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FAST FACTS

Current evidence on dietary intakes of fatty acids and mortality

Findings from the associations between dietary intakes of different fatty acids and longevity are of particular interest to researchers, healthcare providers, and patients. Based on our meta-analysis of 41 articles from cohort studies, dietary intake of alpha linolenic acid (ALA) was associated with a reduced risk of mortality from all causes, cardiovascular disease, and coronary heart disease, and a slightly higher risk of cancer mortality. In a mixed diet, however, ALA is consumed with other fatty acids with different effects. Therefore, finding the effects of other fatty acids might help us to determine the overall effect of a diet that includes fats.

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Why fatty acids matter in healthy diets

Adherence to healthy diets can delay the onset of cardiovascular disease (CVD) and cancer and improve longevity. Fatty acids are the major components of these diets. Findings on the associations between different types of fatty acids and mortality are, however, inconsistent.^{1,2} In this Fast Facts article, we summarize the available findings.

Saturated fatty acids

Saturated fatty acids contain carbon-to-carbon single bonds only. Palmitic acid, stearic acid, and myristic acid are the most common saturated fatty acids found in animal products, including dairy, red meat, egg, coconut and palm oils, and chocolate.² A meta-analysis of cohort studies revealed no evidence of a positive association between intake of saturated fatty acids and deaths from CVD and coronary heart disease.² Disregarding intakes of other types of fats might be a reason for the statistically non-significant associations found in the meta-analysis. This claim was further confirmed when a review study concluded that a lower intake of saturated fatty acids, coupled with a higher intake of polyunsaturated and monounsaturated fatty acids, was associated with a lower risk of CVD and other major causes of death.³ For cancer related mortality, findings are inconclusive. Future studies should therefore determine the link between intake of saturated fatty acids and cancer risk or cancer mortality.

Trans fatty acids

Trans fatty acids are produced by industry through partial hydrogenation of liquid plant oils or are naturally available in meat and dairy products.⁴ Vaccenic acid (natural) and elaidic acid (industrial) are the most common trans fatty acids in diet. A meta-analysis of six cohort studies showed positive associations between intake of trans fatty acids and risks of all cause and coronary heart disease mortality.² Also, evidence suggests a positive association between intake of dietary trans fatty acids and cancer.⁵ In line with these findings, randomised controlled trials have shown that replacement of calories from other types of fats with those from trans fatty acids raises levels of low density lipoprotein cholesterol, apolipoprotein B, triglycerides, and Lp(a)

lipoprotein and lowers levels of high density lipoprotein cholesterol and apolipoprotein A1.³ Overall, the suggestion to restrict trans fatty acids from the diet might be an optimal strategy for reducing the risk of cancer and cardiometabolic disease and increasing longevity. Recent evidence, however, suggests that the adverse effects of trans fatty acids are related to industrial trans fatty acids and that natural trans fatty acids are safe.⁴

Omega 6 fatty acids

Polyunsaturated fatty acids contain more than one double bond in their carbon chain. Biologically relevant families are omega 6 and omega 3 fatty acids.³ These two classes of fatty acids are not converted to each other. The most abundant type of omega 6 fatty acid is linoleic acid, which is metabolised to arachidonic acid and subsequently to some prostaglandins, leukotrienes, and thromboxanes that are involved in inflammatory responses.⁶ The main sources of linoleic acid are plant oils, whole grains, nuts, and seeds. Based on a meta-analysis of 44 prospective cohort studies, a high intake of linoleic acid was associated with a modestly lower risk of mortality from all causes, CVD, and cancer.⁶ A review study considered all fatty acids and reported that dietary intake of linoleic acid, in replacement of saturated fatty acids or carbohydrates, had moderate benefits for preventing CVD.³ However, because linoleic acid is a precursor for producing compounds involved in inflammatory responses, more studies are needed to confirm the health benefits of this fatty acid.

Omega 3 fatty acids

In the family of omega 3 fatty acids, much attention has been paid to ALA, eicosapentaenoic acid, and docosahexaenoic acid. ALA is readily available in soybean, nuts, canola oils, flaxseed, and other plant food sources and is metabolised to eicosapentaenoic acid and docosahexaenoic acid, both of which have anti-inflammatory properties.⁷ Eicosapentaenoic acid and docosahexaenoic acid are long chain polyunsaturated fatty acids available in seafoods. In our meta-analysis, we found that dietary intake of ALA was associated with a reduced risk of mortality from all causes, CVD, and coronary heart disease,

and a slightly higher risk of cancer mortality.⁷ Also, a meta-analysis on marine sources of omega 3 fatty acids indicated an inverse association with all cause mortality.⁸ In line with the meta-analyses of cohort studies, a meta-analysis of 45 clinical trials showed that supplementation with omega 3 fatty acids was associated with improved lipid profile, inflammation, and glycaemia in people with diabetes.⁹ Despite the beneficial effects of omega 3 fatty acids, recommendations for intakes should be made cautiously because ALA intake might slightly increase the risk of cancer mortality. Further studies are, however, needed to confirm the increased risk.

Omega 9 fatty acids

Omega 9 fatty acids often have one double bond and therefore are considered as monounsaturated fatty acids. The major omega 9 fatty acid in the food supply is oleic acid, which is available in nuts and vegetable oils, particularly olive oil.¹ A meta-analysis of 17 cohort studies showed that intake of monounsaturated fatty acids was associated with a reduced risk of all cause mortality, with no statistically significant association with CVD and cancer mortality.¹ In a meta-analysis of 32 cohort studies, however, dietary intakes of monounsaturated fatty acids, olive oil, and oleic acid were associated with an overall risk reduction of mortality from all causes, CVD, and stroke.¹⁰ It seems that the link between intake of monounsaturated fatty acids and cancer is unclear and further studies are needed.

Conclusion

Evidence suggests that a diet with a high amount of omega fatty acids (3, 6, and 9), a low amount of saturated fatty acids, and zero to a low amount of trans fatty acids might improve health outcomes and increase longevity. Further studies are still needed to assess the association between ALA and cancer and between omega 6 fatty acids and inflammatory based diseases. Future studies should also determine the effects of a diet high in fatty acids and low in saturated and trans fatty acids on health outcomes.

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- Lotfi K, Salari-Moghaddam A, Yousefinia M, Larijani B, Esmailzadeh A. Dietary intakes of monounsaturated fatty acids and risk of mortality from all causes, cardiovascular disease and cancer: A systematic review and dose-response meta-analysis of prospective cohort studies. *Ageing Res Rev* 2021; published online 21 September. doi: 10.1016/j.arr.2021.101467. pmid: 34560281
- de Souza RJ, Mente A, Maroleanu A, et al. Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *BMJ* 2015;351:h3978. doi: 10.1136/bmj.h3978. pmid: 26268692
- Sacks FM, Lichtenstein AH, Wu JHY, et al. American Heart Association. Dietary Fats and Cardiovascular Disease: A Presidential Advisory From the American Heart Association. *Circulation* 2017;136:e1-23. doi: 10.1161/CIR.0000000000000510. pmid: 28620111
- Bendsen NT, Christensen R, Bartels EM, Astrup A. Consumption of industrial and ruminant trans fatty acids and risk of coronary heart disease: a systematic review and meta-analysis of cohort studies. *Eur J Clin Nutr* 2011;65:773-83. doi: 10.1038/ejcn.2011.34. pmid: 21427742
- Michels N, Specht IO, Heitmann BL, Chajès V, Huybrechts I. Dietary trans-fatty acid intake in relation to cancer risk: a systematic review and meta-analysis. *Nutr Rev* 2021;79:758-76. doi: 10.1093/nutrit/nuaa061. pmid: 34104953
- Li J, Guasch-Ferré M, Li Y, Hu FB. Dietary intake and biomarkers of linoleic acid and mortality: systematic review and meta-analysis of prospective cohort studies. *Am J Clin Nutr* 2020;112:150-67. doi: 10.1093/ajcn/nqz349. pmid: 32020162
- Naghshi S, Aune D, Beyene J, Mobarak S, Asadi M, Sadeghi O. Dietary intake and biomarkers of alpha linolenic acid and risk of all cause, cardiovascular, and cancer mortality: systematic review and dose-response meta-analysis of cohort studies. *BMJ* 2021;375:n2213.

- Chen GC, Yang J, Eggersdorfer M, Zhang W, Qin LQ. N-3 long-chain polyunsaturated fatty acids and risk of all-cause mortality among general populations: a meta-analysis. *Sci Rep* 2016;6:28165. doi: 10.1038/srep28165. pmid: 27306836
- O'Mahoney LL, Matu J, Price OJ, et al. Omega-3 polyunsaturated fatty acids favourably modulate cardiometabolic biomarkers in type 2 diabetes: a meta-analysis and meta-regression of randomized controlled trials. *Cardiovasc Diabetol* 2018;17:98. doi: 10.1186/s12933-018-0740-x. pmid: 29981570
- Schwingshackl L, Hoffmann G. Monounsaturated fatty acids, olive oil and health status: a systematic review and meta-analysis of cohort studies. *Lipids Health Dis* 2014;13:154. doi: 10.1186/1476-511X-13-154. pmid: 25274026