

## The Dual Effect of the Ketogenic Diet in Overweight and Obese Populations: A Systematic Review of Adverse Effects and Weight Loss Outcomes

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### Abstract

**Background:** Obesity and overweight are global public health concerns with serious health and economic consequences. The ketogenic diet (KD), characterized by high-fat and low-carbohydrate intake, has emerged as a popular strategy for weight loss. **Objective:** This systematic review aims to assess the effectiveness and safety of ketogenic diets in reducing body weight and BMI among overweight and obese adults. **Methods:** We conducted a systematic search following the PRISMA 2020 guidelines and PICOS framework. Seven interventional studies met the inclusion criteria, evaluating the effects of various forms of ketogenic diets compared to standard or non-ketogenic diets in adults aged 18–65 years with BMI  $\geq 25$  kg/m<sup>2</sup>. The review protocol was registered in PROSPERO (CRD420251017102) prior to data extraction. **Results:** Across all studies, ketogenic diets led to significant weight loss and BMI reduction compared to control groups. Reported adverse events included mild symptoms such as fatigue, gastrointestinal discomfort, and "keto flu," which were generally transient and manageable. No severe adverse effects were reported. **Conclusion:** The ketogenic diet appears effective for short- and medium-term weight loss in overweight and obese adults, with mostly mild side effects. Professional supervision is recommended to mitigate potential risks. Further high-quality research is needed to assess long-term effects and metabolic outcomes

**Keywords:** Ketogenic diet, Obesity, Weight loss, BMI reduction, Diet therapy, Low-carbohydrate diet

## Background

Overweight and obesity are long-term health conditions marked by excessive fat accumulation in the body, typically measured using the Body Mass Index (BMI). BMI is determined by dividing a person's weight in kilograms by the square of their height in meters. As defined by the World Health Organization (WHO), individuals with a BMI of 25 kg/m<sup>2</sup> or higher are considered overweight, while a BMI of 30 kg/m<sup>2</sup> or more is classified as obesity [1]. Obesity has become a major global health issue, affecting nearly 30% of the global population, regardless of age, gender, or socioeconomic factors [2]. It is linked to approximately 4.7 million premature deaths each year and is the fifth leading preventable cause of death, accounting for 8.4% of all global fatalities [3].

Since 1975, the global rate of obesity has tripled, with over 1.9 billion adults considered overweight and more than 650 million classified as obese by 2016 [1]. Obesity, which was initially more common in high-income countries, is now rapidly increasing in low- and middle-income regions. This rising trend is a serious public health issue, given the heightened risk of chronic diseases such as cardiovascular diseases, type 2 diabetes, certain cancers, musculoskeletal disorders, and sleep apnea [4]. Furthermore, obesity has significant psychological consequences, as it is associated with an increased risk of depression, anxiety, and reduced self-esteem. Additionally, it places a considerable economic strain on healthcare systems and negatively affects overall productivity [4].

Combating obesity requires a comprehensive approach that incorporates prevention and management strategies aimed at fostering healthy eating habits, improving access to nutritious foods, and promoting physical activity. Effective intervention necessitates coordinated efforts among governments, healthcare systems, and communities to implement evidence-based solutions that mitigate the health and economic consequences of obesity [5]. Dietary modifications and increased physical activity play a fundamental role in achieving sustainable weight management [6].

The ketogenic diet (KD), first introduced in the early 20th century to manage epilepsy, has recently gained attention as a weight-loss and therapeutic strategy. This high-fat, low-carbohydrate diet triggers ketosis, a metabolic state where the body primarily burns fat for energy instead of glucose [1]. During ketosis, the body metabolizes fat to produce ketone bodies, which serve as an alternative

energy source. This metabolic shift is associated with both neuroprotective benefits and enhanced weight loss [7]. A standard ketogenic diet typically comprises 70-80% of total daily calories from fats, 20-25% from proteins, and only 5-10% from carbohydrates, emphasizing a high-fat, moderate-protein, and low-carbohydrate macronutrient distribution [8].

Several variations of the ketogenic diet exist, including the classic ketogenic diet, the medium-chain triglyceride (MCT) diet, the modified Atkins diet (MAD), and the low-glycemic index treatment (LGIT). While all these approaches aim to induce ketosis, they differ in macronutrient composition and clinical application. Notably, not all low-carbohydrate diets qualify as ketogenic, as those with higher protein intake may inhibit ketosis by promoting gluconeogenesis, a process in which certain amino acids are converted into glucose [9].

The increasing adoption of the ketogenic diet for weight management and metabolic health has also prompted concerns regarding its safety and long-term implications. Common short-term side effects, collectively known as "keto flu," include fatigue, nausea, and electrolyte imbalances. Moreover, prolonged adherence to the diet, if not carefully managed, may lead to nutrient deficiencies, gastrointestinal disturbances, and an elevated risk of kidney stone formation or osteoporosis [10], [4]. Despite these challenges, the ketogenic diet continues to be a widely utilized approach for weight management, highlighting the need for further research to better understand its benefits, potential risks, and underlying mechanisms [11].

The current review aims to evaluate the evidence on the ketogenic diet's impact on obesity and related health outcomes. Specifically, the objectives are to (i) evaluate the diet's effectiveness in facilitating weight loss and (ii) investigate its potential adverse effects, offering a comprehensive perspective on both its benefits and limitations.

## Materials and Method

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA) 2020 guidelines [12]. the protocol was prospectively registered in PROSPERO under the registration number CRD420251017102. The Population, Intervention, Comparison, Outcomes, and Study design (PICOS) framework was employed to guide the systematic review process. This framework was chosen to structure the research question and ensure a comprehensive synthesis of evidence related to the effects of the ketogenic diet. Table 1

outlines the key components of our research question: "What are the effects of the ketogenic diet on weight loss and its associated adverse outcomes?" using the PICOS framework.

**Table 1: PICOS framework**

PICOS Component	Description
<b>Population (P)</b>	Adults aged $\geq 18$ years of age to $\leq 65$ years with a BMI $\geq 25$ kg/m <sup>2</sup> (overweight) or $\geq 30$ kg/m <sup>2</sup> (obese).
<b>Intervention (I)</b>	Ketogenic diets, including Classical KD, Modified Atkins Diet (MAD), Low Glycemic Index Treatment (LGIT), Medium-Chain Triglyceride (MCT) diets, and other variations designed to induce ketosis.
<b>Comparison (C)</b>	Placebo, usual care, or non-ketogenic diets.
<b>Outcomes (O)</b>	Primary: Weight loss (e.g., BMI reduction, changes in body weight). Secondary: Adverse effects (e.g., fatigue, constipation, mood swings).
<b>Study Design (S)</b>	Primary interventional studies were included, as well as studies where data underwent secondary analysis related to ketogenic diet adherence, even if this was not the initial focus. Case studies, letters, reviews, and conference abstracts were excluded.

### Inclusion and Exclusion Criteria

In this systematic review, we included studies published in English that evaluated the effects of the ketogenic diet (KD) on weight loss and adverse outcomes in adults. Eligible participants were adults aged  $\geq 18$  years of age to  $\leq 65$  years with a BMI between 25 kg/m<sup>2</sup> and 29.9 kg/m<sup>2</sup> (overweight) or  $\geq 30$  kg/m<sup>2</sup> (obese). The review considered interventions involving any form of ketogenic diet. Comparisons included placebo, usual care, or any non-ketogenic diet. The minimum duration of intervention for inclusion was 7 days, with a follow-up period of at least 7 days. Studies comparing different types of ketogenic diets or different KD regimens were also included. Studies were excluded if they (a) recruited children, adolescents, pregnant or lactating women, or elderly participants; (b) involved participants with a history of eating disorders or those

undergoing treatment for eating disorders; (c) included participants taking medications that could interfere with study outcomes, such as weight-loss medications or medications affecting lipid metabolism; (d) did not report relevant outcomes, including weight loss, BMI reduction, or other health-related outcomes; (e) were non-primary research articles, including review articles, conference abstracts, case reports, letters to editors, and duplicate studies; (f) were in vitro studies.

### Study Selection Strategy

A comprehensive and systematic literature search was conducted to identify studies examining both the therapeutic and adverse effects of the ketogenic diet among overweight and obese populations. The search was finalized in December 2024 and covered multiple high-impact electronic databases, including MEDLINE (Ovid MEDLINE ALL, from 1946 to the most recent daily update), PubMed, ClinicalTrials.gov, the World Health Organization International Clinical Trials Registry Platform (ICTRP), Web of Science Core Collection, Google Scholar, and the Egyptian Knowledge Bank (EKB).

Only articles published in English were considered to ensure consistency in data extraction and interpretation. Additionally, reference lists of all eligible studies were manually screened to identify any relevant articles not retrieved through the database search.

The search strategy incorporated a combination of controlled vocabulary (MeSH terms) and free-text terms tailored to each database. The key search concepts focused on the ketogenic diet, weight-related outcomes, and adverse health events. Examples of expanded and optimized keyword combinations include:

\* ("ketogenic diet" OR "keto diet" OR "low carbohydrate diet" OR "very low carb diet" OR "VLCD")

\* AND ("obesity" OR "overweight" OR "body mass index" OR "BMI" OR "abdominal fat" OR "visceral fat" OR "body composition")

\* AND ("adverse effects" OR "side effects" OR "complications" OR "safety profile" OR "nutritional deficiencies" OR "ketosis complications")

\* AND ("weight loss" OR "weight reduction" OR "fat loss" OR "BMI reduction" OR "clinical outcomes" OR "therapeutic effectiveness")

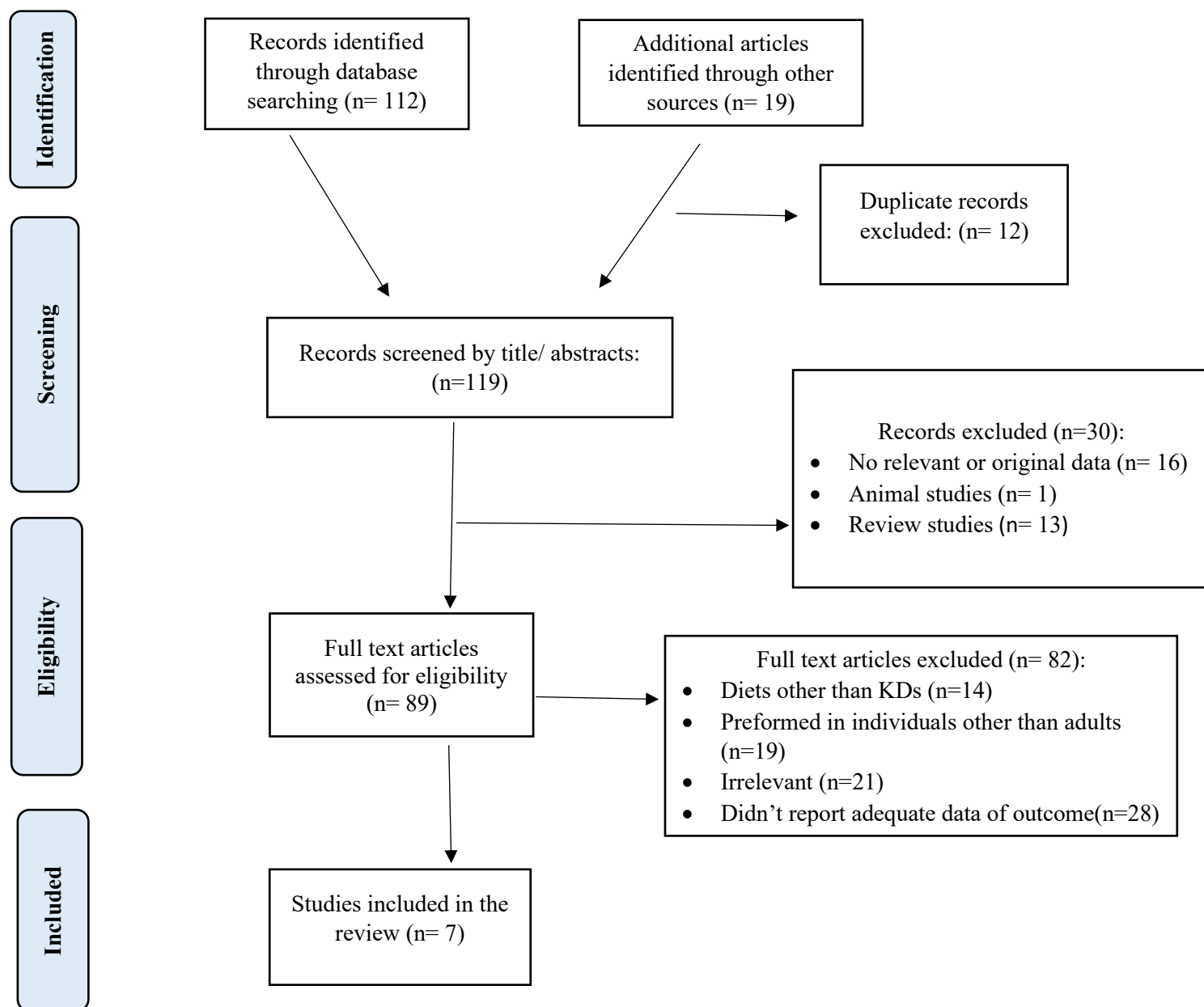
In MEDLINE and PubMed, advanced search filters such as title/abstract fields and publication types were used to enhance specificity, while broader syntax was applied in Google Scholar to include gray literature and conference papers.

Two independent reviewers (AA and AI) screened all retrieved records in two stages. The initial screening assessed title and abstract relevance, followed by a full-text review of potentially eligible studies. Discrepancies were resolved through consensus or consultation with a third reviewer when necessary.

### **Screening Process**

- A. All study titles were screened (AA), and those clearly not eligible for inclusion (e.g., studies involving children, pregnant women, or non-ketogenic diets) were excluded. Abstracts were retrieved and reviewed if there was any ambiguity from the title.
- B. Selected abstracts were then assessed, and if any ambiguity remained, full texts were retrieved and reviewed following discussion with the co-investigators (AA and AI).
- C. Eligibility was confirmed by two investigators (AI and ER).
- D. Reference lists of the included studies were checked for additional potentially suitable articles, and steps B–D were repeated for these studies. The number of articles excluded, along with the reasons for exclusion, was documented (Figure 1).

Figure (1) PRISMA 2020 flow diagram



## Data Extraction

Key information related to participant characteristics, study design, sample size, age range, BMI range, type of ketogenic diet intervention, length of intervention, primary and secondary outcomes (e.g., weight loss, BMI reduction, adverse effects), follow-up duration, and study main findings were extracted by one investigator (AA). A second investigator (AI) then reviewed all the extracted data to ensure accuracy and agreement. The format used for data extraction is shown in Table 2

## Quality Assessment

The quality of each included study was assessed using the SIGN (Scottish Intercollegiate Guidelines Network) checklist <sup>[13]</sup> to ensure methodological rigor. One investigator (AA) conducted the initial assessment, evaluating factors such as the clarity of study objectives, the appropriateness of the ketogenic diet interventions, the consistency of methods, and the reliability of reported outcomes. The second investigator (AI) reviewed the assessments to confirm agreement. Any discrepancies between the investigators were resolved through discussion. This standardized approach ensured consistency and accuracy in evaluating the quality of the studies included in this systematic review.

## Result

### Study Selection

The search strategy identified 112 records through electronic databases, with an additional 19 records identified from other sources. After the removal of 12 duplicate records, 119 records were screened by title and abstract for relevance. Of these, 30 records were excluded for reasons including the absence of original data, use of animal models, or being review studies. Subsequently, 89 full-text articles were assessed for eligibility, leading to the exclusion of 82 articles due to reasons such as the inclusion of non-ketogenic diets ( $n = 14$ ), studies on populations other than adults ( $n = 19$ ), irrelevance to the research question ( $n = 21$ ), or insufficient outcome data ( $n = 28$ ). Ultimately, 7 studies met the inclusion criteria and were included in the systematic review. The study selection process is detailed in the PRISMA flow diagram (Figure 1)



## Study Characteristics

All included studies were published in English and conducted in various countries, including the USA <sup>[14]</sup>, Italy <sup>[15],[16],[17]</sup>, Australia <sup>[6]</sup>, Turkey <sup>[18]</sup> and Iran <sup>[19]</sup>. The ethnicity of participants was not consistently reported across the studies.

A total of 7 trials were included in this systematic review. The intervention durations ranged from 7 days to 2 years, with ketogenic diets compared against non-ketogenic or standard dietary interventions. Detailed characteristics of the included studies are summarized in Table 1.

## Participant Characteristics

Participant characteristics were reported across all studies. Where mean ages were provided, they ranged from 20.7 to 57.5 years. All studies included adults aged  $\geq 18$  years to  $\leq 65$  years. Body mass index (BMI) was reported in all studies and ranged from 22.4 to 37.1 kg/m<sup>2</sup>, classifying participants as overweight or obese. One of the studies reported sex distribution <sup>[17]</sup>, while the remainder included both males and females. The number of participants varied considerably across studies, with sample sizes ranging from 8 to 173.

## Quality Assessment

The study by Cherubino Di Lorenzo <sup>[15]</sup> was considered to be of acceptable quality. The research question and inclusion criteria were clearly defined, and the intervention was well-described. However, scientific quality was not assessed or reported, and there was no evaluation of publication bias, leading to a moderate risk of bias. Luigi Schiavo's <sup>[16]</sup> randomized controlled trial was of high quality. It provided a clear description of randomization and intervention protocols, with systematic data extraction. However, allocation concealment was not detailed, which may introduce a minor risk of bias.

Kade S. Lyman's <sup>[14]</sup> non-randomized study was assessed as high quality. Despite the lack of randomization, a comprehensive literature search and data extraction process were conducted. Dropout rates were high in the control group, but reasons for attrition were well-documented. The study by Garipoğlu <sup>[18]</sup> was of acceptable quality. While the research question and intervention were well-described, the study lacked scientific quality assessment and did not address publication bias, which limits its reliability.

Marco D'Abbondanza's <sup>[17]</sup> pilot study was assessed as low quality. The study lacked a systematic assessment of scientific quality and did not report exclusions or evaluate publication bias, reducing its methodological rigor. While, Maria Perissiou's <sup>[6]</sup> randomized controlled trial was of high quality. It clearly defined research questions and assessed publication bias. However, allocation concealment methods were not reported, leading to a moderate risk of bias.

Amin Valinejad's <sup>[19]</sup> study was of high quality. The research question was clearly defined, and the scientific quality of included data was systematically assessed. However, the lack of reported allocation concealment introduced a minor risk of bias.

### **Relationship Between Ketogenic Diets, Weight Loss, and Adverse Events**

The outcomes considered in the included studies were weight loss, changes in body mass index (BMI), and the occurrence of adverse events, all assessed in overweight or obese individuals. Studies varied in duration, ranging from 7 days to 25 weeks, and were designed to induce ketosis through carbohydrate restriction. Across all interventions, significant differences were observed between ketogenic diet groups and control groups.

#### **Weight Loss and BMI**

Ketogenic diets consistently resulted in significant reductions in weight and BMI across all studies. In the randomized controlled trials (RCTs), participants in the intervention groups experienced weight losses ranging from 5% to 15% of their baseline body weight, significantly outperforming the control groups. For instance, one RCT <sup>[16]</sup> reported a mean weight reduction from  $112.0 \pm 9.2$  kg to  $91.8 \pm 9.6$  kg in the ketogenic diet group over four weeks, compared to less pronounced reductions in the control group. Another study with a non-randomized design <sup>[14]</sup> observed a mean weight loss of  $-12.3 \pm 12.0$  kg over two years in participants following a ketogenic diet, compared to  $-1.4 \pm 4.8$  kg in the control group. Short-term interventions also demonstrated rapid weight loss, primarily attributed to glycogen depletion and water loss, while long-term studies highlighted the sustained efficacy of ketogenic diets in reducing fat mass and BMI.

#### **Adverse Events**

Adverse events were commonly reported but were generally mild and transient. Symptoms such as gastrointestinal discomfort (e.g., constipation), "keto flu" (e.g., headaches, fatigue, and muscle

cramps), and occasional nausea were noted, particularly during the initial adaptation phase. For example, one study [16] reported mild nausea in 73% of participants and vomiting in 50% during the early weeks of the intervention. Another study [17] observed muscle cramps and dizziness, though these did not lead to participant dropout. The majority of adverse events resolved as participants adapted to the diet, and no severe adverse events were reported. In some cases, dietary adjustments and monitoring of electrolyte levels were recommended to mitigate symptoms.

## Discussion

Emerging evidence highlights the effectiveness of ketogenic diets as a tool for weight loss and obesity management. The reviewed studies demonstrate consistent reductions in weight and BMI among participants adhering to a ketogenic diet. These findings emphasize both the potential benefits and challenges of this dietary intervention. The most recent meta-analysis article evaluated the effect of a ketogenic diet on body weight control and glycemic management in overweight patients with type 2 diabetes mellitus (T2DM) [21]. The eight articles included in the study revealed that the KD considered as an effective intervention for lowering body weight and glycemic levels. These eight studies reported parameters in body weight change, with the results demonstrating that T2DM patients exposed to a ketogenic diet were more likely to record a higher body weight loss (SMD,  $-5.63$ ; 95% CI,  $-9.76$  to  $-1.49$ ;  $I^2 = 60\%$ ; moderate heterogeneity) and a reduction in waist circumference (SMD,  $-2.32$ ; 95% CI,  $-4.58$  to  $-0.06$ ;  $I^2 = 52\%$ ; moderate heterogeneity) when compared to those on other types of diets.

The most similar article to this systematic review was published by Natalia Drabinska, et al [9] that evaluated efficacy and safety of KD. Noted that ketogenic diets, particularly VLCKD were effectively reduce body weight, BMI, and fat mass. However, the study noted mild, transient adverse effects that result from short-term adherence to KD such as hunger, fatigue, constipation, muscle cramps, and headaches, which decrease over time. Long-term risks, including kidney stones and osteoporosis, remain a concern primarily for epilepsy patients on prolonged KD. While studies suggest VLCKD maintains normal kidney function and acid-base balance in obese individuals [22]. Other study by Emmanuelle. et al, focused on the pattern of symptoms, severity and time course of keto flu. They reported that Keto flu symptoms peak in the first week of a ketogenic diet and fade within a month common issues include headache, fatigue, nausea, dizziness, and brain fog [23].

Yves Schutz. et al <sup>[24]</sup>, found that KD may not only cause constipation, a commonly described side-effect, but also promote diverticular disease of the colon and colon cancer and alter the microbiome. In addition, the diet lacks a well-balanced intake of fruits and vegetables, a source of antioxidants. Mohammad. et al <sup>[25]</sup>, evaluate the effects of a KD on body composition and anthropometric measures in adults, that found a significant reduction in body weight, BMI, waist circumference but he mentioned that further research is needed to examine the maintenance of these effect in a long period of time <sup>[25]</sup>.

Furthermore, Hany. Et al, reported that KD significantly reduce HbA1c levels and promote greater weight loss in T2DM patients compared to low-carb diets. This effect is linked to stricter carbohydrate restriction. However, potential cardiovascular risks due to unfavorable lipid profiles should be considered <sup>[26]</sup>. Other article was showed the efficacy of KD on weight loss published by Luigi. Et al, where she reported VLCKD has shown promising results in weight loss for patients with overweight and obesity, contributing to significant reductions in body weight <sup>[27]</sup>

The findings support the use of KD as an effective strategy for weight management, particularly for individuals with obesity. However, the potential for adverse events and the requirement for strict adherence emphasize the importance of professional guidance <sup>[28]</sup>. Future research should focus on long-term outcomes, the diet's impact on metabolic health markers, and its effectiveness in specific populations, such as individuals with diabetes or metabolic syndrome. Studies with larger sample sizes and standardized definitions of adherence and adverse events will improve the reliability and applicability of the results <sup>[29]</sup>. Overall, ketogenic diets show promise as a weight management tool, with consistent evidence demonstrating their effectiveness in reducing weight and BMI. Although adverse events are common, they are typically manageable with appropriate monitoring and care <sup>[30]</sup>. While all included studies reported consistent findings regarding weight loss and minor adverse effects, the overall certainty of the evidence is considered moderate due to variability in study design, sample size, and reporting quality.

## Conclusion

This review highlights the significant potential of ketogenic diets as an effective strategy for weight loss and obesity management. Consistent findings across various study designs emphasize the effectiveness of ketogenic diets in achieving substantial reductions in weight and BMI,

establishing them as valuable clinical tools for addressing obesity and related metabolic disorders. However, challenges remain, including transient adverse events and the need for strict adherence to the diet. Addressing these issues through professional guidance, structured support, and individualized care is essential to optimize outcomes and ensure safety.

The variability in study methodologies, durations, and participant characteristics highlights the need for standardized protocols and further high-quality research. Future studies should focus on exploring the long-term metabolic benefits of ketogenic diets, their impact on comorbid conditions such as diabetes and metabolic syndrome, and their efficacy across diverse populations. Additionally, further investigation into the mechanisms underlying both the benefits and potential risks of the diet is needed to refine its application.

Despite these limitations, the evidence supports ketogenic diets as a promising and clinically relevant approach to obesity management. With proper implementation and monitoring, ketogenic diets can provide significant health benefits, offering a viable solution for individuals seeking effective and sustainable weight loss strategies.

### **Author Contributions**

Aya A.Salama contributed to the conceptualization of study design and methods, screened all study titles, assessed study abstracts, excluded studies clearly not eligible for inclusion, checked for further potentially suitable articles in reference lists of included studies, interpreted the results, critically reviewed the results, drafted the manuscript, and critically reviewed the full text. Amel I.Ahmed contributed to the conceptualization of study design and methods, confirmed the eligibility of included studies, and critically reviewed the full text. Eman R.El-Refaay contributed to the conceptualization of study design and methods, assessed study abstracts, excluded studies clearly not eligible for inclusion, confirmed the eligibility of included studies, interpreted the results, critically reviewed the results, and critically reviewed and edited the full text.

### **Conflicts of Interest Statement**

The authors declare that there are no conflicts of interest.

### **Ethical Approval and Transparency Declaration**

This systematic review did not involve primary data collection from human subjects. However, all included studies were peer-reviewed interventional trials, and ethical approval for those studies was obtained by their respective authors. The current review was conducted following PRISMA 2020 standards

The lead author affirms that the manuscript is an honest, accurate and transparent account of the study being reported. No important aspects of the study have been omitted, and all discrepancies have been explained. No funding was received.

### **Data availability**

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

### **Acknowledgment**

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