VIEWPOINT

Childhood Obesity at the Crossroads of Science and Social Justice

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Treatment focused on the root cause of disease generally achieves the best outcomes for efficacy and safety, a precept that has guided medical research and clinical practice for centuries. Earlier this year, the American Academy of Pediatrics (AAP) published a clinical practice guideline for the evaluation and treatment of children with obesity.[1] This guideline emphasizes weight loss drugs and bariatric surgery even though the prevalence of childhood obesity has increased far too fast to be attributable to otherwise untreatable genetic predisposition. Diet received relatively little specific attention beyond advice to follow the US Department of Agriculture's MyPlate recommendations and limit intake of sugar-sweetened beverages.

This emphasis does not indicate a bias or oversight of the guideline committee per se. Evidence-based reviews such as the guideline must, of course, base recommendations on available evidence, and the results for weight loss obtained with drugs and surgical procedures seem superior to those for diet. However, few high-quality studies of scope and rigor comparable to that of a phase 3 drug trial have ever been conducted to test novel dietary obesity treatment in any age group. Total National Institutes of Health research expenditure for childhood obesity, approximately $250 million in 2022, pales in comparison to the investments of the pharmaceutical industry.

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Even so, the physiologic actions of antiobesity drugs and surgery may have similarities to diet, among which a low–glycemic load diet (reduced in carbohydrate or glycemic index) shows promise (**Table**). Recently, the US Food and Drug Administration approved the use of glucagon-like polypeptide-1 receptor agonists (GLP-1 RAs) for obesity in adolescents. GLP-1, an incretin hormone, is believed to increase insulin secretion according to its isolated actions on islet cells. However, studies have shown that insulin secretion is actually reduced in the more clinically relevant context of mixed meals for 2 reasons. First, GLP-1 RAs improve beta cell sensitivity to glucose so that the same amount of insulin will be released at a lower glucose concentration. Second, although considerable tachyphylaxis occurs, the long-acting GLP-1 RAs persistently slow gastric emptying rate,[2,3] especially during the critical initial postprandial phase, producing a better match between nutrient absorption and insulin secretion. In other words, the lower glucose excursions arising from delayed gastric emptying reduce overall insulin demand. Controversy in the literature on the persistence of this effect relates to use of indirect methods for measurement of gastric emptying, such as paracetamol (acetaminophen) absorption, instead of scintigraphy, the criterion standard technique. Indeed, a longer delay in gastric emptying time is associated with greater weight loss with GLP-1 RA treatment, providing evidence for the importance of this effect.[3]

With slower gastric emptying, the stomach remains fuller longer and the duration of nutrient absorption is extended after a meal. Both of these effects, together with more stable blood glucose concentration, would tend to delay the return of hunger after eating and may augment satiety induced by the direct actions of long-acting GLP-1 RA in the brain. A low–glycemic load diet has analogous effects. Slower-digesting carbohydrate must travel farther down the intestinal tract before being fully absorbed, resulting in lower postprandial blood glucose levels and insulin secretion. Protein and fat also digest more slowly, and stimulate less insulin secretion, than the same amount in calories of high–glycemic index carbohydrate. Additional similarities between low–glycemic load diets and the GLP-1 RA include decreasing leptin levels (suggestive of lower leptin resistance) and ghrelin levels and increasing adiponectin levels.[4,5] Moreover, this dietary strategy shares mechanisms with gastric bypass surgery, which shifts nutrient absorption from a proximal to more distal location in the intestines. Of special relevance, secretion of GLP-1 is increased with a low–glycemic load diet[6] (which would slow gastric emptying, further enhancing satiety) and bariatric surgery.

Could a low–glycemic load diet approach the efficacy of the GLP-1 RAs in weight loss (ie, 10%-15% placebo-adjusted decrease in weight after 1 year)? Meta-analyses of clinical trials show only a modest advantage in weight loss for low- vs high-carbohydrate diets. However, most of these trials used weak behavioral interventions that produce limited dietary change and little differentiation between diet groups. Among the few studies with high-intensity dietary interventions, the low–glycemic load diets produced substantial improvements in weight loss (eg, the Dietary Intervention Randomized Controlled Trial[7]) or weight loss maintenance (eg, Diet, Obesity, and Genes Project, DiOGenes[8]). In the pediatric arm of DiOGenes (n = 465 completers 5-18 years), the prevalence of overweight or obesity decreased after 6 months only in the group with the lowest glycemic load.[9] Among 262 patients with type 2 diabetes treated with a ketogenic diet and intensive behavioral supports,

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Table. Examples of Low–Glycemic Load Diets

Diet type	Carbohydrate proportion, %[a]	Decrease these foods	Increase these foods
Low GI/moderate carbohydrate	40-50	Reduce processed grains, white potato, added sugar	Minimally processed grains, root vegetables (other than white potato), legumes, whole fruits
Low carbohydrate	20-<40	Reduce grains, potatoes, added sugar	Fats (olive oil, nuts, avocado, full-fat dairy, etc)
Very low carbohydrate	<20	Greatly reduce grains, potatoes, added sugar	Fats (olive oil, nuts, avocado, full-fat dairy, etc)
Ketogenic	<10[b]	Eliminate most sources of digestible carbohydrate except for small amounts in nonstarchy vegetables, unsweetened dairy, nuts, and low-sugar fruits (eg, 1 serving of berries)	Fats (olive oil, nuts, avocado, full-fat dairy, etc)

Abbreviation: GI, glycemic index.

[a] Percentage of total energy intake. Macronutrient cutoffs for these categories vary in the medical literature.

[b] Typically ≤50 g carbohydrate per day; protein limited to ≤20%.

weight had decreased by 12% vs 0.2% for a nonrandomized usual care group after 1 year.[10] High-quality clinical trials, with intensive support to facilitate long-term dietary adherence, will be needed to know the full potential of low–glycemic load diets.

The justified excitement surrounding new-generation weight loss drugs should not lead to deprioritizing development of nonpharmacologic interventions aimed at the root causes of the epidemic. At $1400 per month, GLP-1 RA treatment of all adolescents with obesity in the US would cost approximately $100 billion annually. Treatment of all adults with obesity would cost approximately $1 trillion. In the US, substantial costs may fall to government through health care reimbursement programs at the state and federal level. These public resources could be used not only to enhance diet quality (eg, supplemental nutrition programs) but also create an environment that encourages spontaneous physical activities and outdoor play (eg, through construction of parks and recreation facilities) as an alternative to screen time and electronic gadgets, with benefits to physical and mental health. Although the costs of new obesity drugs may eventually decrease, they appear to have already exacerbated health care disparities. A spate of media stories suggests widespread use of GLP-1 RAs by high-income individuals with little excess weight for cosmetic reasons even as those with severe obesity-related complications (who disproportionately come from low-income and disadvantaged minority groups) cannot access or afford treatment.

Beyond cost considerations, reliance on drugs for weight control could require lifelong treatment because rapid weight regain occurs after their discontinuation. Although GLP-1 RAs have a good track record of safety, we cannot yet know the potential risks of long-term treatment, begun in adolescence, with this or any drug that modulates fundamental metabolic pathways. Efficacious dietary and behavioral strategies will be needed, if only to prevent weight regain, as people discontinue drug treatment. Furthermore, diet affects health beyond weight control. Even with a population-level decrease in weight from GLP-1 RAs, a low-quality diet could still leave this generation of adolescents at elevated lifetime risk for cardiovascular disease, cancer, and other chronic conditions, independent of weight.

The shared physiologic mechanisms considered earlier raise the intriguing possibility of therapeutic synergy, wherein a low–glycemic load diet might increase the efficacy of GLP-1 RAs, allowing for their use at a lower dosage and thereby reducing acute adverse effects, likelihood of drug intolerance, and long-term risks of unanticipated adverse events.

With their remarkable efficacy, the new GLP-1 RAs inaugurate an era in which obesity could be reconceptualized as a treatable medical condition, lessening social stigma. This class of drugs, now available to adolescents, provides an important option to bariatric surgery for youth experiencing weight-related complications. To advance science and social justice, we must also better fund research into new dietary treatments and overcome obstacles to reimbursement for the intensive behavioral interventions considered necessary by the AAP guideline. Especially for children, diet and lifestyle must remain at the forefront of obesity prevention and treatment.

ARTICLE INFORMATION

Published Online: May 1, 2023. doi:10.1001/jama.2023.7592

Conflict of Interest Disclosures: Dr Ludwig reported receiving royalties from Hachette Book Group for books that recommend a carbohydrate-modified diet and receiving consulting fees for providing advice on pediatric obesity prevention initiatives from the Novo Nordisk Foundation (a charitable foundation). Dr Holst reported serving on the advisory board for Novo Nordisk; being a consultant for AlphaSights, Eli Lilly, and ShouTi/Structure Therapeutics within the last year; and being an unpaid member of the board of directors of Antag Therapeutics and Bainan Biotech outside the submitted work.

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