Reducing Cardiovascular Disease Risk with Therapeutic Carbohydrate Restriction

'Studies have shown that reducing carbohydrate intake is the most effective dietary approach for managing atherogenic dyslipidemia, particularly in individuals with excess adiposity and/or metabolic syndrome'. Kim et al. (2025)

Nutrition Network

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Introduction

Despite significant medical advances, cardiovascular disease (CVD) is the leading cause of mortality globally. Markers of insulin resistance are associated with increased CVD risk on a population level (with similar findings in women) and hyperinsulinaemia is an independent risk factor for CVD. This supports the findings of Gerald Reaven, who was one of the first to outline the role of insulin resistance in human disease. TCR effectively addresses the core features of hyperinsulinaemia and metabolic syndrome (central adiposity; elevated fasting glucose, triglycerides, and blood pressure; reduced HDL-c; and increased small, dense LDL-c), key drivers of CVD. In addition, hyperglycaemia is implicated in glycocalyx integrity, endothelial function, and clotting activation. Glycaemic variability has also been studied in the context of CVD and has been associated with an increased risk of heart failure. In another study impaired fasting glucose variability was independently associated with CVD and mortality in a general population without diabetes. Inflammation also plays a key role in CVD and TCR, particularly in the ketogenic range, has significant anti-inflammatory effects.

1. Dyńka, D. *et al.* (2023) 'The Ketogenic Diet and Cardiovascular Diseases', *Nutrients*, 15(15), p. 3368. Available at: https://doi.org/10.3390/nu15153368.

Systematic Reviews and Meta-Analyses

A number of systematic reviews and meta-analyses have examined the efficacy of TCR approaches in reducing CVD risk in patients both with and without type 2 diabetes. Examples are below (also see this reference resource from Nutrition Network).

1. Gjuladin-Hellon, T. *et al.* (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), pp. 161–180. Available at: https://doi.org/10.1093/nutrit/nuy049.

2. Ghasemi, P. *et al.* (2024) 'Impact of very low carbohydrate ketogenic diets on cardiovascular risk factors among patients with type 2 diabetes; GRADE-assessed systematic review and meta-analysis of clinical trials', *Nutrition & Metabolism*, 21(1), p. 50. Available at: https://doi.org/10.1186/s12986-024-00824-w.
3. Dong, T. *et al.* (2020) 'The effects of low-carbohydrate diets on cardiovascular risk factors: A meta-analysis', *PLOS ONE*, 15(1), p. e0225348. Available at: https://doi.org/10.1371/journal.pone.0225348.

Studies

Other studies examining TCR show improvements in CVD risk factors across different populations, including healthy adults, women, and children (may be nutritionally sufficient). Examples include:

1. Athinarayanan, S.J. *et al.* (2020) 'Impact of a 2-year trial of nutritional ketosis on indices of cardiovascular disease risk in patients with type 2 diabetes', *Cardiovascular Diabetology*, 19(1), p. 208. Available at: https://doi.org/10.1186/s12933-020-01178-2. (5-year data on Lipid, Inflammatory, Hepatic, and Renal Markers)
2. Unwin, D.J. *et al.* (2019) 'Substantial and Sustained Improvements in Blood Pressure, Weight and Lipid Profiles from a Carbohydrate Restricted Diet: An Observational Study of Insulin Resistant Patients in Primary Care', *International Journal of Environmental Research and Public Health*, 16(15), p. 2680. Available at: https://doi.org/10.3390/ijerph16152680.

What about Fat?

The diet-heart hypothesis, in the context of saturated fat and CVD risk, is an outdated and flawed paradigm, which has been debunked in several studies. It is now recognised that the type of fat consumed, in conjunction with the food matrix, provides context for the metabolic effects of dietary fat. Recent reviews and meta-analyses do not demonstrate benefits from restricting dietary fat. These findings are also observed in studies of women, which include a re-analysis of the Women's Health Initiative. In a similar way, studies increasingly find dairy products to be either neutral or beneficial in CVD risk. Though rarely discussed, there is no association between dietary cholesterol and plasma cholesterol, and there are no recommendations to limit dietary cholesterol (removed from guidelines in 2015).

1. Yamada, S. *et al.* (2025) 'Saturated Fat Restriction for Cardiovascular Disease Prevention: A Systematic Review and Meta-analysis of Randomized Controlled Trials', *JMA Journal*, 8(2), pp. 395–407. Available at: https://doi.org/10.31662/jmaj.2024-0324.

Atherogenic dyslipidemia and lean mass hyper-responders

Atherogenic dyslipidaemia, as described by **elevated serum triglycerides** and **decreased HDL-c** and an increase in **small dense LDL-c** (also known as **pattern B**), may be effectively

improved using TCR, demonstrating a reduction in triglycerides, increased HDL-c, and increased large, buoyant LDL-c (pattern A).

1. Kim, S., Shin, M.-J. and Krauss, R.M. (2025) 'Dietary Management of Atherogenic Dyslipidemia', *Current Atherosclerosis Reports*, 27(1), p. 93. Available at: https://doi.org/10.1007/s11883-025-01335-6.

In contrast, a group of individuals have been identified as developing significant elevations in LDL-c on a carbohydrate-reduced diet, notably in the context of good metabolic health, with lipid profiles comprised of **low serum triglycerides** (≤70 mg/dL [0.8 mmol/L]), **high HDL-c** (≥80 mg/dL [2.1 mmol/L]), and **high LDL-c** (≥200 mg/dL [5.2 mmol/L]) with a predominance of large buoyant particles (**pattern A**). Those identified with this phenotype have been labelled as Lean Mass Hyper-Responders (LMHRs). This group reflects a physiological response to carbohydrate restriction, which requires more study. Features common in this phenotype are a normal bodyweight, a higher lean mass (often athletic), good metabolic health, and LDL-c elevations occurring with dietary change (reduced carbohydrates). Data are lacking for this phenotype and specific studies for this group are warranted.

What is known is that LDL-c, as an isolated metric, is not a good measure of CVD risk, with CVD occurring across a range of LDL-c concentrations. Rather, measures of insulin resistance, which may be reflected in lipid ratios, are better predictors of risk, namely the triglyceride:HDL-c ratio (target <1.5 in mmol/L, or <3.0 in mg/dL).

A possible physiological, as opposed to pathological, mechanism behind this cholesterol response has been suggested, namely, the lipid-energy model, which remains a subject of study. Early studies of the LMHR phenotype are promising, emphasising considerations for a wide range of biomarkers when determining CVD risk. Regular monitoring, including a coronary artery calcium (CAC) score (a CAC score of zero reflecting lower risk), is essential for stratifying risk in this understudied cohort. Recent LMHR studies:

1. Budoff, M. *et al.* (2024) 'Carbohydrate Restriction-Induced Elevations in LDL-Cholesterol and Atherosclerosis', *JACC: Advances*, 3(8), p. 101109. Available at: https://doi.org/10.1016/j.jacadv.2024.101109.
2. Soto-Mota, A. *et al.* (2025) 'Plaque Begets Plaque, ApoB Does Not', *JACC: Advances*, 0(0). Available at: https://doi.org/10.1016/j.jacadv.2025.101686.

Other factors contributing to CVD risk

While hyperinsulinaemia and dysglycaemia are key drivers of increased CVD risk, other factors contribute to the development of disease, including stress, sleep disturbances, alcohol consumption, smoking (includes vaping), and environmental factors such as pollution.

Individual responses to dietary composition can vary, so appropriate medical monitoring is advised. Patients who are taking medication should consult with their doctor, as the following guidelines (Society of Metabolic Health Practitioners) may need to be considered.