



Dietary intake by patients taking GLP-1 and dual GIP/GLP-1 receptor agonists: A narrative review and discussion of research needs

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ABSTRACT

Background: Obesity and type 2 diabetes mellitus (T2DM) are increasingly common in the United States and worldwide. Because both conditions are associated with serious health consequences, weight reduction is recommended by professional medical and nutrition societies to improve outcomes. Due to the striking efficacy of glucagon-like peptide receptor agonists (GLP-1RAs) and dual mechanism glucose-dependent insulinotropic polypeptide/glucagon-like peptide receptor agonists (GIP/GLP-1RAs) for weight reduction and glycemic control, there is increased utilization for patients with obesity and/or T2DM. Yet, the impact of these medications on dietary intake is less understood.

Methods: This narrative literature review summarizes clinical studies quantifying and characterizing dietary intake in people with obesity and/or T2DM using GLP-1 or GIP/GLP-1 RAs.

Results: Though data from these studies reveal that total caloric intake was reduced by 16–39 %, few studies evaluated the actual composition of the diet.

Conclusions: Further research is needed to understand the unique nutritional needs of adults on GLP-1 or dual GIP/GLP-1RAs and to support the development of nutritional guidelines for these individuals.

1. Introduction

1.1. Background and objectives for this review

Obesity and type 2 diabetes mellitus (T2DM) are increasingly common in the United States (US), as in other developed countries worldwide [1,2]. In the US, obesity prevalence is estimated at 42 % of the adult population [3], while 38 million US adults (10 %) have diabetes, mostly T2DM (>90 %) [4]. Obesity and T2DM are interrelated clinical conditions with overlapping etiologies and pathophysiology [5]. Both are associated with serious health consequences such as metabolic impairments, cardiovascular dysfunction, physical disability, sarcopenia, declining quality of life, and decreased survival [2,6–10]. The adverse health consequences of obesity and diabetes can be lessened by reduction of excess body weight, particularly excess adiposity; professional

guidelines recommend weight reduction of at least 5–10 % to improve outcomes [11].

Comprehensive obesity management utilizes a spectrum of treatments, including nutrition therapy, physical activity, behavioral interventions, pharmacotherapy, and surgical devices and procedures. Glucagon-like peptide receptor agonists (GLP-1RAs) and dual mechanism GIP/GLP-1 RAs are effective for promoting weight reduction and for improving glycemic control, which has led to heightened usage by people with obesity and/or T2DM. Physiologically, GLP-1 and GIP/GLP-1 RAs stimulate insulin secretion and inhibit glucagon release in a dose-dependent manner and bind to the appetite-regulating centers in the hindbrain, hypothalamus, and mesolimbic pathway [12–15]. The effects of GLP-1 and GIP/GLP-1 RAs include appetite reduction [16], increased satiety [17], and decreased food cravings [18–21]. However, a remaining knowledge gap is how these medications impact the quantity

Abbreviations: AOMs, Anti-Obesity Medications; BMI, Body Mass Index; GLP-1, glucagon-like peptide-1; GIP RA, glucose-dependent insulinotropic polypeptide receptor agonist; GLP-1 RA, glucagon-like peptide receptor agonist; T2DM, type 2 diabetes mellitus; GIP/GLP-1 RAs, glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 receptor agonists; IBT, intensive behavioral therapy; MNT, medical nutrition therapy; RCT, randomized controlled trial; RDN, registered dietitian nutritionist; RA, receptor agonist.

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and quality of dietary intake, i.e., the intake of vitamins, minerals, and macronutrients [22,23]. Reduction in overall dietary intake while taking these medications may contribute to shortfalls in micronutrient intake, while lower protein intake may not be sufficient to sustain muscle health [24].

This narrative review sought to determine what is presently known about the dietary intake of individuals with obesity, overweight, and T2DM who were taking GLP-1 or GIP/GLP-1 RAs. We aimed to: (1) characterize how dietary interventions were implemented, (2) examine if and how dietary intake was quantified, (3) summarize changes in dietary intake, and (4) identify potential gaps in nutritional care among individuals who were taking GLP-1 or GIP/GLP-1 RAs. Further, this review sought to recognize research gaps and opportunities to enhance guidance for healthcare providers who treat people with obesity, overweight, and T2DM.

2. Methods

2.1. Review of dietary intake in individuals taking GLP-1 or GIP/GLP-1 RAs

This narrative review describes studies quantifying and characterizing dietary intake in people with obesity and/or T2DM who were taking GLP-1 or GIP/GLP-1 RAs, as compared to those on other treatments or placebo. Study parameters included medication dose, delivery, timing, concurrent dietary recommendations (if any), and duration of treatment. Study outcomes included data collection on dietary intake, assessment method, and duration of dietary intake versus comparator with focus on energy and nutrient intake. We also collected subjective data on participant appetite, cravings, and food preferences. The involvement of a registered dietitian nutritionist (RDN) in the study was also identified.

2.2. Search strategy

This narrative review of clinical research studies was conducted using the search terms: “Glucagon-like peptide-1 receptor agonist” OR “GLP-1” OR “semaglutide” OR “liraglutide” OR “tirzepatide” AND “intake” OR “diet” OR “nutrition”. Reference lists of relevant publications were also reviewed for studies missed during the initial search. There was no cutoff year for the search. Studies were included if the medication was provided to patients with obesity or T2DM and if dietary intake was reported; details were collected on energy intake, involvement of an RDN, dietary guidance, and patient-reported outcomes (appetite/cravings/eating behavior), if available. Papers must have been published in the English language to be included.

3. Results

3.1. Findings from 10 studies reviewed

The results of 10 eligible research studies are summarized in Table 1. In eight studies, the use of GLP-1 or GIP/GLP-1 RAs by people with obesity or T2DM resulted in decreased calorie intake compared to placebo [16–19,25–30]. The remaining two studies compared intake for people using GLP-1 or GIP/GLP-1 RAs to patients who received dietary counseling and/or behavioral counseling and reported no difference in energy intake between groups [29,30]. Of the 10 studies included, the most common measurement of food intake was a standardized test meal followed by an ad libitum lunch, dinner, or snack [16–19,25–28,30]. One study included a validated instrument for dietary intake assessment, i.e., 24-h dietary recall [29]. Only one study described the dietary counseling and guidance used along with medication [30], whereas others either did not describe if an intervention was provided or stated that patients were advised not to change dietary or physical activity behaviors while taking medication. Just 2 of the 10 included studies

reported involvement of an RDN in delivering a nutrition intervention or counseling either in the intervention or control group.

Participants on GLP-1 or GIP/GLP-1 RAs reduced caloric intake by 16–39 % compared to those receiving placebo treatment [16–19, 25–31]. Beyond changes in caloric intake, 4 studies evaluated changes in macronutrient intake [16,18,25,29]. Two studies compared ad libitum intake at a meal for patients on GLP-1 RA medication or on placebo and found no between-group differences in macronutrient intake [18,25]. Although no between-group difference was found in macronutrient intake, Blundell et al. [18] showed a 35 % lower intake from high-fat and non-sweet foods which was corroborated with a lower explicit liking and wanting for these foods and a higher implicit wanting for low-fat and sweet foods in the semaglutide group compared to placebo group (Table 1). Quast et al. [16] had no control group, instead comparing ad libitum intake between groups on 2 different GLP-1RAs (liraglutide and lixisenatide). Pooled data from both groups showed a significant reduction in carbohydrate, protein, and fat intake; the liraglutide group showed a 17.1 % reduction in protein intake, a 22.7 % reduction in fat intake and a 12.2 % reduction in carbohydrate intake compared to baseline. Although changes in macronutrient intake were not evaluated, Gibbons et al. reported a significant reduction (40.7 %) in energy intake from high-fat foods during meals and snacks for participants on semaglutide compared to those on placebo [17]. Finally, Silver et al. used 24-h recall to compare dietary intake and reported a greater reduction in total and added sugars and greater increase in protein in the dietitian-guided caloric restriction group compared to the medication-alone group [29].

4. Discussion

4.1. Overview

Our review of studies showed that treatment with GLP-1 or GIP/GLP-1 RAs reduced caloric intake by 16–39 %. Due to methodology and the reliance on measuring dietary intake at a standardized meal, specific changes in macro- or micronutrient intake remain to be elucidated. More research is needed to explore changes in quality of the overall dietary intake, intake of macronutrients and micronutrients, and eating patterns in people using GLP-1 or GIP/GLP-1 RAs.

Although this review did not seek to gather all studies evaluating change in appetite perception, multiple studies appeared during the initial search which assessed patient-reported outcomes such as food cravings, emotional eating, and food preoccupation [20,21,32]. For example, an observational study reported that the addition of dietary counseling combined with regular exercise for patients on semaglutide was associated with reduced emotional eating (72.5 % vs 11.5 %; $p < 0.0001$), less external eating (27.5 % vs 10.1 %; $p < 0.0001$), and fewer binge-eating episodes (47.8 % vs 10.1 %; $p < 0.0001$) [20]. Patients also had a reduction in cravings for savory foods (53.6 % vs 14.5 %; $p < 0.001$) as measured by a food craving questionnaire [20]. Another randomized controlled trial (RCT) comparing patients taking liraglutide with intensive behavioral therapy (IBT) versus those just receiving IBT, found that the combination of medication with IBT led to reduced reports of hunger and food preoccupation [32]. Wharton et al., 2023 [21], conducted a double blind RCT of semaglutide with lifestyle modification compared to placebo with lifestyle modification. This study concluded that control of eating questionnaire scores significantly improved with semaglutide along with significant decreases in cravings for salty, spicy, dairy, and starchy foods. Although the results of these studies support the hypothesis that the quality of dietary intake is altered for patients on GLP-1 or GIP/GLP-1 RAs, they did not objectively measure dietary intake so these, as well as similar studies evaluating appetite perception, were not included in this review.

Table 1
Summary of Included Studies that evaluated dietary intake of patients on GLP-1 or GIP/GLP-1 RAs.

Author/Year/ Country	Study Design/ Outcomes/Duration	Participants/ Condition/ Age	Medication	Control	Dietary Assessment Method	Dietary Outcomes/Results	Conclusion
Quast et al. [16], 2021/Germany	Single center, randomized, investigator blinded and parallel group	N = 50/T2DM	Liraglutide (1.8 mg daily (qd))	Lixisenatide (20 µg qd)	Overnight fast followed by ad libitum breakfast at baseline and after 10 weeks (wks)	Pooled analysis of both groups showed reduced energy (-582.3 kJ; 95 % CI -886.8, -277.8; p = 0.0003), carbohydrate (14.7 ± 4.6 g; p = 0.0015), protein (-5.2 ± 2.0 g; p = 0.011), and fat (-9.1 ± 2.8 g]; p = 0.0032) intake from baseline. Liraglutide reduced energy intake by 16.7 % (-690.7 kJ, 95 % CI -1114.5, -266.9; p = 0.0025), carbohydrate by 14.1 % (-14.1 g; 95 % CI -26.9, -1.3; p = 0.032), protein by 17.1 % (-6.5 g; 95 % CI -12.3, -0.7; p = 0.03), and fat intake by 22.7 % (-9.1 g; 95 % CI -14.8,-3.4; p = 0.0032) compared to baseline. Lixisenatide significantly reduced energy (-464.9 kJ; 95 % CI -931.6, 1.7; p = 0.051) and carbohydrate (-15.4 g; 95 % CI -28.3, -1.3; p = 0.022) but not protein or fat intake compared to baseline.	Significant reduction in energy and macronutrient intake occurred with liraglutide and lixisenatide.
	Appetite, satiety, macronutrient	18–70 years (yrs)	BMI 18–40 kg/m ²	No mention of whether dietary guidance was provided with medication	No mention of whether dietary guidance was provided with medication		
Gibbons et al. [17], 2021/United Kingdom	Intake in people with T2DM 10 weeks duration	BMI 18–40 kg/m ²	No mention of whether dietary guidance was provided with medication	No mention of whether dietary guidance was provided with medication			
	Single center, randomized, double- blind, placebo controlled, 2-period cross-over	N = 15/T2DM	Semaglutide (qd oral,	Placebo	Standardized breakfast followed by ad libitum lunch, evening meal, snack box after 12 wks	Total energy intake from the standardized breakfast was significantly lower (38.9 %) in 13 evaluable participants using semaglutide compared to those using placebo (-5096.0 kJ; 95 % CI -7000.0, -3192.1; p = 0.0001). During meals and snacks, energy intake from high-fat foods was significantly reduced by 40.7 % compared to placebo (-1381.9 kJ; 95 % CI -2248.6, -515.1; p = 0.0026). VAS postprandial score for overall appetite significantly lower after a fat-rich breakfast for semaglutide versus placebo (p = 0.0059). No difference in fasting and postprandial thirst score between groups. Palatability VAS scores were similar between groups with no indication of food aversion.	Improved satiety and eating control resulted in weight loss and lower body fat mass with semaglutide use.
Blundell et al. [18], 2017/United Kingdom-	Energy intake, food preference, appetite, control of eating in people with T2DM	18–75 yrs	4-wk dose escalation from 3 to 14 mg)				
	12 weeks duration	BMI 20–38 kg/m ²	No mention of whether dietary guidance was provided with medication				
Blundell et al. [18], 2017/United Kingdom-	Single center, randomized, double blind, placebo- controlled, 2- period crossover	N = 30/ Obesity	Semaglutide (1 mg subcutaneously (SC) once weekly)	Placebo	Standardized breakfast followed by ad libitum lunch, evening dinner, snack box at the end of 12 wks.	Ad libitum energy intake was significantly reduced at lunch, snack, and dinner in the intervention group resulting in a relative 24 % reduction in total	Weight loss from semaglutide results from reduced energy intake and appetite, improved control of eating, fewer food

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Table 1 (continued)

Author/Year/ Country	Study Design/ Outcomes/Duration	Participants/ Condition/ Age	Medication	Control	Dietary Assessment Method	Dietary Outcomes/Results	Conclusion
	Energy intake, appetite, and food preference in people with obesity without diabetes.	≥18 yrs 12 weeks duration	BMI 30–45 kg/m ²			caloric intake –3036 kJ; 95 % CI -4209, –1864; (p < 0.0001) over the day compared to the placebo group. No significant differences in between-group proportional intake of macronutrients at dinner or snack or postprandial thirst between groups. No mention of whether dietary guidance was provided with medication	cravings, and lower preference of fatty, energy dense foods.
4	Energy intake by food category for the evening ad libitum snack box showed a 35 % relative difference in intake from high-fat and non-sweet foods for semaglutide vs. placebo (–368.4 kJ; 95 % CI -674, –62.7; p = 0.0184). The Leeds Food Preference Task showed a lower explicit liking for high-fat and non-sweet foods for semaglutide vs. placebo (–13.9 mm; 95 % CI -22.5, –5.4; p = 0.0016). Ratings of implicit wanting were lower for high-fat and non-sweet foods (–15.8 mm; 95 % CI -29.1, –2.5; p = 0.0203) and higher for low-fat and sweet-foods (13.9 mm; 95 % CI 0.6, 27.3; p = 0.0401) with semaglutide vs. placebo. The overall appetite suppression score was significantly						

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Table 1 (continued)

Author/Year/ Country	Study Design/ Outcomes/Duration	Participants/ Condition/ Age	Medication	Control	Dietary Assessment Method	Dietary Outcomes/Results	Conclusion
						higher in the intervention compared to the placebo group (p = 0.0023).	
Friedrichsen et al. [19], 2021/Germany	Single center, randomized, double-blind, placebo-controlled, parallel-group, trial. Appetite and energy intake in adults with obesity 20-week treatment duration, 7-week follow-up	N = 72/ Obesity 18–65 yrs BMI 30–45 kg/m ²	Semaglutide (2.4 mg once weekly SC) No mention of whether dietary guidance was provided with medication	Placebo	Standardized breakfast followed by ad libitum lunch	Mean percent change from baseline in energy intake at ad libitum lunch was reduced by 47.1 % in intervention vs. 18.6 % in placebo (95 % CI 28.5 %; –42.3, –14.7; p = 0.0001). Intervention group reported higher overall appetite score (Estimated treatment difference [ETD] 13 mm; p = 0.001) and lower cravings for dairy (p = 0.0231) and savory foods (p = 0.0076)	Improved eating behavior control, suppressed appetite, reduced food cravings led to weight loss with semaglutide use.
Flint et al. [25], 2013/Germany	Randomized, placebo-controlled, double blind, two-period, crossover study Appetite, energy intake, and macronutrient composition in patients with T2DM 3 weeks duration	N = 18/T2DM 18–70 years (yrs) BMI 18.5–40 kg/m ²	Liraglutide (qd SC), doses escalated weekly from 0.6 to 1.8 mg) No mention of whether dietary guidance was provided with medication	Placebo	Standardized breakfast test meal weekly, ad libitum lunch measured at the end of each treatment week (wk)	Mean estimated energy intake was 18 % lower in intervention than placebo group [intervention: 4019 kJ, placebo: 4855 kJ; estimated ratio 0.82 (95 % CI 0.73, 0.94); p = 0.004]. No significant difference in macronutrient intake, or postprandial thirst. Mean postprandial [intervention: 44 mm, placebo: 51 mm; estimated ratio –7.3 (95 % CI –11.8, –2.7); p = 0.002] and minimum hunger ratings [intervention: 25 mm, placebo: 33 mm; estimated ratio –8.9 (95 % CI –15.0, –2.8); p = 0.005] significantly lower for the intervention group. Mean overall appetite score [intervention: 48 mm, placebo: 43 mm; estimated ratio 4.5 (95 % CI 0.0003; 9.0); p = 0.05] significantly higher which indicated reduced appetite in intervention group.	The use of liraglutide decreased hunger and appetite, which reduced oral intake and resulted in weight loss.
Van Can et al. [26], 2014/Netherlands	Single center, randomized, double blind, two period incomplete cross-over study Appetite and energy intake in people having obesity, without diabetes	N = 49/ Obesity 18–75 yrs	Liraglutide (qd SC, doses escalated to 1.8 mg or 3 mg/d) with no dietary or exercise changes recommended	Placebo	Standardized breakfast test meal followed by ad libitum lunch at baseline and after 5 wks	Energy intake during ad libitum lunch was reduced by 588 [95 % CI –951, –224; p = 0.002] and 568 kJ [95 % CI –937, –199; p = 0.003] (~16 % compared to placebo) in the groups receiving 1.8 and 3 mg liraglutide compared to placebo.	Reduced appetite and decreased energy intake resulted in weight loss with the use of liraglutide.

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Table 1 (continued)

Author/Year/ Country	Study Design/ Outcomes/Duration	Participants/ Condition/ Age	Medication	Control	Dietary Assessment Method	Dietary Outcomes/Results	Conclusion
	<i>5 weeks duration</i>	BMI 30–40 kg/m ²				Mean, maximum and postprandial visual analog scores were significantly improved ($p < 0.01$) for overall appetite (reduced appetite), satiety, fullness, and prospective food consumption in liraglutide groups compared to placebo.	
Saxena et al. [27], 2021/United States	Randomized, double-blind, placebo-controlled, two-arm, parallel-group.	N = 61/ Obesity	Liraglutide (up to 3 mg/d); patients were advised to maintain their normal diet and physical activity	Placebo	Standardized breakfast, followed by ad libitum lunch at wk 3 and wk 6	Mean difference in energy intake change from baseline between intervention and placebo was -236 kcal (95 % CI $-322, -149$; $p < 0.0001$) at wk 3 and -244 kcal (95 % CI $-339, -148$, $p < 0.0001$) at wk 6.	Single meal intake was a predictor of weight change in patients with obesity.
	Energy intake in adults with obesity <i>6-week duration</i>	18–75 yrs BMI 30–40 kg/m ²				Compared to placebo, mean differences in change from baseline body weight was significantly reduced with treatment (-3.85 kg; 95 % CI $-4.71, -2.99$; $p < 0.001$) at 6 wks.	
Heise et al. [28], 2023/United States	Secondary analysis of a randomized, double-blind, parallel-arm study	N = 121/ T2DM	Semaglutide (1 mg) or Tirzepatide (15 mg) once weekly	Placebo	Ad libitum intake at buffet lunch at baseline, and wks 8, 16, and 28	Semaglutide group had greater reductions in energy intake from baseline compared to placebo at wk 8 (-130.2 kcal; SE $-257.4, -3.0$; $p = 0.045$), wk 16 (-143.4 kcal; standard error (SE) $-282.4, -4.4$; $p = 0.043$) and wk 28 ($p < 0.001$). The tirzepatide group had greater reductions in energy intake from baseline compared to placebo at wks 8 (-185.3 kcal; SE $-312.7, -57.8$; $p = 0.005$) and 28 (-309.8 kcal SE $-423.0, -196.6$; $p < 0.001$). Although appetite reduced from baseline with both tirzepatide and semaglutide ($p < 0.001$), but not placebo, only tirzepatide significantly reduced appetite compared to placebo (15.0; SE 4.1, 25.9; $p = 0.007$).	Significant weight reduction (fat mass loss) along with reduced appetite and energy intake occurs with the use of either semaglutide or tirzepatide.
	Energy intake and appetite in adults with T2DM	52–69 yrs					
	<i>28-week duration</i>	BMI 24–45 kg/m ²	No mention of whether dietary guidance was provided with medication				
Silver et al. [29], 2023/United States	Prospective, randomized, parallel-group intervention trial	N = 88/ Prediabetes	Medical intervention groups used either liraglutide (1.8 mg/d) or sitagliptin (100 mg/d) without other dietary advice.	A comparator calorie restricted (CR) group had a nutritional counseling session with a registered dietitians who also provided a daily calorie intake goal to achieve a 390-calorie deficit below resting energy expenditure.	Dietary intakes were assessed for all three groups by averaging three 24-h diet recalls obtained within 10 days of the baseline and final testing visits (including two non-consecutive weekdays and one weekend day).	All groups reduced energy intake with an average reduction of 300 ± 891.8 kcal/d ($p = 0.007$) from baseline. Changes in energy intake were not significantly different between groups. Intake of total sugars (CR vs. liraglutide: -29.5 g [95 % CI $-5.0, -54.8$], $p = 0.02$; CR vs. sitagliptin: -25.1 g [95 % CI $-25.9, -75.2$], $p = 0.02$; liraglutide vs sitagliptin:	Calorie restriction alone led to weight loss and improved body composition. Liraglutide and calorie restriction combined can reduce cardio-metabolic risk.
	Energy and dietary intake in adults with obesity and prediabetes	18–65 yrs					

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Table 1 (continued)

Author/Year/ Country	Study Design/ Outcomes/Duration	Participants/ Condition/ Age	Medication	Control	Dietary Assessment Method	Dietary Outcomes/Results	Conclusion
						<p>–9.9 g [95 % CI -14.4, 34.2], p = 0.42) and added sugars (CR vs. liraglutide: –31.1 g [95 % CI -9.7, –52.5], p = 0.005; CR vs. sitagliptin: –23.0 g [95 % CI -67.4, –21.4], p = 0.005; liraglutide vs sitagliptin: –5.6 g [95 % CI -42.9, 31.6], p = 0.43) was decreased significantly and to a greater extent in the calorie-restricted group than in groups receiving medication with no dietary guidance. Protein intake as % kcals was significantly increased in the CR group compared to the other groups (difference CR vs. liraglutide: 4.0 % kcal [95 % CI 0.3, 7.7], p = 0.03; CR vs. sitagliptin 5.4 % kcal [1.7, 12.6], p = 0.03; liraglutide vs. sitagliptin: 1.4 % kcal [95 % CI -2.3, 4.9], p = 0.46).</p>	
Kadouh et al. [30], 2020	<p>14-week duration</p> <p>Sub-study of a single-center, double-blind, placebo-controlled, parallel group, randomized trial Appetite and taste preference in adults with obesity</p> <p>16-week duration</p>	<p>BMI ≥30 kg/m²</p> <p>N = 35/ Obesity</p> <p>18–65 yrs</p> <p>BMI >30 kg/m²</p>	Liraglutide (3 mg) with behavioral weight management and dietetic counseling at baseline, wks 4, 8 and 12	Placebo with behavioral weight management and dietetic counseling at baseline, wks 4, 8 and 12	Standardized breakfast, followed by ad libitum lunch at wk 16. Appetite and taste preferences measured after standardized meal.	<p>Compared to placebo, liraglutide showed significant reductions in maximum tolerated volume (MTV) (liraglutide: 750.0 mL [651.0, 908.0] vs placebo: 1126.0 mL [944.0, 1185.0]; p = 0.054), prospective food consumption score (liraglutide: –4461.0 [-7560.0, –460.0] vs placebo 420.0 [-3945.0, 3838.5]; p = 0.03), desire to eat something sweet (liraglutide: 420.0 [-3945.0, 3838.5] vs placebo: –1245.0 [-4636.0, 510.0]; p = 0.02), salty (liraglutide: 5235.0 [–230.0, 9705.0] vs –2565.0 [-6053.5, 1027.5]; p = 0.005), or savory (liraglutide: 3165.0 [-1830.0, 6735.0] vs placebo –2580.0 [-7830.0, 795.0]; p = 0.006) or fatty (liraglutide: 6000.0 [2614.0, 12975.0] vs placebo: –1350.0 [-4852.5, 4177.5]; p = 0.002), and an increase in perceived fullness (liraglutide: 4065.0 [1513.0, 6870.0] vs placebo: 1650.0 [-3352.5, 3367.5]; p = 0.02).</p>	The combined use of liraglutide with dietetic and behavioral counseling increased the feeling of fullness and modulated taste preference
Halawi et al. [31], 2017/United States	<p>Randomized, double-blind, placebo-controlled pilot trial Energy intake in adults with obesity</p> <p>16-week duration</p>	<p>N = 35/ Obesity</p> <p>18–65 yrs</p> <p>BMI >30 kg/m²</p>	Liraglutide (3 mg qd) with behavioral weight management and dietetic counseling at baseline, wks 4, 8 and 12	Placebo with behavioral weight management and dietetic counseling at baseline, wks 4, 8 and 12	Standardized breakfast, followed by ad libitum lunch at wk 16.	<p>Ad libitum energy intake was not significantly different between liraglutide (median 554 kcal [IQR 406–687]) and placebo (680 kcal [513–1002]) (p = 0.27)</p>	Energy intake was not significantly different after 16 wks of combined liraglutide with behavioral weight management and dietetic counseling vs behavioral weight management and dietetic counseling alone.

4.2. Future studies needed

To fill existing research gaps, we recommend future studies to examine not only the quantitative change in calorie intake but the qualitative changes in macro- and micronutrient intake including dietary patterns for patients using highly effective anti-obesity medications. Moreover, given the vital role that protein plays in maintaining muscle health and function, the quantity and quality of protein intake is especially important to monitor. To date, some studies report lower intake of certain micronutrients in people with obesity [33–35], but future studies need to examine risk of worsening nutrient status following use of anti-obesity medications and protocols. Such knowledge is needed to guide optimal nutritional support for patients undergoing treatment with GLP-1 or GIP/GLP-1 RAs.

Another question for future research is whether intake differs for patients using GLP-1 or GIP/GLP-1 RAs for obesity management versus diabetes management. People with diabetes, for example, may have different dietary intake due to greater access to RDN intervention through diabetes self-management education and support courses. Depending on the specific GLP-1 or GIP/GLP-1 RA medication prescribed and the indication for which it is prescribed, the dose of medication may vary, which could indirectly impact weight reduction through differences in appetite, side effects, or the mechanism of action of the medication itself. Risk for muscle loss increases as people age, especially in those with diabetes, who also have an increased risk for sarcopenia [36,37]. A possible contributor to muscle loss in patients with T2DM is insulin resistance, which impairs glucose uptake by muscle and can reduce its mass, strength, quality, and function [38]. Other potential contributors to low muscle mass include fat accumulation in the muscle, mitochondrial and stem cell dysfunction, weight cycling, physical inactivity and inadequate intake of energy and protein [2,39,40]. Low muscle mass, strength, and function are associated with risk of incident T2DM [36] and predict risk of poor outcomes in adults with T2DM [10]. Outside of people with T2DM, sarcopenia in older adults is associated with poor outcomes including poor physical function, poor quality of life, and reduced survival, therefore, adequate protein is emphasized to support muscle health [6,10,39,41].

4.3. Nutritional concerns

4.3.1. Nutritional concern #1: inadequate protein intake to maintain muscle mass, strength, and function

Low food intake and poor diet quality may contribute to loss of muscle in individuals taking GLP-1 or GIP/GLP-1 RAs. Increased risk of muscle loss is seen in people who report a history of weight cycling (bouts of weight reduction and regain, i.e., “yo-yo” dieting) or those who reduce weight without accompanying exercise [9,24,42–45]. While muscle loss or sarcopenia is often associated with older age, obesity-associated sarcopenia can also occur in young and middle-aged women in weight management settings [46]. Studies of various weight reduction interventions showed that 11–50 % of total weight reduction can be attributed to loss of lean body mass, which may include loss of skeletal muscle [24,47–49].

4.3.2. Nutritional concern #2: inadequate dietary quality: poor intake of micronutrients, fiber, and fluids

According to the Dietary Guidelines for Americans, fiber, vitamin D, iron, calcium, and potassium are nutrients of public health concern, i.e., they may be under-consumed in the American diet. In fact, fewer than 5 % of adults consume more than the RDA for fiber. Fiber intake is even lower among people with obesity [33]. This data was collected from adults in the general population who were not necessarily reducing dietary intake for weight reduction, so intake may be even less among those intentionally pursuing weight reduction.

With reduced caloric intake and reduced appetite, it is possible that individuals taking GLP-1 or GIP/GLP-1 RAs may reduce the overall

intake of micronutrients. Compared to normal-weight adults, those with obesity had 5–12 % lower usual intake of vitamins A, C, D and E, calcium, magnesium, and potassium [33]. They were also less likely to meet the estimated average requirement for vitamins A, C, D and E, calcium, and magnesium. These patients were not necessarily pursuing weight reduction through calorie restriction, therefore, intake may be even less while pursuing weight reduction.

4.4. Nutrition guidelines for patients on anti-obesity medications

Although multiple nutritional concerns exist for individuals with overweight/obesity, little guidance is available for those pursuing treatment with GLP-1 or GIP/GLP-1 RAs [50]. For patients with T2DM pursuing weight reduction through dietary restriction, the American Diabetes Association guidelines advise dietary interventions and discuss structured, low-calorie meal plans (800–1000 kcal/day) and incorporation of high-protein foods and meal replacement products to support weight reduction and glycemic improvement compared to standard behavioral modifications only [51]. While agents from the GLP-1 and GIP-1/GLP RA classes are advised for treatment of T2DM and overweight/obesity, specific dietary needs for this population are not discussed [51].

The Obesity Medicine Association (OMA) publishes management guidance on nutrition, physical activity, behavioral therapy, and pharmacotherapy, including anti-obesity medications [52–54]. A guideline from the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society was published in 2014, but recently approved pharmacological treatments for obesity were not included [55]. More recently, the efficacy of newer generation anti-obesity medications was reviewed, but nutrition management protocols were not included [56]. Clinical practice guidelines also exist for patients pursuing obesity treatment via bariatric devices and surgery [57]. In summary, while diet is an essential aspect of obesity management, recommendations for optimal dietary intake are lacking for patients using anti-obesity medications. Specific nutritional questions remain: (i) What changes occur in dietary intake patterns for these patients, especially diet quality? (ii) Are patients meeting macronutrient needs, especially protein? (iii) Are patients meeting micronutrient intake needs?

As we await guidelines and further research results, clinicians should discuss the importance of balanced nutritional intake with all patients prescribed GLP-1 and GIP/GLP-1 RAs and provide access to an RDN whenever possible. Dietary counseling can also include ways to provide variety and nutritional adequacy. Likely, guidance needs to emphasize intake of adequate protein with complete amino acid profile, as well as optimal protein intake timing. Fruits and vegetables may also be prioritized, along with reduction of energy intake, and provision of fiber, vitamins, and minerals. Supplementation can help meet protein and micronutrient needs for patients who are unable to consume adequate nutrition through usual dietary intake. Monitoring should consider changes in body composition, physical function, and potential signs of malnutrition or micronutrient deficiencies (hair loss, fatigue). Due to the potential loss of lean body mass with the use of GLP-1 and GIP/GLP-1 RAs, the OMA advises baseline body composition analysis with reassessment at regular intervals, if there is a substantial weight reduction in a short period of time, or if weight reduction is considered to be excessive [58,59]. This is particularly important for those who have or are at risk for sarcopenia. Laboratory tests (e.g., vitamin B12, 25(OH) vitamin D, iron, folic acid) can be ordered to monitor for micronutrient insufficiencies [60]. Dietary counseling by an RDN or trained clinician is essential to improve outcomes for patients with obesity and/or T2DM. The Academy of Nutrition and Dietetics calls on the medical community, including pharmaceutical manufacturers of anti-obesity medications, obesity medicine providers and other health care practitioners who treat obesity, “to enhance the efficacy of these medications and maximize patient success rates by including a referral for medical nutrition

therapy from a registered dietitian nutritionist alongside prescriptions for anti-obesity medication.” [61].

Physical activity. The OMA advises healthcare professionals conduct pre-exercise medical evaluations and provide suggestions regarding types and recommended amounts of dynamic (aerobic) training, resistance (anaerobic) training, and leisure time physical activities for patients seeking obesity treatment [52]. Physical activity is key to achieving optimal health outcomes including preservation of muscle during weight reduction, therefore, involvement of physical therapists

essential vitamins and minerals for overall health. One of the limitations of this narrative review is the absence of definitive data on outcomes related to dietary intake in this population. Additional studies are needed to describe changes in dietary patterns and diet quality in individuals using GLP-1 or GIP/GLP-1 RAs, including macronutrient and micronutrient intake. Studies are also needed to determine whether differences exist in nutritional status, weight reduction, health, and quality of life when GLP-1 or GIP/GLP-1 RAs are used concurrently with Medical Nutrition Therapy guided by an RDN.

Box 1. Summary of key messages on dietary changes for patients on GLP-1 or GIP/GLP-1 RAs.

What is known about dietary intake of patients on GLP-1 RA or GIP/GLP-1 RAs.

- In 10 studies of patients using GLP-1 or GIP/GLP-1 RAs, calorie intake was reduced by 16 to 39 % compared to placebo treatment. [16–19,25–30].
- Intake in these studies was most commonly measured using ad libitum intake rather than the gold-standard of 24-h recall.
- Only 1 study described dietary counseling and guidance provided along with taking GLP-1RA medications, [30] and just 2 studies specified involvement of a registered dietitian. [29,30].
- Just 4 studies evaluated changes in macronutrient intake in addition to changes in energy intake. [16,18,25,29] Changes in macronutrient intake were inconsistent among studies.

Remaining questions about dietary intake of patients on GLP-1 or GIP/GLP-1 RAs.

- How do GLP-1 or GIP/GLP-1 RAs impact eating patterns and diet quality (macro/micronutrients)?
- Are changes in dietary intake (i.e., protein) associated with altered body composition during weight reduction?
- What is the most appropriate dietary guidance for people taking GLP-1 or GIP/GLP-1 RAs

or clinical exercise physiologists should be considered to improve patient movement and functionality by enhancing engagement in age- and ability-adjusted exercises [61].

Behavior therapy. Behavior therapy, as part of intensive lifestyle interventions, helps support patients as they adopt or maintain healthful behaviors. Behavioral counseling with a mental health professional can help address mood disturbance or disordered eating and can also provide strategies to tackle environmental or emotional triggers for food seeking behaviors [62].

4.5. Recommendation: multi-modal healthcare is needed to manage people with obesity and T2DM

Multiple healthcare professionals—physicians, nurse practitioners, and physician associates who specialize in obesity management, primary care, endocrinology, and diabetology, as well as RDNs, physical therapists, and behavioral therapists—need to work as a team to achieve effective, holistic care. Clinicians increasingly need training to provide the latest comprehensive, evidence-based care for people with obesity and T2DM. With increased awareness and utilization of GLP-1 or GIP/GLP-1 RAs, up-to-date educational programs are needed to educate healthcare professionals on not only medication selection and dosing but also the importance of nutritional support and adequacy [61].

5. Conclusions

With the emergence of GLP-1 and GIP/GLP-1 RAs, there are more treatment options for obesity and T2DM. Results of studies in individuals with obesity (with or without T2DM) taking GLP-1 or GIP/GLP-1 RAs showed significant reductions in energy intake, appetite, and food cravings. Nonetheless, there is a paucity of data on the adequacy of protein intake for maintenance of muscle mass and function or intake of

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CRedit authorship contribution

KR and ST conducted the literature review and wrote draft materials. All authors reviewed the final manuscript and approved the final submission and publication.

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