as an important intervention for the prevention/early intervention of EDs

Wilfley et al., 2007; *JAMA*; Wilfley et al., 2017, *JAMA Peds*; Epstein, Wilfley, et al., 2023, *JAMA*

Future Research

Next Steps Needed

- Inclusion of Broader Samples that are Representative of Youth with Obesity and Mental Health Co-Morbidities
- Establish a System of Screening and Monitoring for Possible ED & MH Safety Concerns
- Optimize Assessment Outcomes Tools to Include Comprehensive Psychosocial Measures Collected at all Time Points
- Evaluate IHBLTs as a Complement to AOMs at the Intensity (i.e., Dose & Duration) Required to Build and Sustain Long-Term Lifestyle Habits
- Assess Risk for EDs in AOMs, and Develop Standards for Safe Titration of AOMs Based on Rapidity & Extent of Weight Loss
- Overcome Barriers to Reimbursement for Comprehensive Care for Obesity, as well as to Address Social Needs, ACEs, and Stigma

Thank You!

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