GUHES 2025; 7 (2): 37-45
DOI: 10.59124/guhes.1595201

Review

Journal of Gazi University Health Sciences Institute
journal homepage*:* https://dergipark.org.tr/tr/pub/guhes

Carbohydrate-Insulin Model in Obesity- An Updated Review

Buket Akyakar[1*], Yasemin Akdevelioğlu[2]

[1]Gazi University, Health Sciences Institute. Ankara, Türkiye
[2]Gazi University, Faculty of Health Sciences, Department of Nutrition and Dietetics. Ankara, Türkiye

Article info:

Received: 02.12.2024

Accepted: 06.05.2025

Keywords:

carbohydrate quality,
carbohydrate quantity,
carbohydrate-insulin,
model,
obesity.

Abstract

The prevalence of obesity is increasing rapidly worldwide and represents a serious public health problem. In order to prevent obesity, the causes of obesity should be identified and appropriate interventions developed. In this review, the carbohydrate-insulin model, which is one of the causal perspectives to obesity, and recent studies on this approach are discussed and evaluated together with the energy balance model. Reduced total energy expenditure when adhering to healthy dietary recommendations without energy restriction or dietary energy restriction interventions makes it difficult to understand the energy-independent insulinaemic effect of diet. Although more studies are needed on the causal approaches to obesity, it was concluded that high-fibre and low-glycaemic load diets, rather than carbohydrate-restricted diets in the carbohydrate-insulin model, may give more favorable results in trials. In addition, individualized nutritional and dietary models should be developed under the guidance of a dietician in the treatment of obesity.

Buket Akyakar **(Corresponding author);** ORCID: 0000-0003-0545-5680, e-mail: buketakyakar@hotmail.com
Yasemin Akdevelioğlu; ORCID: 0000-0002-2213-4419, e-mail: ydemirci@gazi.edu.tr

Citation: Akyakar, B. & Akdevelioğlu, Y. (2025). Carbohydrate-insulin model in obesity- an updated review. *Journal of Gazi University Health Sciences Institute*, 7(2), 1-6. https://doi.org/10.59124/guhes.1595201

1. Introduction

Obesity and obesity-related deaths are increasing rapidly around the world. According to the World Health Organization, at least 2.8 million people die each year because they are overweight or obese (WHO, 2023). To prevent obesity, the causes of obesity should be identified and individual and societal interventions should be developed to address these causes. In addition to the Energy Balance Model (EBM) in identifying the causes of obesity, the Carbohydrate Insulin Model (CIM), which is a more recent approach, is also discussed. This review analyses the CIM, which has been proposed as one of the causes of obesity, and compares it with the EBM. The EBM approach to obesity is more concerned with positive energy balance, while CIM focuses on hormonal and metabolic responses rather than calorie intake (Ludwig et al., 2021, Ludwig et al., 2022). The CIM model proposes metabolic processes that cause insulin resistance. In the CIM, high circulating fatty acids and other metabolites activate protein kinases such as Protein Kinase C (PKC), Jun kinase (JNK), and inhibitor of nuclear factor-κB (NF-κB) kinase-β (IKKβ), and may cause these kinases to impair insulin signaling by increasing inhibitory serine phosphorylation of insulin receptor substrates (IRS) (key mediators of insulin receptor signaling) (Petersen & Shulman, 2006). It is also reported that TNF-induced insulin resistance is associated with increased IL-18 gene expression in muscle tissue (Krogh-Madsen et al., 2006). It is suggested that this is due to the transcription of miR-146b, an intergenic miRNA that can regulate the inflammatory process by attenuating cytokine signaling via nuclear factor-κB (Shi et al., 2014).

2. Methodology

PubMed, Sciencedirect and Wiley databases were used to search for relevant literature. Keywords included carbohydrate-insulin model, energy balance model, obesity, complex carbohydrates, carbohydrate quality, glycemic index, glycemic load, insulin resistance, blood glucose, type 2 diabetes and various combinations of these terms. Research articles, narrative reviews, systematic reviews and meta-analyses published in the last 10 years were analysed. Only articles published in English were included.

3. Carbohydrate Insulin Model

There are two different views to explain the causes of obesity: EBM and the CIM. In the EBM, an increased intake of energy-dense, palatable, ultra-processed foods with a change in dietary pattern provides a positive energy balance and causes an increase in the amount of body fat (Ludwig et al., 2021). The CIM hypothesis is that increased fat content triggers the desire to overeat (Ludwig et al., 2022). In the energy balance approach, dietary interventions take the form of energy restriction, since a positive energy balance increases the body weight of individuals. However, CIM argues that carbohydrates that stimulate insulin release should be reduced to reduce body fat (Hall et al., 2015). Insulin plays a key role in this model. Insulin reduces ketone production in the liver, stimulates glycogen and fat accumulation by allowing circulating glucose to be taken into the cell (Ludwig

& Ebbeling, 2018). Refined carbohydrates in particular are insulinaemic and have a very high glycaemic load (GL).

When these high-GL foods enter the body, they are digested very quickly and induce the release of insulin and glucagon-like peptide-1 (GLIP-1), inhibit lipolysis and promote fat accumulation in adipose tissue (Ludwig & Friedman, 2014). Therefore, this dietary pattern causes hyperinsulinemia, which leads to an increase in adipose tissue and sheds light on the relationship between obesity and hormonal response (Taubes, 2007).

4. Carbohydrate Quantity/Quality in the Carbohydrate-Insulin Model and Comparison with the Energy Balance Model

In the CIM approach, it has been reported in the literature that foods with a high glycaemic load trigger obesity. In this approach, research generally focuses on dietary carbohydrate ratio and carbohydrate quality. This is a controversial topic because the research is very conflicting.

4.1. Carbohydrate Quantity

Dietary carbohydrate intake is reduced in three categories (reduced carbohydrate diet, low carbohydrate diet and very low carbohydrate diet). In a reduced carbohydrate diet, at least 130 g of carbohydrates are consumed daily and the amount of carbohydrates does not exceed 45% of total energy intake. The carbohydrate restriction in a low-carbohydrate diet is between 30-130 g per day. Very low carbohydrate diets contain <30 g of carbohydrate per day. Studies have generally compared low-carbohydrate diets with low-fat diets (10-15% of total daily energy intake from fat) (Hite et al., 2011).

In a study by Hall et al. (Hall et al., 2015) of 19 obese American subjects, which examined the effects of fat-restricted and carbohydrate-restricted diets of equivalent energy on fat oxidation and body fat loss, it was found that fat oxidation did not change in those on the low-fat diet (LFD) compared with those on the carbohydrate-restricted diet, despite the equivalent energy, but there was a greater rate of body fat loss. In contrast, another study showed that those who consumed a low-carbohydrate diet for 12 months had a significant decrease in body weight and fat mass compared with those who consumed a low-fat diet (Bazzano et al., 2014). The same contradiction exists in the relationship between low-carbohydrate diets and fasting blood glucose, serum insulin and other glucose parameters. A decline in body weight, HbA1c and fasting plasma glucose levels was observed in people with HbA1c levels of 6.0-6.9% who were not receiving diabetes treatment compared with the control group (no change in diet) after consuming less than 40 g of carbohydrate per day for 6 months (Dorans et al., 2022). On the contrary, no significant difference in serum glucose and insulin levels was observed in the low-carbohydrate and low-fat diet groups over 12 months in the study by Bazzano et al. (Bazzano et al., 2014). A meta-analysis of 13 randomised controlled trials comparing low-carbohydrate diets with low-fat diets for at least 12 months showed significant reductions in body weight, triglycerides and diastolic blood pressure in those on very low-carbohydrate diets compared with those on low-fat diets (Bueno et al., 2013). A systematic review and meta-analysis of 22 randomised controlled trials in South Africa showed that high carbohydrate intake (compared with low carbohydrate intake) was associated with a small increase in the risk of obesity.

Limitations of the study included the non-standardised categorisation of dietary intake across studies and confounding factors such as total energy intake, activity level, age and sex (Sartorius et al., 2018). Therefore, further studies are needed to classify carbohydrate intake by type in detail and to examine the direct effect of dietary carbohydrate ratios on insulin secretion and its relationship with obesity.

When healthy eating recommendations are followed, even in the absence of energy restriction (regardless of diet type), individuals' daily energy intake decreases by an average of 500-600 kcal (Gardner et al., 2018). In addition, the low-carbohydrate diet contains less simple sugars than the control group due to carbohydrate restriction, so the glycaemic load is low and energy intake is significantly reduced (Dorans et al., 2022). Moreover, energy restriction is applied to individuals in the studies (Hall et al., 2015; Tricò et al., 2021). Therefore, it is difficult to interpret the insulinaemic effect of diet alone, independent of the energy intake of the carbohydrate insulin model under these conditions. In this case, studies evaluating the carbohydrate ratio or glycaemic load of the diet without energy restriction/alteration are needed. The American Diabetes Association has published a guideline for adults with type 2 diabetes that includes low and very low carbohydrate dietary patterns (Siverhus, 2019). This guideline includes low-very low-carbohydrate dietary patterns and plans of experts in adults with type 2 diabetes. According to European recommendations, there are relationships between very low carbohydrate ketogenic diets and hypoglycaemia, ketoacidosis and vitamin-mineral deficiencies; also a relationship between extremely high carbohydrate or low carbohydrate dietarty approaches and high mortality (Aas et al., 2023).

The ESPEN 2021 guideline states that hospitalised patients with diabetes should avoid diets with a carbohydrate content of less than 40% of total energy intake, as this is associated with low energy intake and risk of malnutrition (Thibault et al., 2021). Although adaptation to long-term low-carbohydrate diets is not a problem (Ebrahimpour-Koujan et al., 2019), as they generally have short-term metabolic benefits and are of limited efficacy and practicality in the long term (Barber et al., 2021), it is important for professionals to be aware of these issues when applying low-carbohydrate diets to obese people and people with type 2 diabetes.

4.2. Carbohydrate Quality

High quality carbohydrate sources (whole grains, legumes or fruits), low glycaemic index (GI) and glycaemic load (GL), high dietary fibre and low sugar content are the determinants of carbohydrate quality (Sievenpiper, 2020). Low-carbohydrate diets reduce the consumption of whole grains, which are a source of high-quality carbohydrates, and consequently reduce the daily intake of dietary fibre. Low-carbohydrate diets contain significantly fewer whole grains than diets with no restrictions on any food group (DASH diet, Mediterranean diet, etc.) (Turner-McGrievy et al., 2021). In addition, the group who were in low-carbohydrate diet had a lower total fibre intake comparing the low-fat diet group (Gardner et al., 2018). A systematic review and meta-analysis conducted to identify markers that explain the association between carbohydrate quality and health found that high dietary fibre intakes have significant benefits in protecting against type 2 diabetes, cardiovascular disease and cancer, and that body weight, blood pressure and total cholesterol levels benefits in protecting against type 2 diabetes, cardiovascular disease and cancer, and that body weight, blood pressure and total cholesterol levels decreased significantly with increasing dietary fibre intake (Reynolds et al., 2019). As dietary fibre is thought to regulate glucose and lipid parameters in individuals by supporting the gut microbiota through the production of short-chain fatty acids (Cronin et al., 2021) daily fibre consumption is particularly important in the prevention of obesity and obesity-related diseases.

In a review of carbohydrate quality studies in the literature, HOMA index, serum diacylglycerols and triacylglycerols, insulin, leptin and proinflammatory cytokines increased more in rats fed a high GI diet for 4 weeks than in those fed a low GI diet. In addition, an increase in fatty liver and overall adipose tissue was observed in obese rats fed rapidly digested carbohydrates (Manzano et al., 2022). In a randomised trial of 121 mildly obese adults, those fed a low-GI diet for 6 months had greater weight loss and greater progression in insulin resistance and sensitivity comparing low-fat diet group (Juanola-Falgarona et al., 2014). It is thought that low glycaemic index diets increase pregnancy rates in women and have an effect on the weight of babies to be born when used during pregnancy. A study of adult women who were with a body mass index (BMI) of 25-40 kg/m^2 undergoing In Vitro Fertilisation (IVF) reported that a hypocaloric low-glycaemic index diet improved oocyte development and pregnancy rates (Juanola-Falgarona et al., 2014).

As a result of a meta-analysis of 5 randomised controlled trials and 302 participants, it was reported that low glycaemic index diets contributed to a reduced risk of macrosomia in patients with gestational diabetes compared with the control group.

It was also reported that low glycaemic index diets with added dietary fibre further reduced the risk of macrosomia (Wei et al., 2016). According to these results, focusing on the quality of carbohydrates in the diet seems to be more beneficial than focusing on the quantity of carbohydrates (Sievenpiper, 2020).

4.3. Carbohydrate Insulin Model-Energy Balance Model

As shown in Figure 1, it has been reported that unhealthy dietary patterns can trigger either inflammatory or insulinaemic responses in the development of obesity and type 2 diabetes; with this view, the EBM shows the inflammatory response of individuals to diet, while the CIM explains the hormonal and metabolic responses. Evaluating these models together, rather than comparing them, may be a more accurate approach to assessing the development of obesity and associated diabetes (Ss, 2023). It has also been suggested that diets that focus on dietary models (taking into account the quality of carbohydrates) rather than a single type of diet are more appropriate (Sievenpiper, 2020). For the prevention of obesity and its complications, it seems more appropriate to develop individual dietary plans under the guidance of a dietician.

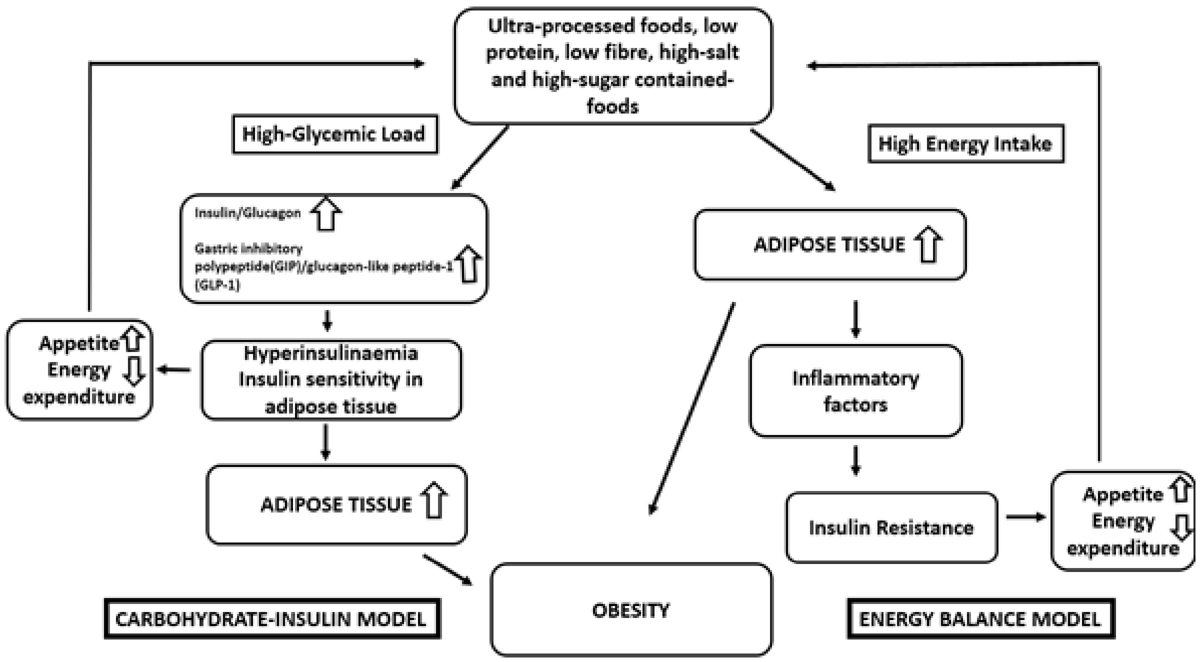

Figure 1. Causal Approaches of Obesity

The figure was adapted from Ludwig DS, Aronne LJ, Astrup A, de Cabo R, Cantley LC, Friedman MI, et al. (2021) The carbohydrate-insulin model: a physiological perspective on the obesity pandemic. Am J Clin Nutr.114(6):1873-85 and Ludwig DS, Apovian CM, Aronne LJ, Astrup A, Cantley LC, Ebbeling CB, et al. (2022) Competing paradigms of obesity pathogenesis: energy balance versus carbohydrate-insulin models. Eur J Clin Nutr. 76(9):1209-21. Adapted with permission.

4.4. Long-Term Risk Assessment of Low Carbohydrate Diet and The Importance of Personalised Diets

Low-carbohydrate diets are promoted in CIM in order to reduce the hyperinsulinemic effect. Some studies indicate beneficial metabolic effects of low-carbohydrate diets (Bazzano et al., 2014; Dorans et al., 2022), yet a contradictory finding exists as well (Hall et al., 2015). First of all, there is a lack of standardization of carbohydrate classification in studies (Feinman et al., 2015). This makes it difficult to compare low-carb diets with other dietary models, which in turn makes it difficult to explain the CIM approach.

Second, low-carbohydrate diets pose sustainability concerns because they increase the proportion of the diet coming from protein and fat. Low-carbohydrate diets cause some side effects, such as fatigue, headache and muscle pain, and serious side effects, such as ketoacidosis (Teicholz et al., 2025). Carbohydrate restriction may also result in low intakes of dietary fibre, minerals, vitamins, trace elements and PUFAs (Sampaio, 2016).

Moreover, It may cause a decrease in dietary fiber, mineral, vitamin, trace element and PUFA intake due to carbohydrate restriction (Sampaio, 2016). Another concern is the negative lipid response that can occur with low-carbohydrate diets, which is an increase in LDL cholesterol (LDL-C).

Although a systematic review and meta-analysis found no significant difference in serum LDL-C in people on a 20-40% carbohydrate diet for up to 24 months (Teuta et al.,2019), dietary saturated fat should be considered as it poses a risk for cardiovascular disease. Finally, it is necessary to take into consideration both the economic and environmental damages of increased meat consumption due to carbohydrate restriction (Barber, 2021).

Given these potential outcomes, personalized nutrition planning should prioritise individual health status, metabolic needs, lifestyle and preferences. Since a uniform diet will not be effective in the long term, a dietitian plays an important role in evaluating components such as genomes, gut microbiota, health biomarkers, socio-economic and cultural factors when designing a diet (Chen & Chen, 2022). This is because while restricting carbohydrates in the diet, it is also necessary to maintain adequate levels of fibre, vitamins, minerals and essential fatty acids. A study of 800 people between the ages of 18 and 70 reported that personalized dietary interventions, rather than general recommendations, can lead to lower postprandial glycaemic responses and positive changes in gut microbiota (Zeevi et al., 2015). In addition to the creation of personalized diet plans, individual self-monitoring of diet and follow-up is also important for research results (Popp et al., 2022).

5. Conclusion

Very low-carbohydrate diets have been associated with several concerns regarding their long-term sustainability, potential health risks, and economic as well as environmental implications. The long-term effects of such dietary patterns continue to be debated in the literature.

From a CIM perspective, diets rich in dietary fiber and low glycemic load carbohydrate sources may be considered more effective in obesity management compared to traditional low-carbohydrate approaches. Furthermore, the development of personalized dietary interventions by dietitians is essential for the effective treatment of obesity. However, further research is needed to evaluate and improve dietary patterns used to investigate the multifactorial causes of obesity.

Funding Information

No funding was received for this study.

Conflict of Interest

There are no conflicts of interest to declare.

Author Contributions

BA contributed to research, article writing and figure creation. YA contributed to topic identification, writing process and evaluation.

References

Aas, A, M., Axelsen, M., Churuangsuk, C., Hermansen, K., Kendall, C. W. C., Kahleova, H., Khan, T., Lean, M. E. J., Mann, J. I., Pedersen, E., Pfeiffer, A., Rahelić, D., Reynolds, A. N., Risérus, U., Rivellese, A. A., Salas-Salvadó, J., Schwab, U., Sievenpiper, J. L., Thanopoulou, A., & Nutrition Study Group of the European Association for the Study of Diabetes. (2023). Evidence-based European recommendations for the dietary management of diabetes. *Diabetologia, 66*(6), 965-985. https://doi.org/10.1007/s00125-023-05894-8

Barber, T. M., Hanson, P., Kabisch, S., Pfeiffer, A. F., & Weickert, M. O. (2021). The low-carbohydrate diet: Short-term metabolic efficacy versus longer-term limitations. *Nutrients*, 13(4), 1187. https://doi.org/10.3390/nu13041187

Bazzano, L. A., Hu, T., Reynolds, K., Yao, L., Bunol, C., Liu, Y., Chen, C.-S., Klag, M. J., Whelton, P. K., & He, J. (2014). Effects of low-carbohydrate and low-fat diets: A randomized trial. *Annals of Internal Medicine, 161*(5), 309-318. https://doi.org/10.7326/M14-0180

Bueno, N. B., de Melo, I. S., de Oliveira, S. L., & da Rocha Ataide, T. (2013). Very-low-carbohydrate ketogenic diet vs. low-fat diet for long-term weight loss: A meta-analysis of randomized controlled trials. *British Journal of Nutrition*, 110(7), 1178-1187. https://doi.org/10.1017/s0007114513000548

Cronin, P., Joyce, S. A., O'Toole, P. W., & O'Connor, E. M. (2021). Dietary fibre modulates the gut microbiota. *Nutrients*, 13(5), 1655. https://doi.org/10.3390/nu13051655

Chen, R., & Chen, G. (2022). Personalized nutrition for people with diabetes and at risk of diabetes has begun. *Journal of Future Foods*, 2(3), 193-202.

Dorans, K. S., Bazzano, L. A., Qi, L., He, H., Chen, J., Appel, L. J., Chen, C.-S., Hsieh, M.-H., Hu, F. B., & Mills, K. T. (2022). Effects of a low-carbohydrate dietary intervention on hemoglobin A1c: A randomized clinical trial. *JAMA Network Open*, 5(10), e2238645-e2238645. https://doi.org/10.1001/jamanetworkopen.2022.38645

Ebrahimpour-Koujan, S., Keshteli, A. H., Afshar, H., Esmaillzadeh, A., & Adibi, P. (2019). Adherence to low carbohydrate diet and prevalence of psychological disorders in adults. *Journal of Nutrition*, 18(1):87.https://doi.org/10.1186/s12937-019-0513-8

Feinman, R, D., Pogozelski, W, K., Astrup, A., Bernstein, R, K., Fine, E, J., Westman, E, C., Accurso, A., Frassetto, L., Gower, B, A., McFarlane, S, I., Nielsen, J, V., Krarup, T., Saslow, L., Roth, K, S., Vernon, M, C., Volek, J, S., Wilshire, G, B., Dahlqvist, A., Sundberg, R., Childers, A., Morrison, K., Manninen, A, H., Dashti, H, M., Wood, R, J., Wortman, J., Worm, N. Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base. *Nutrition*. 2015 Jan;31(1):1-13. doi: 10.1016/j.nut.2014.06.011.

Gardner, C. D., Trepanowski, J. F., Del Gobbo, L. C., Hauser, M. E., Rigdon, J., Ioannidis, J. P., Desai, M., & King, A. C. (2018). Effect of low-fat vs low-carbohydrate diet on 12-month weight loss in overweight adults and the association with genotype pattern or insulin secretion: The dietdits randomized clinical trial. *JAMA*, 319(7), 667-679. https://doi.org/10.1001/jama.2018.0245

Hall, K. D., Bemis, T., Brychta, R., Chen, K. Y., Courville, A., Crayner, E. J., Goodwin, S., Guo, J., Howard, L., & Knuth, N. D. (2015). Calorie for calorie, dietary fat restriction results in more body fat loss than carbohydrate restriction in people with obesity. *Cell Metabolism*, *22*(3), 427-436. https://doi.org/10.1016/j.cmet.2015.07.021

Hite, A. H., Berkowitz, V. G., & Berkowitz, K. (2011). Low-carbohydrate diet review: Shifting the paradigm. *Nutrition in Clinical Practice*, 26(3), 300-308. https://doi.org/10.1177/0884533611405791

Juanola-Falgarona, M., Salas-Salvadó, J., Ibarrola-Jurado, N., Rabassa-Soler, A., Díaz-López, A., Guasch-Ferré, M., Hernández-Alonso, P., Balanza, R., & Bulló, M. (2014). Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: A randomized controlled trial. *The American Journal of Clinical Nutrition, 100*(1), 27-35. https://doi.org/10.3945/ajcn.113.081216

Ludwig DS, Ebbeling CB. (2018). The Carbohydrate-Insulin Model of Obesity: Beyond "Calories In, Calories Out". *JAMA Internal Medicine*, Aug 1;178(8):1098-1103. doi: 10.1001/jamainternmed.2018.2933. PMID: 29971406; PMCID: PMC6082688.

Ludwig, D. S., Apovian, C. M., Aronne, L. J., Astrup, A., Cantley, L. C., Ebbeling, C. B., Heymsfield, S. B., Johnson, J. D., King, J. C., & Krauss, R. M. (2022). Competing paradigms of obesity pathogenesis: Energy balance versus carbohydrate-insulin models. *European Journal of Clinical Nutrition*, 76(9), 1209-1221. https://doi.org/10.1038/s41430-022-01179-2

Ludwig, D. S., Aronne, L. J., Astrup, A., de Cabo, R., Cantley, L. C., Friedman, M. I., Heymsfield, S. B., Johnson, J. D., King, J. C., & Krauss, R. M. (2021). The carbohydrate-insulin model: A physiological perspective on the obesity pandemic. *The American Journal of Clinical Nutrition*, 114(6), 1873-1885. https://doi.org/10.1093/ajcn/nqab270

Ludwig, D. S., & Friedman, M. I. (2014). Increasing adiposity: Consequence or cause of overeating? *JAMA*, 311(21), 2167-2168. https://doi.org/10.1001/jama.2014.4133

Krogh-Madsen R, Plomgaard P, Møller K, Mittendorfer B, Pedersen BK. (2006). Influence of TNF-alpha and IL-6 infusions on insulin sensitivity and expression of IL-18 in humans. *Am Journal Physiol Endocrinol Metabolisma*. Jul;291(1):E108-14. doi: 10.1152/ajpendo.00471.2005.

Manzano, M., Giron, M. D., Salto, R., Vilchez, J. D., Reche-Perez, F. J., Cabrera, E., Linares-Pérez, A., Plaza-Díaz, J., Ruiz-Ojeda, F. J., & Gil, A. (2022). Quality more than quantity: The use of carbohydrates in high-fat diets to tackle obesity in growing rats. *Frontiers in Nutrition, 9*, 112-119. https://doi.org/10.3389/fnut.2022.809865

Petersen KF, Shulman GI. (2006). Etiology of insulin resistance. *Am Journal Medicine*. May; 119(5 Suppl 1): S10-6. doi: 10.1016/j.amjmed.2006.01.009.

Popp, C. J., Hu, L., Kharmats, A. Y., Curran, M., Berube, L., Wang, C., & Sevick, M. A. (2022). Effect of a personalized diet to reduce postprandial glycemic response vs a low-fat diet on weight loss in adults with abnormal glucose metabolism and obesity: a randomized clinical trial. *JAMA*, 5(9), e2233760-e2233760.

Reynolds, A., Mann, J., Cummings, J., Winter, N., Mete, E., & Te Morenga, L. (2019). Carbohydrate quality and human health: A series of systematic reviews and meta-analyses. *Lancet, 393*(10170), 434-445. https://doi.org/10.1016/S0140-6736(18)31809-9.

Sampaio, L.P. (2016). Ketogenic diet for epilepsy treatment. *Arquivos de Neuro-Psiquiatria*. 74, 842–848. doi: 10.1590/0004-282X20160116.

Sartorius, K., Sartorius, B., Madiba, T. E., & Stefan, C. (2018). Does high-carbohydrate intake lead to increased risk of obesity? A systematic review and meta-analysis. *BMJ Open, 8*(2), e018449. https://doi.org/10.1136/bmjopen-2017-018449.

Shi C, Zhu L, Chen X, Gu N, Chen L, Zhu L, Yang L, Pang L, Guo X, Ji C, Zhang C. (2014). IL-6 and TNF-α induced obesity-related inflammatory response through transcriptional regulation of miR-146b. *Journal of Interferon & Cytokine Research.* May;34(5):342-8. doi: 10.1089/jir.2013.0078.

Sievenpiper, J. L. (2020). Low-carbohydrate diets and cardiometabolic health: The importance of carbohydrate quality over quantity. *Nutrition Reviews,* 78 (Supplement_1), 69-77. https://doi.org/10.1093/nutrit/nuz082.

Siverhus, K. (2019). Low-carbohydrate and very low carbohydrate eating patterns in adults with diabetes. Houston, Texas.

Ss, P. (2023). Energy-balance and carbohydrate-insulin models of obesity are not competing propositions. *International Journal of Obesity*, *47*(2), 95-97. https://doi.org/10.1038/s41366-022-01249-2

Taubes G. (2007). Good calories, bad calories: challenging the conventional wisdom on diet, weight control, and disease. https://archive.org/details/goodcaloriesbadc0000taub.

Teicholz, N., Croft, S. M., Cuaranta, I., Cucuzzella, M., Glandt, M., Griauzde, D. H., Jerome-Zapadka, K., Kalayjian, T., Murphy, K., Nelson, M., Shanahan, C., Nishida, J. L., Oh, R. C., Parrella, N., Saner, E. M., Sethi, S., Volek, J. S., Williden, M., & Wolver, S. (2025). Myths and Facts Regarding Low-Carbohydrate Diets. *Nutrients*, *17*(6), 1047. https://doi.org/10.3390/nu17061047

Teuta Gjuladin-Hellon, Ian G Davies, Peter Penson, Raziyeh Amiri Baghbadorani, (2019). Effects of carbohydrate-restricted diets on low-density lipoprotein cholesterol levels in overweight and obese adults: a systematic review and meta-analysis, *Nutrition Reviews*, 77(3) ,161–180), https://doi.org/10.1093/nutrit/nuy049

Thibault, R., Abbasoglu, O., Ioannou, E., Meija, L., Ottens-Oussoren, K., Pichard, C., Rothenberg, E., Rubin, D., Siljamäki-Ojansuu, U., & Vaillant, M.-F. (2021). ESPEN guideline on hospital nutrition. *Clinical Nutrition*, *40*(12), 5684-5709. https://doi.org/10.1016/j.clnu.2021.09.039

Tricò, D., Moriconi, D., Berta, R., Baldi, S., Quinones-Galvan, A., Guiducci, L., Taddei, S., Mari, A., & Nannipieri, M. (2021). Effects of low-carbohydrate versus Mediterranean diets on weight loss, glucose metabolism, insulin kinetics and β-cell function in morbidly obese individuals. *Nutrients, 13*(4), 1345. https://doi.org/10.3390/nu13041345

Turner-McGrievy, G., Wirth, M. D., Hill, K. L., Dear, E. R., & Hébert, J. R. (2021). Examining commonalities and differences in food groups, nutrients, and diet quality among popular diets. *Clinical Nutrition Reports* .ESPEN.2021Feb:41:377-385. https://doi.org/10.1016/j.clnesp.2020.10.017

Wei, J., Heng, W., & Gao, J. (2016). Effects of low glycemic index diets on gestational diabetes mellitus: A meta-analysis of randomized controlled clinical trials. *Medicine, 95*(22), e3792. https://doi.org/10.1097/MD.0000000000003792

World Health Organization (WHO). (2023, June 28). *6 facts on obesity*. Retrieved from. https://www.who.int/news-room/facts-in-pictures/detail/6-facts-on-obesity

Zeevi, D., Korem, T., Zmora, N., Israeli, D., Rothschild, D., Weinberger, A., & Segal, E. (2015). Personalized nutrition by prediction of glycemic responses. *Cell*, 163(5), 1079-1094.