NOJEK, Pawel, ZAWÓŁ, Monika, ZIMONCZYK, Mariusz, PAWLIK, Wiktoria, NOWOTARSKA, Agnieszka and BLASZCZYŃSKI, Gustaw. Ketogenic diet and metabolic health: A review of its impact on type 2 diabetes and obesity. Analysis of research on the ketogenic diet in the context of treating metabolic disorders. Journal of Education, Health and Sport. 2024;71:55923. eISSN 2391-8306.

https://dx.doi.org/10.12775/JEHS.2024.71.55923 https://apcz.umk.pl/JEHS/article/view/55923

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences). Punktivy Ministeriante 40 punktivy. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulture firzycznej (Diedzian nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Diedzian nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Diedzian nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Diedzian nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Diedzian nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Diedzian nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Diedzian nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Diedzian nauk medycznych i nauk o zdrowiu); Noncommercial License which permits any noncommercial use, distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distributed under the terms of the Creative Commons Attribution Non commercial use, distributed under sciences Shy-nc-sa/4.0) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited. The authors declare that three is no conflict of interests regarding the publication of this paper. Received:02.10.2024. Revised:15.11.2024. Accepted:18.11.2024. Published:19.11.2024.

# Ketogenic diet and metabolic health: A review of its impact on type 2 diabetes and obesity. Analysis of research on the ketogenic diet in the context of treating metabolic disorders

#### Monika Zawół,

Lower Silesian Center for Oncology, Pulmonology, and Hematology in Wrocław, plac Hirszfelda 12, 53-413 Wroclaw, Poland https://orcid.org/0009-0003-9854-5083, monikazawol315@gmail.com

# Mariusz Zimonczyk,

Muncipal Hospital in Zabrze, ul. Zamkowa 4, 41-803 Zabrze, Poland https://orcid.org/0009-0004-9256-3798, mariusz.zimonczyk1@gmail.com

# Wiktoria Pawlik,

Muncipal Hospital in Siemianowice Śląskie, ul. 1 maja 9, 41-100 Siemianowice Sląskie, Poland https://orcid.org/0009-0006-8756-5398, wikipawlik@gmail.com

#### Paweł Nojek.

Muncipal Hospital in Siemianowice Śląskie, ul. 1 maja 9, 41-100 Siemianowice Sląskie, Poland https://orcid.org/0009-0005-4460-3406, pawel.nojek98@gmail.com

# Agnieszka Nowotarska,

Katowice Oncology Center, Katowice, Poland <u>https://orcid.org/0009-0009-2698-9519</u>, nowotarska.agnieszka@o2.pl

# Gustaw Błaszczyński,

Muncipal Hospital in Siemianowice Śląskie, ul. 1 maja 9, 41-100 Siemianowice Sląskie, Poland <u>https://orcid.org/0009-0001-3017-3514</u>, gustawblaszczynski@gmail.com

#### Abstract

This paper aims to review current research on the ketogenic diet as a potential therapeutic approach for obesity and type 2 diabetes. This diet is characterized by high fat intake, moderate protein, and minimal carbohydrates, leading to a state of ketosis in which the body utilizes ketone bodies as its primary energy source. Studies indicate that the ketogenic diet may positively influence blood glucose control, enhance insulin sensitivity, and facilitate weight reduction, particularly relevant in the context of insulin resistance. The paper discusses the biological mechanisms underlying these effects, as well as potential risks associated with long-term adherence to the diet. It underscores that, despite promising results, further research is necessary to better understand the long-term effects of the ketogenic diet and its applicability across various patient populations. Conclusions highlight the need for patient monitoring during the dietary regimen and the potential for integrating the ketogenic diet into a broader strategy for managing metabolic diseases.

**Keywords:** Ketogenic diet, ketosis, ketone bodies, obesity, type 2 diabetes, metabolism, insulin sensitivity, glucose control, insulin resistance, biological mechanisms, metabolic processes, long-term use, inflammation, gut microbiota, neuroprotection, therapeutic effects, dietary changes, fat intake, carbohydrates, scientific research, lipid profile, side effects, supplementation, weight management, physical activity, dietary programs, patient education, dietary interventions.

# **1.Introduction**

The ketogenic diet, characterized by high fat intake, moderate protein, and very low carbohydrates, is gaining popularity as a potential therapeutic approach for the treatment of obesity and type 2 diabetes. The objective of this diet is to induce a state of ketosis in which ketone bodies, rather than glucose, serve as the primary energy source. In recent years, numerous studies have investigated the effects of the ketogenic diet on metabolic health, with results suggesting that it may positively influence blood glucose control and enhance insulin sensitivity (1)(2).

Type 2 diabetes and obesity are prevalent health issues that significantly impact patients' quality of life and healthcare systems. Both conditions are closely interconnected, making them a critical focus for research on the efficacy of various dietary strategies, including the ketogenic diet.

This paper will conduct a detailed review of current research regarding the impact of the ketogenic diet on metabolic health. This analysis will encompass both the positive and negative aspects of employing this diet in the management of type 2 diabetes and obesity. It will also be essential to discuss the biological mechanisms underlying the beneficial effects of the ketogenic diet, as well as potential risks associated with its long-term use.

Given the growing interest in the ketogenic diet as a tool for the therapy of metabolic diseases, understanding its effects on health becomes crucial for developing effective treatment and prevention strategies for these conditions. This work aims to contribute to a broader discussion on the ketogenic diet, its advantages and limitations, and its role in the context of current trends in medicine and healthy living (1)(2).

# 2. Theoretical background

# 2.1. Mechanisms of action of the ketogenic diet

The ketogenic diet operates through a series of complex mechanisms that significantly influence bodily functions. A key aspect of this diet is the substantial reduction of carbohydrate intake, which leads to decreased blood glucose levels. In response to this condition, the body enters a state of ketosis, during which it begins to produce ketone bodies, such as  $\beta$ -hydroxybutyrate, acetoacetyl-CoA, and acetone. These substances become the primary energy source for cells, including neurons, which may enhance their functionality and metabolism.

In the context of the nervous system, ketones exhibit neuroprotective properties, which are particularly relevant in the treatment of epilepsy and other neurodegenerative diseases. Changes in glucose and fat metabolism result in reduced inflammation, which is beneficial in numerous chronic conditions. The ketogenic diet also affects neurotransmission by modifying the levels of neurotransmitters such as GABA and glutamate, which may contribute to the stabilization of neuronal electrical activity and the reduction of seizures.

Increased consumption of long-chain fats promotes improved insulin homeostasis, which is especially important for individuals with insulin resistance. Furthermore, this diet may influence the gut microbiome, with implications for metabolic health, including body weight regulation and blood lipid levels. Long-term adherence to the ketogenic diet leads to metabolic adaptations that may enhance the body's capacity to burn fat as an energy source.

These transformations can also support better performance during physical activity. Additionally, the ketogenic diet may assist in reducing feelings of hunger and increasing satiety, facilitating weight management. There are also suggestions that ketone bodies may have protective effects on neuronal cells, potentially slowing the progression of neurodegenerative diseases such as Alzheimer's and Parkinson's.

Due to its anti-inflammatory and metabolism-stabilizing properties, the ketogenic diet may serve as a valuable tool in the therapy of individuals with metabolic disorders, including obesity and type 2 diabetes. Research into these mechanisms is ongoing, and findings may contribute to a deeper understanding of the ketogenic diet's impact on health. As knowledge in this area expands, it becomes possible to tailor therapeutic strategies that utilize the ketogenic diet to enhance patients' quality of life. Future studies are anticipated to shed light on its long-term effects and potential clinical applications (2)(3)(4).

#### 2.2. Epidemiology of type 2 diabetes and obesity

The epidemiology of type 2 diabetes and obesity indicates a rising prevalence worldwide, presenting a significant public health challenge. Type 2 diabetes is currently one of the most frequently diagnosed metabolic disorders, and its occurrence is closely associated with obesity, which serves as a primary risk factor. Over the past few decades, there has been a notable increase in obesity rates, contributing to the escalating incidence of type 2 diabetes, particularly in low- and middle-income countries. Obesity not only heightens the risk of developing diabetes but also affects its progression and treatment efficacy.

Specifically, adipocytes produce pro-inflammatory substances that can lead to insulin resistance, a key mechanism in the development of type 2 diabetes. In 2021, it was reported that approximately 537 million adults globally were living with diabetes, a figure projected to rise to 783 million by 2045. This increase is particularly concerning in the context of an aging population and lifestyle changes, such as poor diet and lack of physical activity. Epidemiological data suggest that individuals with obesity are up to five times more likely to develop type 2 diabetes compared to those with a normal body weight.

Variations in the incidence of type 2 diabetes can also be observed based on geographical region, gender, and ethnic groups, indicating that environmental and genetic factors play a significant role in this epidemic. In response to the growing issue, coordinated actions at both public and individual levels are essential to effectively combat the development of obesity and type 2 diabetes. Understanding the epidemiology of these conditions is crucial for developing effective preventive strategies and therapeutic interventions (6)(7)(8).

#### 2.3. The role of diet in managing metabolic diseases

Diet plays a crucial role in managing metabolic diseases, particularly in the context of obesity and type 2 diabetes. A well-balanced diet can significantly influence weight control and the improvement of metabolic parameters. Research has demonstrated that dietary patterns, such as the Mediterranean diet, can contribute to the prevention of diabetes development and slow its progression (12). Specifically, this diet, rich in fiber, healthy fats, and antioxidants, positively impacts insulin sensitivity (12). Moreover, diet can support physical activity, which is vital for maintaining metabolic health in older adults (10). Studies indicate that dietary interventions in older populations can enhance physical functions and quality of life (10).

It is also essential that dietary approaches are tailored to individual patient needs, as the effectiveness of a diet can vary from person to person (9). In addition to diet, regular physical activity is a key element in the prevention and treatment of metabolic diseases (13). The combination of diet and exercise can significantly increase the likelihood of preventing or delaying the onset of diabetes (13). It is noteworthy that dietary changes, such as reducing carbohydrate and saturated fat intake, can lead to significant weight loss and improved health (11). Research has also shown that pharmacotherapy combined with dietary management may be more effective in reducing body weight and improving health parameters (11).

Another important aspect is patient awareness regarding healthy eating, which can be supported through appropriate educational dietary programs (9). Systematic reviews have indicated that individuals at high risk for diabetes should be included in dietary interventions and support programs (14).

In the context of obesity, the diet should be balanced and tailored to taste preferences to enhance its acceptance and long-term adherence (11). Studies suggest that diets based on natural products with limited processed foods may yield the best health outcomes (12).

Finally, it is important to emphasize the value of regular consultations with a dietitian, who can assist in developing an individualized nutrition plan (10). Maintaining a healthy body weight, along with monitoring blood glucose levels, is critical for individuals with diabetes (14). Patient education about the effects of diet and lifestyle can significantly influence their self-discipline and motivation to implement positive changes (9). Collaboration between health professionals and patients is essential for achieving long-term outcomes in the management of metabolic diseases (13). Understanding the mechanisms by which diet affects the body allows for more effective approaches to treatment and prevention (12).

# 3. Review of scientific research

# 3.1. Ketogenic diet and type 2 diabetes

The ketogenic diet, characterized by low carbohydrate intake and high fat consumption, is gaining increasing attention as a supportive method for the treatment of type 2 diabetes. Numerous studies, including meta-analyses and systematic reviews, affirm its positive effects on glycemic control and improved insulin sensitivity in individuals with diabetes (15). By drastically reducing carbohydrate intake, the ketogenic diet lowers blood glucose levels, leading to stabilized glycemia and a reduction in insulin requirements (16). Patients adhering to this diet also exhibit lower levels of glycated hemoglobin (HbA1c), a key indicator of long-term diabetes control (17).

The restriction of carbohydrates results in an increased concentration of ketone bodies, which serve as an alternative energy source, contributing to reduced glycemic fluctuations and improved insulin response (18). Consequently, the ketogenic diet enhances insulin sensitivity, potentially alleviating the symptoms of insulin resistance, one of the primary causes of type 2 diabetes (20). Weight loss, frequently observed in patients following this diet, also plays a significant role in improving insulin sensitivity, as supported by review studies (15).

Research by Jing et al. (2023) (19) indicates that the ketogenic diet is among the most effective dietary interventions for enhancing glycemic control, surpassing other nutritional strategies. The stabilization of blood sugar levels resulting from this diet also helps to limit postprandial glucose spikes, which may lead to reduced oxidative stress and decreased inflammation associated with type 2 diabetes (16). The reduction in carbohydrate intake allows for lower fasting insulin levels and diminishes the need for insulin therapy, potentially improving treatment outcomes and preventing complications (17).

Furthermore, the ketogenic diet influences the reduction of visceral and hepatic fat, which contribute to insulin resistance and metabolic disorders (18). These mechanisms enhance glycemic control and enable better regulation of blood sugar levels by the body. The increased insulin sensitivity allows for more effective glucose management without the necessity of high doses of insulin or antidiabetic medications (20).

#### 3.2. Ketogenic diet and obesity

The ketogenic diet (KD), particularly in the form of very low-calorie ketogenic diet (VLCKD), has proven effective for weight reduction, with its mechanisms of action differing from those of other low-calorie diets. It consists of minimal carbohydrate intake and induces a state of ketosis, in which the body utilizes fats as its primary energy source, thereby promoting the burning of adipose tissue (21). Ketosis contributes to appetite suppression by decreasing levels of ghrelin, the hunger hormone, which facilitates the control of caloric intake (22). Additionally, the KD influences insulin levels by stabilizing its secretion, a critical factor for individuals with insulin resistance and type 2 diabetes, conditions often associated with obesity (23).

Research conducted by Cunha et al. (2020) (21) demonstrated that VLCKD exhibited greater efficacy in reducing visceral and hepatic fat compared to traditional low-calorie diets. Patients on a ketogenic diet lost more weight in a shorter time frame, which is advantageous for those with severe obesity or metabolic diseases. Furthermore, a meta-analysis by Choi et al. (2020) (22) indicated that the ketogenic diet is more effective in improving metabolic parameters, such as triglyceride and HDL cholesterol levels, which also supports weight reduction. Studies have also shown that the ketogenic diet helps preserve muscle mass during weight loss, which is beneficial for maintaining physical activity and basal metabolic rate (23).

In comparing KD to the Mediterranean diet, research by Lambadiari et al. (2024) (24) revealed that both diets can effectively reduce inflammation in patients with obesity and conditions such as psoriatic arthritis. However, KD was found to be more effective for rapid weight loss and inflammation reduction, while the Mediterranean diet better supports long-term cardiovascular health. Compared to standard low-calorie diets, KD demonstrates higher efficacy in short-term weight loss but requires a more restrictive approach, which may limit its long-term adherence (22). Although vegetarian diets offer numerous health benefits, they do not match the ketogenic diet in terms of reducing blood sugar levels. The carbohydrate restrictions in the ketogenic diet allow for more stable glucose levels, which is particularly important for individuals with type 2 diabetes (27).

The ketogenic diet is also distinguished by its influence on biochemical changes that contribute to its effectiveness in weight reduction, such as the regulation of blood glucose levels and the reduction of insulin resistance. In the context of sustained weight loss and metabolic benefits, KD offers unique mechanisms, though the Mediterranean diet may be a better option for patients with cardiovascular diseases seeking a more sustainable long-term dietary approach (24).

#### 4. Benefits and risks of the ketogenic diet

The ketogenic diet, characterized by its low carbohydrate and high fat content, is gaining popularity due to its potential health benefits. One of the primary advantages of this diet is its ability to support glucose control, which is particularly important for individuals with type 2 diabetes (27). Research indicates that the ketogenic diet can improve insulin sensitivity and stabilize blood sugar levels, leading to enhanced glycemic management (28). Additionally, it is noteworthy that this diet may positively influence gut microbiota, which could confer further health benefits (25). Weight loss is another frequently cited effect of the ketogenic diet, potentially contributing to a reduced risk of cardiovascular diseases (26).

However, the adoption of a ketogenic diet is associated with certain risks, including the possibility of nutrient deficiencies, particularly of vitamins and minerals (30). Prolonged adherence to this diet may also lead to fat accumulation in the liver, which is undesirable, especially in individuals with pre-existing health conditions (29). The phenomenon commonly referred to as "keto flu," characterized by fatigue and headaches, is a prevalent issue that may arise during the initial stages of the diet (26). Furthermore, for some individuals, the restrictions associated with the ketogenic diet can be challenging to maintain, leading to a yo-yo effect (27). It is crucial to consult a healthcare professional or a dietitian prior to initiating the diet, to tailor it to individual needs (28). Education regarding the diet and monitoring one's well-being are essential to avoid potential pitfalls (25). While the ketogenic diet may yield rapid results, its long-term health effects remain the subject of ongoing research (30). In the context of health, a balanced and individualized approach is critical to determine whether this diet is suitable for a given individual (29). Therefore, it is valuable to analyze both the benefits and risks associated with the ketogenic diet to make informed health decisions (26).

# **5.** Conclusions

The ketogenic diet (KD) is gaining popularity as a therapeutic approach in the treatment of obesity and type 2 diabetes. It is characterized by high fat intake, moderate protein consumption, and minimal carbohydrate intake. Transitioning into a state of ketosis, in which the body utilizes ketone bodies as its primary energy source, leads to a reduction in blood glucose levels and an improvement in insulin sensitivity. Numerous studies confirm that this diet positively influences glycemic control and promotes weight loss. The mechanisms of action include a reduction in inflammation, enhancement of insulin homeostasis, and beneficial changes in the gut microbiome. Long-term adherence to the ketogenic diet may result in metabolic adaptations that increase the body's capacity to burn fat.

The ketogenic diet may serve as an effective intervention in the management of type 2 diabetes and obesity. Its efficacy in stabilizing glycemia and reducing insulin resistance renders it a valuable therapeutic tool. The reduction in appetite and improvement in satiety contribute to effective weight management. Research indicates that this diet may be more effective in reducing visceral fat compared to standard low-calorie diets. However, the implementation of the ketogenic diet should be monitored by specialists to minimize the risk of side effects, such as nutrient deficiencies.

Despite promising results, there is a need for further research regarding the long-term effects of the ketogenic diet. Future studies should focus on assessing the impact of this diet on various patient populations, including individuals with comorbid conditions. Additionally, investigating the ketogenic diet's effects on mental health and neurodegenerative disorders is recommended. It is crucial to determine the optimal approach to its application, including potential use as short-term interventions or as part of a broader treatment strategy. Research should also account for variations in dietary effects based on genetics, lifestyle, and other risk factors.

The ketogenic diet holds potential as an effective strategy for the treatment of obesity and type 2 diabetes; however, its use requires caution and appropriate medical supervision. Regular monitoring and meal planning are essential to prevent potential deficiencies.

As research progresses, we can anticipate a better understanding of its long-term effects and its role in metabolic health.

#### Summary

The article discusses the ketogenic diet as a potential therapeutic method for treating obesity and type 2 diabetes, emphasizing its mechanism of action through inducing a state of ketosis, where ketone bodies become the primary energy source. Research suggests that this diet may improve blood glucose control and insulin sensitivity, which are critical in the context of insulin resistance. The article also outlines the mechanisms of the diet, such as the reduction of inflammation, its impact on the gut microbiome, and the satiety effect that supports weight management.

The ketogenic diet, particularly in its low-caloric form, demonstrates greater efficacy in weight loss and the improvement of metabolic parameters compared to traditional low-calorie diets. Despite these promising outcomes, the authors highlight the risk of nutrient deficiencies and potential long-term side effects, such as "keto flu." They emphasize the necessity for diet monitoring by specialists and further research into its long-term health effects. The conclusion drawn is that the ketogenic diet may serve as an effective therapeutic strategy but requires caution and a personalized approach to patient care.

#### Dislocure

Author's contribution: Conceptualization: Mariusz Zimonczyk, Paweł Nojek, Gustaw Błaszczyński Methodology: Agnieszka Nowotarska Software: Monika Zawół, Wiktoria Pawlik Check: Mariusz Zimonczyk, Wiktoria Pawlik, Monika Zawół Formal analysis: Paweł Nojek, Gustaw Błaszczyński Investigation: Agnieszka Nowotarska, Wiktoria Pawlik Resources: Mariusz Zimonczyk Data curation: Monika Zawół, Paweł Nojek Writing-rough preparation: Gustaw Błaszczyński, Agnieszka Nowotarska Writing review and ending: Mariusz Zimonczyk, Wiktoria Pawlik Visualization: Mariusz Zimonczyk, Paweł Nojek, Agnieszka Nowotarska Project administration: Monika Zawół, Wiktoria Pawlik, Gustaw Błaszczyński Receiving funding-no specific funding.

All authors have read and agreed with the published version of the manuscript.

# **Financing statement:**

the study received no specific funding

# **Institional Review Board Statement:**

Not applicable- not required

#### **Informed Consent Statement:**

Informed Consent was obtained from all subjects involved in the study

#### **Data Availability Statement:**

Not applicable

# **Conflict of Interest:**

The authors deny any conflict or interest

# References

- 1. O'Neill, B., & Raggi, P. (2020). The ketogenic diet: Pros and cons. *Atherosclerosis*, 292, 119–126. <u>https://doi.org/10.1016/j.atherosclerosis.2019.11.021</u>
- Di Raimondo, D., Buscemi, S., Musiari, G., Rizzo, G., Pirera, E., Corleo, D., Pinto, A., & Tuttolomondo, A. (2021). Ketogenic Diet, Physical Activity, and Hypertension-A Narrative Review. *Nutrients*, *13*(8), 2567. <u>https://doi.org/10.3390/nu13082567</u>
- Masino, S. A., & Rho, J. M. (2012). Mechanisms of Ketogenic Diet Action. In J. L. Noebels (Eds.) et. al., *Jasper's Basic Mechanisms of the Epilepsies*. (4th ed.). National Center for Biotechnology Information (US).
- 4. Nylen, K., Likhodii, S., & Burnham, W. M. (2009). The ketogenic diet: proposed mechanisms of action. *Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics*, 6(2), 402–405. <u>https://doi.org/10.1016/j.nurt.2009.01.021</u>
- Tiulganova, D. A., Nasaev, S. S., Chugreev, I. A., Rodionova, M. A., & Zavyalov, G. A. (2018). Mekhanizmy deĭstviia ketogennoĭ diety [Mechanisms of ketogenic diet action]. *Zhurnal nevrologii i psikhiatrii imeni S.S. Korsakova*, *118*(10. Vyp. 2), 72–75. https://doi.org/10.17116/jnevro201811810272
- Chandrasekaran, P., & Weiskirchen, R. (2024). The Role of Obesity in Type 2 Diabetes Mellitus-An Overview. *International journal of molecular sciences*, 25(3), 1882. <u>https://doi.org/10.3390/ijms25031882</u>
- 7. Ruze, R., Liu, T., Zou, X., Song, J., Chen, Y., Xu, R., Yin, X., & Xu, Q. (2023). Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. *Frontiers in endocrinology*, *14*, 1161521. <u>https://doi.org/10.3389/fendo.2023.1161521</u>
- Tinajero, M. G., & Malik, V. S. (2021). An Update on the Epidemiology of Type 2 Diabetes: A Global Perspective. *Endocrinology and metabolism clinics of North America*, 50(3), 337–355. <u>https://doi.org/10.1016/j.ecl.2021.05.013</u>
- Sandouk, Z., & Lansang, M. C. (2017). Diabetes with obesity--Is there an ideal diet?. *Cleveland Clinic journal of medicine*, 84(7 Suppl 1), S4–S14. <u>https://doi.org/10.3949/ccjm.84.s1.02</u>
- Bales, C. W., & Porter Starr, K. N. (2018). Obesity Interventions for Older Adults: Diet as a Determinant of Physical Function. *Advances in nutrition (Bethesda, Md.)*, 9(2), 151–159. <u>https://doi.org/10.1093/advances/nmx016</u>

- 11. Aaseth, J., Ellefsen, S., Alehagen, U., Sundfør, T. M., & Alexander, J. (2021). Diets and drugs for weight loss and health in obesity An update. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*, 140, 111789. https://doi.org/10.1016/j.biopha.2021.111789
- Martín-Peláez, S., Fito, M., & Castaner, O. (2020). Mediterranean Diet Effects on Type
  Diabetes Prevention, Disease Progression, and Related Mechanisms. A Review. *Nutrients*, 12(8), 2236. <u>https://doi.org/10.3390/nu12082236</u>
- Hemmingsen, B., Gimenez-Perez, G., Mauricio, D., Roqué I Figuls, M., Metzendorf, M. I., & Richter, B. (2017). Diet, physical activity or both for prevention or delay of type 2 diabetes mellitus and its associated complications in people at increased risk of developing type 2 diabetes mellitus. *The Cochrane database of systematic reviews*, *12*(12), CD003054. https://doi.org/10.1002/14651858.CD003054.pub4
- 14. Esposito, K., Maiorino, M. I., Bellastella, G., Chiodini, P., Panagiotakos, D., & Giugliano, D. (2015). A journey into a Mediterranean diet and type 2 diabetes: a systematic review with meta-analyses. *BMJ open*, 5(8), e008222. <u>https://doi.org/10.1136/bmjopen-2015-008222</u>
- 15. Zhou, C., Wang, M., Liang, J., He, G., & Chen, N. (2022). Ketogenic Diet Benefits to Weight Loss, Glycemic Control, and Lipid Profiles in Overweight Patients with Type 2 Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trails. *International journal of environmental research and public health*, 19(16), 10429. https://doi.org/10.3390/ijerph191610429
- 16. Dashti, H. M., Mathew, T. C., & Al-Zaid, N. S. (2021). Efficacy of Low-Carbohydrate Ketogenic Diet in the Treatment of Type 2 Diabetes. *Medical principles and practice : international journal of the Kuwait University, Health Science Centre*, 30(3), 223–235. <u>https://doi.org/10.1159/000512142</u>
- Yuan, X., Wang, J., Yang, S., Gao, M., Cao, L., Li, X., Hong, D., Tian, S., & Sun, C. (2020). Effect of the ketogenic diet on glycemic control, insulin resistance, and lipid metabolism in patients with T2DM: a systematic review and meta-analysis. *Nutrition & diabetes*, *10*(1), 38. <u>https://doi.org/10.1038/s41387-020-00142-z</u>
- Paoli, A., Bianco, A., Moro, T., Mota, J. F., & Coelho-Ravagnani, C. F. (2023). The Effects of Ketogenic Diet on Insulin Sensitivity and Weight Loss, Which Came First: The Chicken or the Egg?. *Nutrients*, 15(14), 3120. <u>https://doi.org/10.3390/nu15143120</u>
- Jing, T., Zhang, S., Bai, M., Chen, Z., Gao, S., Li, S., & Zhang, J. (2023). Effect of Dietary Approaches on Glycemic Control in Patients with Type 2 Diabetes: A Systematic Review with Network Meta-Analysis of Randomized Trials. *Nutrients*, 15(14), 3156. <u>https://doi.org/10.3390/nu15143156</u>
- 20. Skow, S. L., & Jha, R. K. (2023). A Ketogenic Diet is Effective in Improving Insulin Sensitivity in Individuals with Type 2 Diabetes. *Current diabetes reviews*, 19(6), e250422203985. <u>https://doi.org/10.2174/1573399818666220425093535</u>
- 21. Cunha, G. M., Guzman, G., Correa De Mello, L. L., Trein, B., Spina, L., Bussade, I., Marques Prata, J., Sajoux, I., & Countinho, W. (2020). Efficacy of a 2-Month Very Low-Calorie Ketogenic Diet (VLCKD) Compared to a Standard Low-Calorie Diet in Reducing Visceral and Liver Fat Accumulation in Patients With Obesity. *Frontiers in endocrinology*, 11, 607. <u>https://doi.org/10.3389/fendo.2020.00607</u>

- 22. Choi, Y. J., Jeon, S. M., & Shin, S. (2020). Impact of a Ketogenic Diet on Metabolic Parameters in Patients with Obesity or Overweight and with or without Type 2 Diabetes: A Meta-Analysis of Randomized Controlled Trials. *Nutrients*, 12(7), 2005. https://doi.org/10.3390/nu12072005
- 23. Murphy, E. A., & Jenkins, T. J. (2019). A ketogenic diet for reducing obesity and maintaining capacity for physical activity: hype or hope?. *Current opinion in clinical nutrition and metabolic care*, 22(4), 314–319. https://doi.org/10.1097/MCO.00000000000572
- Lambadiari, V., Katsimbri, P., Kountouri, A., Korakas, E., Papathanasi, A., Maratou, E., Pavlidis, G., Pliouta, L., Ikonomidis, I., Malisova, S., Vlachos, D., & Papadavid, E. (2024). The Effect of a Ketogenic Diet versus Mediterranean Diet on Clinical and Biochemical Markers of Inflammation in Patients with Obesity and Psoriatic Arthritis: A Randomized Crossover Trial. *International journal of molecular sciences*, 25(5), 2475. <u>https://doi.org/10.3390/ijms25052475</u>
- Santangelo, A., Corsello, A., Spolidoro, G. C. I., Trovato, C. M., Agostoni, C., Orsini, A., Milani, G. P., & Peroni, D. G. (2023). The Influence of Ketogenic Diet on Gut Microbiota: Potential Benefits, Risks and Indications. *Nutrients*, 15(17), 3680. <u>https://doi.org/10.3390/nu15173680</u>
- 26. Batch, J. T., Lamsal, S. P., Adkins, M., Sultan, S., & Ramirez, M. N. (2020). Advantages and Disadvantages of the Ketogenic Diet: A Review Article. *Cureus*, 12(8), e9639. <u>https://doi.org/10.7759/cureus.9639</u>
- 27. Rafiullah, M., Musambil, M., & David, S. K. (2022). Effect of a very low-carbohydrate ketogenic diet vs recommended diets in patients with type 2 diabetes: a meta-analysis. *Nutrition reviews*, *80*(3), 488–502. <u>https://doi.org/10.1093/nutrit/nuab040</u>
- Merovci, A., Finley, B., Hansis-Diarte, A., Neppala, S., Abdul-Ghani, M. A., Cersosimo, E., Triplitt, C., & DeFronzo, R. A. (2024). Effect of weight-maintaining ketogenic diet on glycemic control and insulin sensitivity in obese T2D subjects. *BMJ open diabetes research & care*, *12*(5), e004199. https://doi.org/10.1136/bmjdrc-2024-004199
- 29. Berk, K. A., van der Louw, E. J. T. M., Olieman, J. F., & van der Lely, A. J. (2021). Comment on Moriconi et al. Very-Low-Calorie Ketogenic Diet as a Safe and Valuable Tool for Long-Term Glycemic Management in Patients with Obesity and Type 2 Diabetes. *Nutrients* 2021, *13*, 758. *Nutrients*, *13*(10), 3613. https://doi.org/10.3390/nu13103613
- Zhang, X., Qin, J., Zhao, Y., Shi, J., Lan, R., Gan, Y., Ren, H., Zhu, B., Qian, M., & Du, B. (2016). Long-term ketogenic diet contributes to glycemic control but promotes lipid accumulation and hepatic steatosis in type 2 diabetic mice. *Nutrition research (New York, N.Y.)*, *36*(4), 349–358. <u>https://doi.org/10.1016/j.nutres.2015.12.002</u>