Nutritional Interventions to Address Deficiencies and Side Effects Associated with the Use of GLP-1 Receptor Agonist: A Systematic Review

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Abstract

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have transformed the management of obesity and type 2 diabetes by promoting weight loss and improving cardiometabolic outcomes. However, gastrointestinal adverse effects and reduced dietary intake may contribute to micronutrient deficiencies, lean body mass loss, poor adherence, and compromised long-term health. This systematic review evaluated nutritional strategies for mitigating these risks in accordance with PRISMA guidelines. PubMed, Scopus, Web of Science, and Google Scholar were searched for studies published between 2010 and 2025. Eligible studies included adults receiving GLP-1 RAs and reporting nutritional deficiencies, gastrointestinal adverse events, dietary intake, lean-mass outcomes, or nutrition interventions. Data were extracted and synthesized thematically. Deficiencies of vitamin D, calcium, magnesium, potassium, iron, and vitamin B12 were frequently reported, together with nausea, vomiting, and delayed gastric emptying. Lean body mass represented approximately 30–40% of total weight loss, emphasizing the importance of adequate protein intake and structured resistance exercise. Individualized micronutrient supplementation, small frequent meals, dietary modification, and comprehensive nutrition counseling helped correct deficiencies, manage symptoms, and improve treatment adherence. Evidence and implementation gaps were particularly apparent for socioeconomically disadvantaged individuals, older adults, and pediatric populations. Although GLP-1 RAs provide substantial metabolic benefits, they may create clinically important nutritional risks. Routine nutritional assessment, symptom monitoring, protein optimization, appropriate supplementation, and exercise support are therefore essential. Future research should establish standardized protocols and evaluate integrated nutrition-care models across diverse real-world populations.

Keywords: GLP-1 receptor agonist, Nutritional deficiencies, Protein intake, Micronutrient supplementation, Gastrointestinal side effects, Obesity, Type II diabetes.

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1. Introduction

The agonists of glucagon-like peptide-1 receptor (GLP-1 RAs) have emerged as a central component of the treatment plan of obesity and type 2 diabetes, with semaglutide, liraglutide, and tirzepatide showing significant effectiveness in the elicitation of clinically meaningful weight loss and cardiometabolic index improvement (Gorgojo-Martinez et al., 2022). Weight losses of between 5 -18 per cent placebo-adjusted have been reported, which coincides with improvements in glycaemic control, lipid metabolism and renal status. Due to their clinical importance, GLP -1 RA have been added to the Essential Medicines List of the World Health Organization, supporting their implementation as part of a multidisciplinary, long-term obesity management strategy (World Health Organization, 2025).

Despite these benefits, GLP-1 RA treatment is associated with severe nutritional and gastrointestinal safety incidents. Appetite suppression, early satiety, gastrointestinal issues such as nausea, vomiting, diarrhoea and constipation do not spare 40-70% of patients and trigger reduced caloric intake, micronutrient loss, and discontinuation of the therapy (Gorgojo-Martinez et al., 2022; Ismaiel et al., 2025). There is evidence that there will be a considerable number of patients who develop a deficiency in vitamin D, calcium, magnesium, iron, and vitamin B12 during the first year of treatment, and disproportionate depletion of lean body mass further worsens metabolic health and physical functionality (Butsch et al., 2025; Spreckley et al., 2025).

The pharmacodynamic effectiveness of GLP-1 RAs is undeniable, however there is a lack of a rigorous dietary curriculum. Instead of being proactive in using evidence-based treatments, modern healthcare practice has been more reactive in addressing deficiencies and GIT sequelae (Mozaffarian et al., 2025). Therefore, there is a pressing need of specific nutritional measures, which could be optimized protein intake, micronutrient supplement, and changes in the diet directed at improving gastrointestinal tolerability. The current study critically examines these interventions in a bid to prevent GLP 1 RA related failures and adverse outcomes thus promoting safe, efficient and effective treatment.

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2. Materials and Methods

2.1 Study Design and Review Framework

To provide transparency, methodological rigor, and reproducibility, the systematic literature review was conducted in compliance with the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The PRISMA protocol provides a systematic and universal way of determining relevant literature, filtering studies, using inclusion and exclusion criteria, and retrieving data as well as synthesizing outcomes. A rigorous compliance with the given framework can increase the reliability and validity of the review process by reducing the selection bias, recording the decision pathways, and providing the methodological reliability (Thomé et al., 2016).

A systematic review approach was chosen due to the emerging nature of the studies that examine nutritional interventions in patients receiving GLP-1 receptor agonists, in order to gather fragmented evidence and come up with a synthesis of dietary interventions aimed to alleviate the effects of micronutrient deficits, gastrointestinal adverse effects, and lean mass loss in patients treated with GLP-1 RA. The thematic framework was used to analyze and identify, interpret, and organize recurrent patterns in different study designs.

2.2 Data Sources and Search Strategy

The literature review included academic databases as PubMed, Scopus, Web of Science, and Google Scholar that are known to be covered with a significant amount of clinical, nutritional, and pharmacological inquiries (Gusenbauer and Haddaway, 2020). The search strategy focused on articles published in 2010-2025 to include current evidence related to GLP -1 RA therapy and nutritional management. Combination of search terms was transmitted by means of keywords, Boolean operators, and MeSH terms. Keywords like, GLP-1 receptor agonists, semaglutide, liraglutide, tirzepatide, nutritional deficiency, micronutrient deficiency, lean mass loss, sarcopenia, gastrointestinal side effects, nutrition intervention, protein assimilation, micronutrient supplementation, dietary modification, dietary strategies, obesity pharmacotherapy, and nutritional management. Each database had its search strings modified in order to achieve maximum sensitivity and relevancy. Additional articles were manually screened as reference lists of the qualifying articles and pivotal reviews to provide completeness.

2.3 Eligibility Criteria

The selection of the studies was based on PECO model (Population, Exposure, Comparator, Outcome), which offers a systematic way of finding relevant studies.

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Table 1: Eligibility Criteria Based on PECO Framework

Criteria	Inclusion	Exclusion
Population	Patients using GLP-1 RAs for obesity or type 2 diabetes	Studies involving animals, or non-GLP-1 RA therapies
Exposure	Use of GLP-1 receptor agonists (e.g., semaglutide, liraglutide, tirzepatide) associated with nutritional deficiencies or side effects	Studies examining GLP-1 physiology unrelated to medication use
Comparator	With or without a comparator group	—
Outcomes	Nutritional deficiencies, GI adverse events, protein intake, micronutrient status, lean mass outcomes, or effectiveness of nutritional interventions	Studies without nutrition-related outcomes
Study Design	Randomized controlled trials, observational studies, clinical guidelines, qualitative studies, and systematic reviews	Non-peer-reviewed articles, conference abstracts, editorials, commentaries

2.4 Study Selection and PRISMA Flow Process

The results of all searches were imported into endnote software and duplication removed. Relevance of titles and abstracts was done and full-text evaluated against the eligibility criteria. The causes of exclusion were recorded at every phase. A PRISMA flow diagram was used to record the selection process summarizing the number of identified, screened, eligible and included studies in the final synthesis.

2.5 Quality Assessment

The quality of the incorporated studies was evaluated by the modified version of Quality Assessment Tool of Studies of Varying Design (QATSDD). The tool was chosen due to its suitability for incorporating different study designs within a review. Clarity of purpose, technique suitability, sample description, data collection procedure, analytic rigor, and findings relevance were among the evaluation criteria. Each study's quality score was determined, but it wasn't the sole criterion for inclusion in the synthesis.

2.6 Data Extraction Process and Thematic Analysis

It was created as a structured data-extraction tool to offer the consistency and rigor of approach. The tool collected information on study characteristics, demogphics, the type and dosage of GLP-1 receptor agonist (GLP-1 RA), reported nutritional deficiencies, nutritional intake, gastrointestinal side effects, and specific nutritional interventions under investigation (e.g., protein optimization, micronutrient supplementation, dietary counseling). Error was reduced by cross-verifying the extracted data. Because the study design, study outcomes, and intervention modalities varied, a narrative synthesis was conducted and backed by an official theme analysis. This analytical approach made it possible to identify successful nutrition interventions for GLP-1 RA patients and helped with the methodical interpretation of the results of various techniques.

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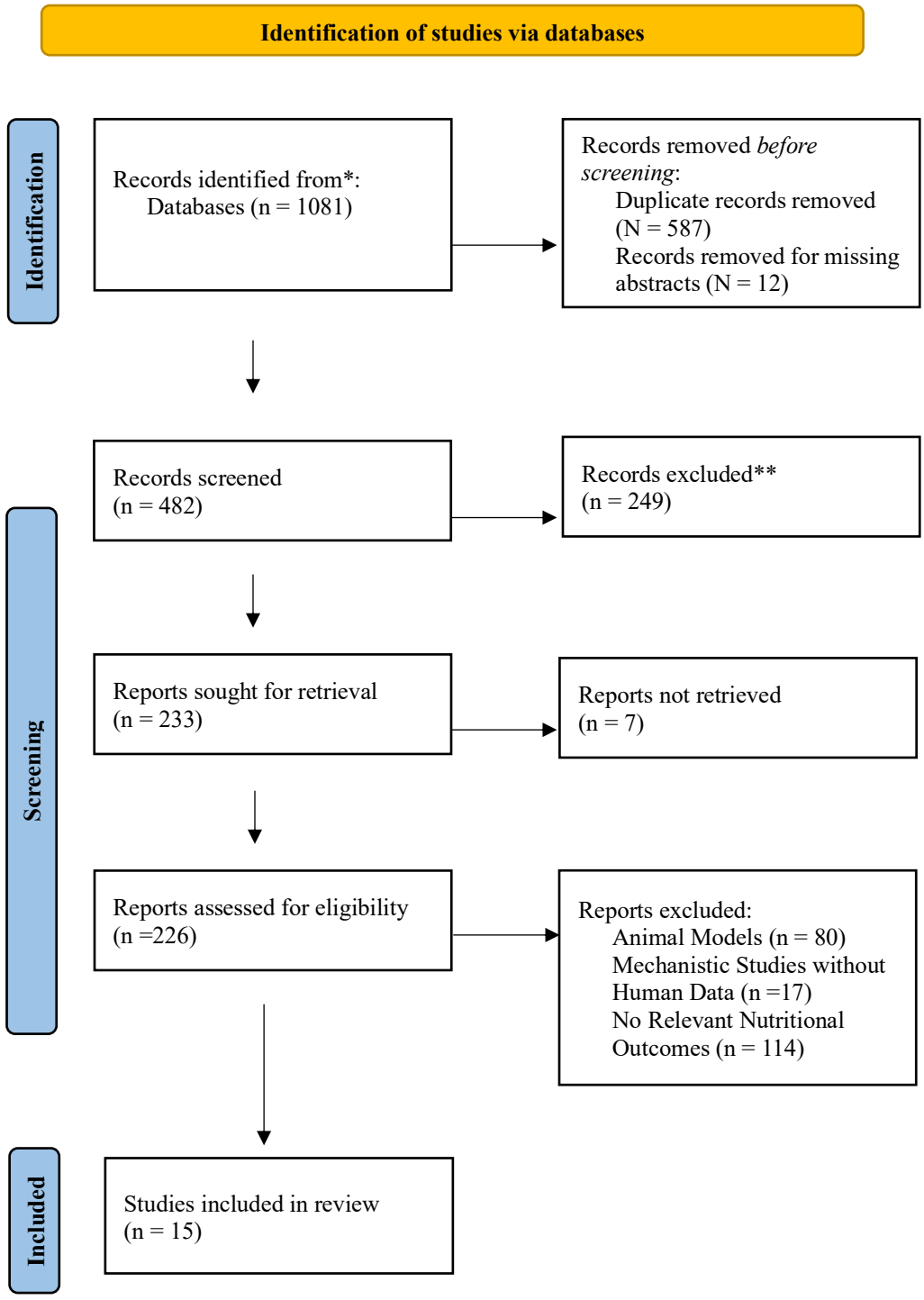

Figure 1: PRISMA Flow Diagram

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3. Results

Significant trends in the dietary effects, physiological ramifications, suggested interventions, and population-specific issues of GLP-1 RA therapy were identified by this synthesis of the evidence in the evaluated papers. The prevalence and types of dietary deficiencies, gastrointestinal and metabolic side effects, nutritional and lifestyle therapies, and special populations and implementation gaps were the four primary topics that emerged.

3.1 Summary of Themes

3.1.1 Prevalence and Types of Nutritional Deficiencies

In all the works that were present in the review, nutritional deficiencies were continuously mentioned to be a severe effect of GLP-1 RA treatment which is mostly due to the decrease in the caloric intake, suppression of the appetite, and change in the dietary habits. Butsch et al. (2025) presented strong real-world data which stated that 12.7% of patients had at least one deficiency in six months, which rose to 22.4% in the first year of treatment. Vitamin D deficiency became the most common with incidence rates of 7.5 percent at six months and 13.6 percent at 12 months and inadequate intakes of calcium, iron, choline, magnesium, fiber, and potassium were reported by Johnson et al. (2025). These micronutrient deficiencies indicate physiological alterations caused by GLP 1 RAs as well as dietary imbalance. Kennedy et al. (2025) also focused on the danger of micronutrient deficiency, whose fast satiety can negatively affect the already inappropriate nutrient baselines. Mozaffarian et al. (2025) have noted that caloric limitation and lack of food variety in the course of treatment may undermine muscle and bone health, which is why the monitoring of micronutrients is essential. Taken together, the evidence suggests that although GLP-1 RA treatment is effective in the management of weight, it is linked to a significant risk of nutrient deficiency that should be assessed proactively and planned in the diet.

3.1.2 Gastrointestinal and Metabolic Side Effects

Gastrointestinal disturbances are one of the most consistent adverse effects of the studies reviewed. Mozaffarian et al. (2025) and Xie et al. (2025) noted that Nausea, vomiting, slow gastric emptying,

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constipation and abdominal discomfort were common particularly when starting and increasing the dose. Additionally, gastrointestinal side effects are the significant predictor of treatment discontinuation and poor adherence. Furthermore, study by Xie et al. (2025) also showed that the use of GLP 1 RA was linked to higher risks of gastrointestinal disorders, pancreatitis, nephrolithiasis, hypotension, syncope, and arthritic symptoms compared to usual antihyperglycaemic treatments. However, such risks were accompanied by a wide range of metabolic advantages, including a lower number of cardiovascular events, a better lipid profile, and a decreased risk of neurocognitive disorders. Mechanistic data provided by Moiz et al. (2025) and Ilias et al. (2025) made it clear that much of this side effects is an expansion of the physiological activity of GLP-1, especially delayed emptying of the stomach, control of central appetite, and hormonal control. Reduced gastrointestinal pace, though advantageous to glycaemic management and satiety, is a direct cause of nausea and early satiety, and decreased food consumption, which further increases nutritional risk. Schooling et al. (2025) and Wang and Wang (2025) emphasized the importance of AMPK (AMP-activated protein kinase) activation and metabolic remodeling, which might be the cause of other system-wide effects other than the gastrointestinal system.

3.1.3 Nutritional and Lifestyle Interventions

The need to use organized nutritional and lifestyle interventions to reduce nutritional risks as well as maximize therapeutic outcomes was stressed in all reviewed studies. Evidence-based nutritional interventions that have been suggested by Kennedy et al. (2025) include protein prioritization, gradual fiber intake, small frequent meals, and monitoring of micronutrients, which are deemed essential to maintain lean body mass and reduce gastrointestinal discomfort. Mozaffarian et al. (2025) also emphasized baseline measurements, such as the quality of the diet, emotional eating habits, muscle strength, and social determinants of health, and continuous lifestyle observation during the therapy. It was found that interdisciplinary care models were critical to effective management. However, Butsch et al. (2025) found that patients with dietitian visits had a higher likelihood of reported deficiencies, which probably was a consequence of the more frequent screening instead of the worsening of the nutritional condition. Recommended supportive

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interventions were resistance training to maintain muscle mass, structured exercise, telehealth-based dietary counseling, and Food-is-Medicine programs. Another issue mentioned in the literature is that more intervention strategies need to be developed, specific to the emerging co-agonists (e.g., GLP-1/GIP dual agents) that can be more effective in terms of appetite suppression. It is proposed by mechanistic studies (Moiz et al., 2025; Liu, 2024) that nutrition-oriented behavioural interventions will be even more important as future pharmaceuticals will be more potent and prevent severe deficits and uphold metabolic health.

3.1.4 Special Populations and Implementation Gaps

Some studies revealed substantive implementational gaps, especially among users of pediatric medicine, those with limited nutritional literacy and those with structural constraints. Kennedy et al. (2025) highlighted a significant evidence gap in children and adolescent diets, which is despite the increasing prescription of GLP-1 RA in these populations. The increased susceptibility of pediatric patients is attributed to their continuous development, increased nutrient needs, and increased vulnerability to deficiencies caused by appetite. Mozaffarian et al. (2025) have found structural barriers that affect treatment outcomes to be broader, such as food insecurity, inadequate access to dietitians, low culinary skills, and inequity in drug affordability. These problems impact low-income populations to a disproportionate extent and could contribute to the increase in inequalities in managing obesity and metabolic diseases. Furthermore, West et al., (2025) and Xie et al., (2025) reported that neurological mechanisms of GLP-1 RAs provided gaps in understanding the long-term effects on cognitive functions, particularly in the vulnerable population. Meanwhile, Chen et al. (2025), Zheng et al. (2024) and Ussher and Drucker (2023) have indicated the growing therapeutic indications in renal, cardiovascular, hepatic, neurological, and inflammatory conditions and it is not clear how nutritional management needs to be tailored to various comorbidities.

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4. Discussion

The results of the review provide great insight into the nutritional risks associated with the use of GLP-1 receptor agonist (GLP-1RA) treatment, explaining the main thematic issues: the nutritional deficiencies, gastrointestinal and metabolic adverse effects, changes in dietary intake, nutritional risks related to weight, and the efficacy of nutritional interventions. Taken together, these themes highlight the sophisticated physiological and behavioural processes through which GLP -1 RAs regulate nutrient status.

4.1 Nutritional Deficiencies and Micronutrient Risks

The most significant result of the review is that deficiencies in vitamin D, calcium, magnesium, potassium, iron, and vitamin B12 are high among users of GLP-1 RA. These are observations that are consistent with the new research. A number of studies reported micronutrient imbalances in patients undergoing GLP-1RA treatment, especially those treated with semaglutide or liraglutide to manage obesity and diabetes. Indicatively, Lupianez-Merly et al. (2024) found higher incidences of vitamin D and magnesium deficiency during treatment, which is similar to our outcome of up to 22 per cent of users developing at least one deficiency in the first year of treatment. Similarly, it was emphasized by Gentinetta et al. (2024) that delayed gastric emptying is one of the major actions of GLP-1 agonists, which may decrease nutrient absorption, especially fat-soluble vitamins like vitamin D.

The observation of the review that the most prevalent is vitamin D deficiency is also correlated with the overall epidemiological data that show high baseline vitamin D insufficiency among obese and type 2 diabetes patients. However, other reports indicate that GLP-1 treatment can indirectly increase the levels of vitamin D through weight loss and reduced fat-soluble vitamin sequestration in adipose tissues (Ali et al., 2024). This is contrary to our findings that suggest that the extent of appetite inhibition and dietary restraint upon GLP -1RAs might counter any weight-loss-related changes in vitamin D bioavailability. The contradicting evidence thus supports the necessity of

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additional controlled experiments that isolate the metabolic versus dietary behaviour-mediated actions of GLP -1 RAs.

The review was also characterized by iron and B12 deficiencies. These results are in agreement with Bain et al. (2023), who have found that levels of ferritin and B12 decrease in GLP-1 RA users, especially those with gastrointestinal side effects like nausea, vomiting, or lack of animal-source food intake. In contrast, Chapman et al. (2016) did not observe clinically significant reduction in B12 and indicated that the risk of deficiency could be determined by the dietary patterns at baseline or co-administration of metformin, which has an independent adverse effect on B12 absorption. This difference suggests that the decrease in B12 may not necessarily be due to GLP-1 physiology but may be increased by dietary modifications with treatment.

4.2 Gastrointestinal and Metabolic Side Effects

The results of this review show that gastrointestinal (GI) disturbances represent the most frequently reported adverse effects in GLP -1 -RA users, which is well-supported across the literature. Similarly, Sun et al., (2015) and Gartner et al., (2025) also point to the same adverse events (nausea, vomiting, constipation, and abdominal discomfort) as typical adverse events, especially in the initial stages of treatment. These symptoms have been widely mentioned as the most common reason leading to discontinuation of treatment, which emphasizes their clinical importance. Chun and Butts (2020) support this point and emphasize that dose-based GI intolerance is one of the primary obstacles to persistent adherence.

Furthermore, Filippatos et al. (2015) disclose greater risks of pancreatitis, nephrolithiasis, hypotension, and syncope in GLP-1RA users, but such incidences are still relatively low. However, they should be understood in the framework of the overall therapeutic process. Ma et al. (2021) and Iorga et al. (2020) also reporting significant metabolic positive outcomes, such as cardiovascular mortality, improved lipids, and possible neuroprotection. This duality is indicative of a crucial clinical trade-off, in that, there are side effects, but they are accompanied by substantial metabolic benefits.

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These side effects are further put in perspective by mechanistic insights. Kim and Yoo (2025) and Zhao et al. (2021) show that a substantial number of GI symptoms are the direct results of the pharmacological effects of GLP-1. Slow gastric emptying, central appetite inhibition, and vagal signaling changes are concomitant causes of nausea, early satiety, and dietary intake. Such mechanisms can also increase micronutrient deficiencies, which connect metabolic activities with nutritional risk. Additionally, Kim and Yoo (2025) and Fadel et al. (2025) point out that, there is the implication of AMPK activation and metabolic remodelling, which explains the systemic manifestations of fatigue, hypotension, or musculoskeletal pain. The literature justifies the idea that GLP-1 RAs have predictable GI and metabolic side effects based on their physiological activity, and the importance of close dose adjustment and nutritional follow-up.

4.3 Altered Dietary Intake and Appetite Suppression

The decreased total dietary intake and intake of foods rich in micronutrients is in line with the established anorexic action of GLP-1 RAs. Some of the studies such as Camilleri (2024) and Horowitz et al. (2012) have shown that energy intake reduces significantly after GLP-1 therapy, mainly due to early satiety, slow gastric emptying, and reduced hedonic eating. Our results expand this evidence by demonstrating that the decreasing consumption of foods high in calcium, magnesium, iron, and vitamin B12, including dairy products, leafy vegetables, legumes, and meat, is not proportional. This is in line with behavioural outcomes of Bettadapura et al. (2025) who found that patients undergoing GLP-1 therapy often develop aversions to meat and high-density foods, which might be the reason why B12 and iron deficiencies are more prevalent.

The decrease in the consumption of micronutrient-contained foods also aligns with the research that demonstrates that GLP-1 treatment changes the dietary habits to simple, easy to digest foods which tend to be deficient in essential minerals (Christensen et al., 2024). Nevertheless, other studies state that decreased consumption is a therapeutic outcome of reduced intake desired as a part of weight loss and enhanced metabolic well-being (Ard et al., 2021; Wong et al., 2025). Although this view is correct in terms of weight-management perspective, the results of this review have indicated that the nutritional implication deserves more clinical consideration.

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4.4 Weight-Loss-Related Nutritional Risks

The weight loss was long related to changes in micronutrient metabolism, such as the depletion of vitamin D reserves due to the decrease in the volume of adipose tissue, the decline in the levels of iron caused by the decrease in consumption, and the disruption of the electrolyte balance (Ciobarca et al., 2024). The current evidence suggests that patients receiving GLP-1 receptor agonists (GLP-1 RAs) seem especially vulnerable to the deficiencies, which is in line with the previous studies that revealed that the rate and the extent of weight loss correlate with the occurrence of micronutrient deficiency (Febrey et al., 2025).

The current body of literature is however divided on whether there is clinical importance on the nutritional risks induced by weight-loss. Some of the research assumes that weight loss induced by GLP-1 is more metabolically favourable and slower than surgery or extreme diets (de Almeida et al., 2024), which may help to avoid dangerous deficiencies. On the other hand, Klair et al., (2023) indicate that semaglutide may provide weight loss just as effective as bariatric surgery in specific patients, thus increasing nutritional risk more than previously predicted (2023). The findings agree with Moetaz et al. (2025), which suggest that clinicians should use bariatric-style-nutritional-monitoring protocols in the management of GLP-1-induced weight loss.

4.5 Efficacy of Nutritional Interventions

The efficiency of the supplementation and lifestyle intervention demonstrates the gaps in the contemporary clinical practice. This has been proven to be effective, with regular monitoring of vitamin D supplementation being found to fix deficiency on GLP-1 RA users (Chavez et al., 2025), which is why our results support the idea that targeted supplementation can make the difference. Conversely, dietary counselling has shown to be less effective with generalized use of multivitamins without behavioural modification, hence the significance of behavioural modification towards the achievement of adequate nutrient status (Acero et al., 2025).

Dietary counselling has been found to be specifically effective, in line with Ismaiel et al. (2025), who report the need to monitor patient with a rapid weight loss, either surgically or pharmacologically induced, under the guidance of a dietitian. The results of the review also support

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the position of Chavez et al. (2025), who propose to include nutritional assessment in the GLP-1 RA treatment protocols, as the negative effects associated with nutrients are increasingly being recognized.

However, some studies, including those by Brown et al. (2024) and Karakasis et al. (2025), claim that routine supplementation might not be necessary in case of no clinically significant deficiencies. Such studies are usually earlier than the common use of GLP-1 agonists in higher doses such as semaglutide and tirzepatide. The present review thus confirms the growing view that nutritional surveillance should become a norm due to the increasing doses and the extended use of GLP-1 drugs.

5. Conclusion

GLP-1 receptor agonists are a disruptive therapeutic agent in obesity and type 2 diabetes, providing significant weight loss and metabolic effects. However, according to this review, their anorexia-inducing and gastrointestinal action presents significant nutritional difficulties. It has been proven that micronutrient deficiencies, specifically vitamin D, calcium, magnesium, potassium, iron, and vitamin B12 are highly prevalent, which is mainly caused by the decreased consumption of these nutrients in the diet, the change in food preferences, and the weight loss. These deficiencies are enhanced by gastrointestinal adverse events such as nausea, vomiting, constipation and early satiety as some of the contributing factors to treatment discontinuation. Moreover, the excessive loss of lean body mass in the case of GLP-1 RA treatment is a matter of concern in terms of sarcopenia, the decline in metabolic rate, and physical functioning, in which case it is essential to maintain sufficient protein consumption and resistance-based exercise.

The review establishes that the lack of micronutrients, protein optimisation, small frequent meals, and dietitian-led counselling, as structured nutritional interventions, have the potential to alleviate deficiencies and aid adherence. The baseline assessment of dietary intake, constant monitoring, and individual approaches play a key role in the retention of lean mass, the avoidance of micronutrient depletion, and metabolic health. However, there are still gaps in evidence, especially in the cases of pediatric patients, socioeconomically disadvantaged, and those taking newer dual

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agonists, which imply that the specific dietary recommendations should be provided, and access to nutritional support should be equal.

In addition, proactive and evidence-based nutritional care should be included in the GLP-1 RA therapy. Individualized supplementation, systematic dietary evaluation, and lifestyle modifications are critical in order to make sure that the deep cardiometabolic effects of GLP-1 RAs are not missed by avoidable dietary complications. Such comprehensive strategies will improve treatment safety, adherence, and long-term outcomes to become a template of optimised, sustainable obesity and diabetes management.

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Author Contributions

W.K did the conceptualisation, data extraction, analysis and manuscript drafting; A.T, A.A, N.S, K.B, I.A and W.K extracted and reviewed the data and did manuscript revision. T.K supervised, revised and approved the manuscript. All authors read and approved the final manuscript.

Declaration of Conflicting Interest

The authors declare no potential conflicts of interest.

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Ethical Approval

Not applicable

Informed Consent

Not applicable.

Data Availability Statement

All data are derived from published studies cited in the references. No new data were generated.

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