THE EFFECT OF KETOGENIC DIETS ON CHOLESTEROL LEVELS, BODY FAT, AND CARDIOVASCULAR RISK

Do high-fat diets increase the risk for cardiovascular disease?

Decades of research have failed to support the long-held hypothesis that higher-fat diets increase risk for cardiovascular disease.

Leading nutrition researchers at Harvard University and Tufts University recommended that dietary advice be updated to reflect the state of the evidence in their paper (Mozaffarian D, Ludwig DS. The 2015 US Dietary Guidelines: Ending the 35% limit on total dietary fat. *JAMA.* 2015), stating:

> *Reducing total fat (replacing total fat with overall carbohydrates) does not lower CVD risk. Dietary advice should put the emphasis on optimizing types of dietary fat and not reducing total fat.*

Dr. Zoë Harcombe published a meta-analysis of 10 RCTs totaling 62,447 patients which found no evidence to support a connection between dietary saturated fat and heart disease: Harcombe Z, Baker JS, Davies B. Evidence from prospective cohort studies does not support current dietary fat guidelines: A systematic review and meta-analysis. *Br J Sports Med.* 2017.

Her detailed analysis of the 2020 Cochrane review of saturated fat and heart disease also found no connection: Cochrane saturated fat reviews. Dr. Zoë Harcombe, PhD.

Dr. Nina Teicholz, a journalist who founded the Nutrition Coalition to advocate for changes to the U.S. Dietary Guidelines, posted this list of scientific studies that have failed to support the metabolic superiority of low-fat diets: Total fat: Is the low fat diet recommended? Nutrition Coalition.

The below excerpt is from my book *Change Your Diet, Change Your Mind* (Balance 2014):

> *For decades, we were told that beef was dangerous because the saturated fat it contains was supposed to drive our blood cholesterol levels up, force cholesterol into our coronary artery walls, and cause heart attacks. Fortunately, this hypothesis is dying a long overdue death. In 2020, the Journal of the American College of Cardiology published a state-of-the-art review of saturated fats and health, concluding that "there is no robust evidence that current population-wide arbitrary upper limits on saturated fat consumption in the United States will prevent CVD [cardiovascular disease] or reduce mortality."* (Astrup A, Magkos F, Bier DM, et al. Saturated fats and health: A reassessment and proposal for food-based recommendations: JACC state-of-the-art review. *J Am Coll Cardiol.* 2020)
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> *In 2021, an international panel of experts—which included two scientists who had previously served on the U.S. Dietary Guidelines Advisory Committee (DGAC)—reviewed the evidence and came to a similar conclusion: "Multiple reviews of the evidence have demonstrated that a recommendation to limit consumption of saturated fats to no more than 10 percent of total calories is not supported by rigorous scientific studies."* (Astrup A, Teicholz N, Magkos F, et al. Dietary saturated fats and health: Are the U.S. Guidelines evidence-based? *Nutrients.* 2021)

To learn about saturated fat and its role in brain health, see *Change Your Diet, Change Your Mind* pp 63-66.

Do high-fat diets increase the risk for obesity?

Fat storage isn't controlled by how much fat is in the diet—fat storage is controlled by insulin levels. When insulin is high, excess energy (whether it comes from fat or carbohydrate) will be stored as fat. When insulin is low, fat will be mobilized for energy.

Carbohydrate is the macronutrient that raises insulin the most. Protein also elicits an insulin response, but minimally processed, non-dairy animal foods like meat, seafood, poultry, and eggs, have a much more modest effect on insulin. Fat elicits little to no insulin response. [See slide #24 in Prof. Ben Bikman's presentation "Hyperinsulinemia Causes," sourced from this paper: Elliott RM, Morgan LM, Tredger JA, Deacon S, Wright J, Marks V. Glucagon-like peptide-1 (7-36)amide and glucose-dependent insulinotropic polypeptide secretion in response to nutrient ingestion in man: Acute post-prandial and 24-h secretion patterns. *J Endocrinol.* 1993.] This means that from a metabolic perspective, fat is the macronutrient least likely to make us fat. A diet high in fat can certainly promote obesity, but only if other elements of the diet are promoting high insulin levels.

Ketogenic diets are typically high in fat, but because they are very low in carbohydrate and contain only moderate (adequate) amounts of protein, they lower insulin levels. Under low-insulin conditions, fat storage systems turn off and lipolysis turns on, mobilizing fat and generating ketones. This is why most people following low-carbohydrate diets tend to lose body fat, reducing the risk for obesity (Comparing low-carb diets of less than 130g carbohydrate per day to low-fat diets of less than 35% fat of total calories. Public Health Collaborative.)

Emerging clinical trials in the field of metabolic psychiatry nicely demonstrate this effect in adults, including these two recent studies in which patients with serious mental illnesses following ketogenic diets lost clinically significant amounts of weight even though most of them were taking antipsychotic medications known to increase appetite and weight in so many people:

Danan A, Westman EC, Saslow LR, Ede G. The ketogenic diet for refractory mental illness: A retrospective analysis of 31 inpatients. *Front Psychiatry.* 2022

Sethi S, Wakeham D, Ketter T, et al. Ketogenic diet intervention on metabolic and psychiatric health in bipolar and schizophrenia: A pilot trial. *Psychiatry Res.* 2024

However, ketogenic diets can also be formulated by skilled dietitians for weight maintenance, or even weight gain, if desired—an important consideration when working with children who do not need to lose body fat.

To learn more about the science and practice of ketogenic diets for mental health, including how ketogenic diets are constructed, how they change brain chemistry, and what clinical trials have shown, please see *Change Your Diet, Change Your Mind*, especially chapters 9 and 18.

Can the ketogenic diet raise LDL cholesterol levels?

Yes, LDL can rise on ketogenic diets—in some cases, to very high levels. However, most people do not experience this effect—at least not people with poor metabolic health. For example, this 2024 review of 29 clinical trials of ketogenic diets in people with type 2 diabetes found no significant change in LDL levels: Ghasemi P, Jafari M, Maskouni SJ, et al. 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. *Nutr Metab (Lond)*. 2024.

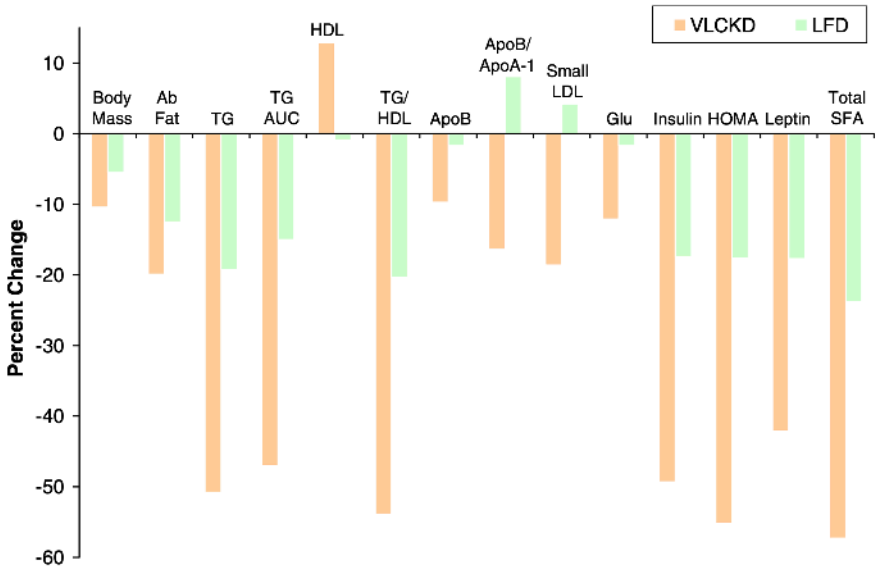
If LDL cholesterol goes up on a ketogenic diet, should you worry?

It's not that LDL levels aren't important, but when evaluating a lipid panel, LDL is the value that gives you the least information about a patient's metabolic health and cardiovascular risk, because the association between LDL levels and cardiovascular disease is so weak. In fact, there is no evidence that LDL is an independent risk factor for heart disease, meaning that LDL on its own doesn't tell you anything about that patient's cardiovascular risk, so LDL must always be interpreted in context. In other words, it's not enough to know that LDL is high—we have to look at the bigger metabolic picture.

Triglycerides, HDL cholesterol, fasting and post-prandial glucose levels, fasting insulin, blood pressure, CRP, and LFTs are all useful indicators of metabolic health and cardiovascular risk. Other measures include the triglyceride-to-HDL ratio (a simple and very good test for insulin resistance) and waist-to-height ratio (an indirect estimate of visceral adiposity). The good news is that the vast majority of people following a well-formulated ketogenic diet see improvements in most or all of these much more reliable values.

In their comprehensive 2008 paper (Volek JS, Fernandez ML, Feinman RD, Phinney SD. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome. *Prog Lipid Res*. 2008), Dr. Volek and Dr. Phinney's group argues that low-carbohydrate diets are metabolically superior to low-fat diets and reduce overall risk for cardiovascular disease. Compared to a low-fat diet, when adults with metabolic syndrome followed a very-low-carb diet, researchers observed all of these beneficial trends:

- Decrease in body fat and abdominal fat
- Decrease in triglycerides
- Increase in HDL cholesterol
- Decrease in small LDL particles (on NMR lipid testing)
- Lower blood glucose levels
- Lower insulin levels
- Increase in insulin sensitivity



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diagnosis:Diet

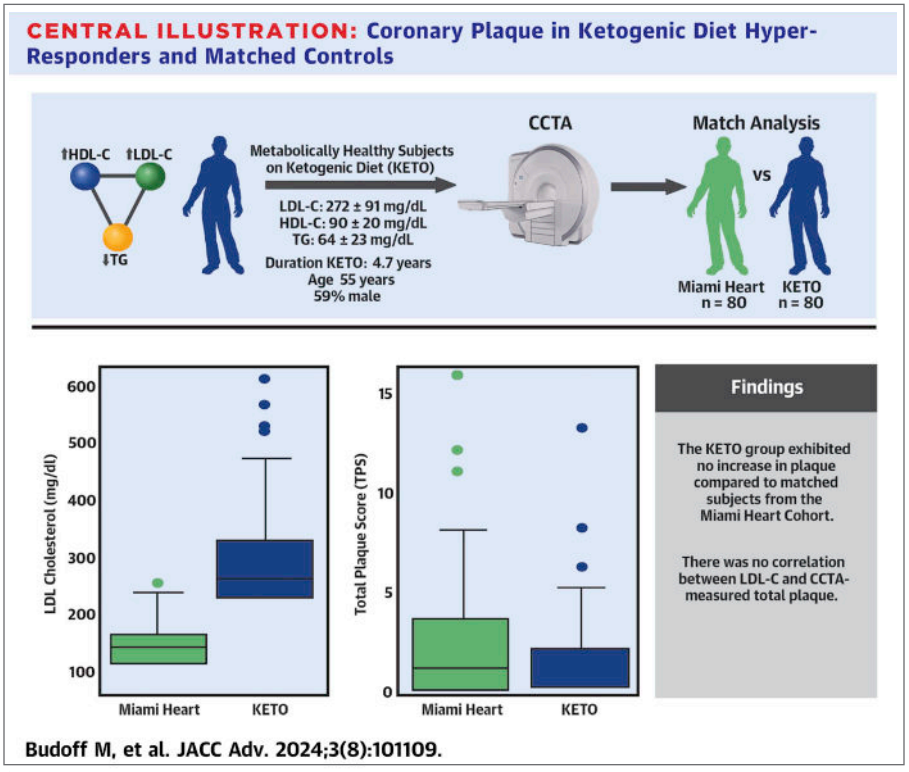
In the 2-year clinical trial of ketogenic diets for type 2 diabetes conducted by Virta Health and published in 2021, (Athinarayanan SJ, Hallberg SJ, McKenzie AL, et al. Impact of a 2-year trial of nutritional ketosis on indices of cardiovascular disease risk in patients with type 2 diabetes. *Cardiovasc Diabetol.* 2020) total average LDL did rise modestly (by about 20 mg/dl), but a closer look at LDL particle characteristics revealed that this was due to a rise in larger LDL particles, which are not associated with increased cardiovascular risk. Also reassuring was that carotid intima-media thickness (a measure of atherosclerosis) did not progress. The authors concluded:

> *Consumption of a very low carbohydrate diet with nutritional ketosis for 2 years in patients with type 2 diabetes lowered levels of small LDL particles that are commonly increased in diabetic dyslipidemia and are a marker for heightened CVD risk. A corresponding increase in concentrations of larger LDL particles was responsible for higher levels of plasma LDL-C. The lack of increase in total LDL particles, ApoB, and in progression of CIMT, provide supporting evidence that this dietary intervention did not adversely affect risk of CVD.*

What about people who develop very high LDL levels on the ketogenic diet?

A subset of individuals will see LDL levels rise substantially—to 200 mg/dl or even much higher, but triglycerides will be nice and low (70 mg/dl or lower) and HDL will be nice and high (80 mg/dl or higher). These people tend to be lean, so they are often referred to as "lean mass hyper-responders" (LMHR for short) (Norwitz NG, Mindrum MR, Giral P, et al. Elevated LDL-cholesterol levels among lean mass hyper-responders on low-carbohydrate ketogenic diets deserve urgent clinical attention and further research. *J Clin Lipidol.* 2022).

Meticulous research conducted by Dave Feldman, Dr. Matthew Budoff, and colleagues is exploring whether these apparently metabolically healthy people whose LDL rises to very high levels are at increased risk for cardiovascular disease. In their landmark 2024 paper (Budoff M, Manubolu VS, Kinninger A, et al. Carbohydrate restriction-induced elevations in LDL-cholesterol and atherosclerosis: The KETO trial. *JACC Adv.* 2024), adults who had been following a ketogenic diet for an average of 4.7 years and had developed very high LDL levels (average 272 mg/dl, max 591 mg/dl)



displayed no evidence of cardiovascular disease on coronary computed tomography angiography (CCTA) compared to very well matched controls (average LDL 123 mg/dl).

Should people who develop high LDL levels on the ketogenic diet be prescribed statins or other cholesterol-lowering medications?

Diamond DM, Ravnskov U, Lorgeril M. Do not treat children with statins. *Arq Bras Cardiol.* 2019

Diamond DM, Bikman BT, Mason P. Statin therapy is not warranted for a person with high LDL-cholesterol on a low-carbohydrate diet. *Curr Opin Endocrinol Diabetes Obes.* 2022

See also Dr. David Diamond's 2023 Low Carb Denver presentation about the relationship between LDL and cardiovascular disease risk and how statistical manipulation is used to greatly exaggerate the benefits of statin medications: "Should low-carbohydrate diet guidelines include concerns over LDL cholesterol?"

What about patients who have genetically high cholesterol levels already (aka familial hypercholesterolemia)?

A 2019 scientific statement by the National Lipid Association Nutrition and Lifestyle Task Force (Kirkpatrick CF, Bolick JP, Kris-Etherton PM, et al. Review of current evidence and clinical recommendations on the effects of low-carbohydrate and very-low-carbohydrate (including ketogenic) diets for the management of body weight and other cardiometabolic risk factors. *J Clin Lipidol.* 2019) lists pre-existing severe hypertriglyceridemia and hypercholesterolemia as absolute contraindications to the ketogenic diet, whereas other authoritative sources view severe dyslipidemias as relative contraindications (Cervenka MC, Wood S, Bagary M, et al. International recommendations for the management of adults treated with ketogenic diet therapies. *Neurol Clin Pract.* 2021 and Watanabe M, Tuccinardi D, Ernesti I, et al. Scientific evidence underlying contraindications to the ketogenic diet: An update. *Obes Rev.* 2020).

Given that the initiation of a low-carbohydrate diet has been reported to exacerbate pre-existing dyslipidemia (Goldberg IJ, Ibrahim N, Bredefeld C, et al. Ketogenic diets, not for everyone. *J Clin Lipidol.* 2021), it is prudent to exercise caution, so additional testing and/or specialist consultation is recommended.

Addtional resources:

Ravnskov U, de Lorgeril M, Kendrick M, Diamond DM. Serious flaws in targeting LDL-C reduction in the management of cardiovascular disease in familial hypercholesterolemia. *Expert Rev Clin Pharmacol.* 2021

Diamond DM, Alabdulgader AA, de Lorgeril M, et al. Dietary recommendations for familial hypercholesterolaemia: An evidence-free zone. *BMJ Evid Based Med.* 2021

Ravnskov U, de Lorgeril M, Kendrick M, Diamond DM. Inborn coagulation factors are more important cardiovascular risk factors than high LDL-cholesterol in familial hypercholesterolemia. *Med Hypotheses.* 2018

Is a simple fasting lipid profile (total cholesterol, LDL, HDL, & triglycerides) sufficient to understand risk, or is more sophisticated lipid and cardiac testing necessary?

If LDL is high, you may wish to order a fractionated lipoprotein panel (aka NMR lipoprofile) which provides more detailed information about lipoproteins including particle size and number. Here's a helpful 2022 review article about the advantages of advanced lipoprotein testing: Emeasoba EU, Ibeson E, Nwosu I, Montemarano N, Shani J, Shetty VS. Clinical relevance of Nuclear Magnetic Resonance LipoProfile. *Front Nucl Med.* 2022.

The authors of this 2020 case report explain why they believe advanced testing is necessary: Norwitz NG, Loh V. A standard lipid panel is insufficient for the care of a patient on a high-fat, low-carbohydrate ketogenic diet. *Front Med (Lausanne).* 2020.

The cost of the panel varies by insurance coverage and lab service, but it can be expensive out-of-pocket (usually at least $100). The out-of-pocket cost through Dave Feldman's ownyourlabs.com (usually the best price available) is $78.61 as of October 2024.

A much more affordable and very good substitute for sophisticated lipoprotein testing is using the standard lipid panel to calculate the triglyceride-to-HDL ratio, which is a strong predictor of future adverse cardiac events. Simply divide triglycerides by HDL; a ratio of less than 2.0 is very reassuring. Here's just one of many papers on this topic: Wan K, Zhao J, Huang H, et al. The association between triglyceride/high-density lipoprotein cholesterol ratio and all-cause mortality in acute coronary syndrome after coronary revascularization. *PLoS One.* 2015.

Another option is a coronary artery calcium scan (CAC). The gold standard is a coronary angiogram, aka computer tomography angiography (CTA). Here is a 2021 review of CTA vs CAC: Incze MA. Should I get a coronary CT scan? *JAMA Intern Med.* 2021.

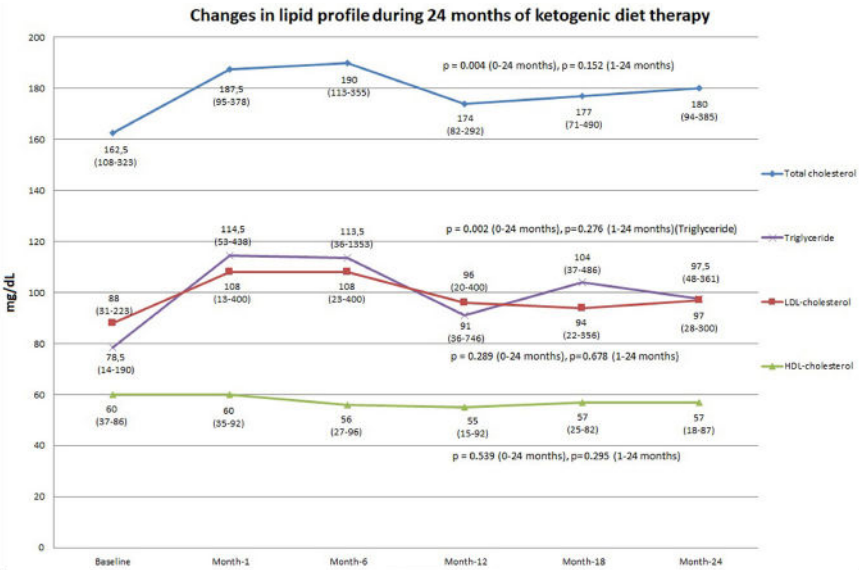
How does the ketogenic diet affect cardiovascular risk profiles in CHILDREN?

According to the Journal of American College of Cardiology, the following are the recommended cholesterol levels for children (all values in mg/dl) (Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol. *Circulation.* 2019):

	Total cholesterol	HDL cholesterol	LDL cholesterol	Triglycerides
Good	170 or less	greater than 45	less than 110	less than 75 in children 0-9; less than 90 in children 10-19
Borderline	170-199	40-45	110-129	75-99 in children 0-9; 90-129 in children 10-19
High	200 or higher	n/a	130 or higher	100 or more in children 0-9; 130 or more in children 10-19
Low	n/a	Less than 40	n/a	n/a

This 2020 review of the safety of ketogenic diets for children with epilepsy includes sections detailing the effect of the ketogenic diet on cardiometabolic profiles in children: Wells J, Swaminathan A, Paseka J, Hanson C. Efficacy and safety of a ketogenic diet in children and adolescents with refractory epilepsy: A review. *Nutrients.* 2020.

This 2021 review focuses specifically on the 2-year effects of ketogenic diets on lipid profiles in children: Yılmaz Ü, Edizer S, Köse M, et al. The effect of ketogenic diet on serum lipid concentrations in children with medication resistant epilepsy. *Seizure.* 2021. The authors concluded:



Theoretically, dyslipidemia may be considered an expected side effect in children on long-term high-fat diet therapy. However, the main concern is whether KD treatment causes serious hyperlipidemia that leads to complications such as pancreatitis or cardiovascular disorders. Aiming to address these questions, this study has demonstrated that, as expected, KD treatment caused an increase in cholesterol and triglyceride concentrations in children with epilepsy. However, although persisted, this increase did not continue after the first month, but set a plateau with a downward trend during the next 24 months. Moreover, none of the patients developed serious complications attributed to dyslipidemia, such as pancreatitis, and no patients had to stop treatment or need to take lipid-lowering medications due to dyslipidemia.

Additional resources about cholesterol metabolism:

- *Change Your Diet, Change Your Mind* pp 67-68, 187-192
- Dave Feldman's website: Cholesterol Code
- Cardiologist/lipidologist Dr. Bret Scher's videos about low-carbohydrate diets, LDL, and cardiovascular risk: "Keto diet and heart disease: What new research reveals about cardiac risk" and "Low carb diets—known benefits, theoretical concerns"
- Interventional cardiologist Dr. Nadir Ali's popular video about low-carbohydrate diets, LDL, and cardiovascular risk: "Why LDL cholesterol goes up with low carb diet and is it bad for health?"