

An Overview on the Role of Nutrition and Food Groups in the Prevention of Cardiovascular Diseases

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ABSTRACT

BACKGROUND AND OBJECTIVE: Nutrition and food consumption patterns have a very important role in the prevention of cardiovascular diseases. There are many clinical and epidemiological evidence regarding to cardiovascular health and food consumption and dietary patterns. Given the importance of this issue, in this study a review of various studies and sources about role of consumption of various food groups in prevention of cardiovascular diseases was performed.

METHODS: In this study, new evidence on the role of major food groups in the prevention of cardiovascular disease were investigated by using various databases including pubmed, pubmed central, scopus, web of science and key words such as cardiovascular disease, food groups, dietary patterns and diet were used.

FINDINGS: According to the results of this study, diets containing fruits and vegetables because of their high fiber, antioxidants and minerals except sodium along with certain food groups such as grains, nuts, fish and low-fat dairy products are appropriate in the prevention of cardiovascular diseases.

CONCLUSION: Taken together, according to the results of this study, it can be considered that appropriate use of the major food groups has a significant role in the prevention of cardiovascular disease and should be an important part of a healthy lifestyle.

KEY WORDS: *Cardiovascular Disease, Nutrition, Food Groups.*

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Introduction

Evidence from Epidemiological evidence suggests that unhealthy lifestyle, smoking, physical inactivity, excessive alcohol consumption, poor diet and lack of ideal weight result in approximately 80 percent risk of cardiovascular disease (1-3) (Fig 1). Information obtained from a cohort study in Sudan have shown that lifestyle and healthy eating almost 80 percent resulted in the prevention of cardiovascular disease (4-6). Change and lifestyle modification in population-based strategies to prevent cardiovascular disease is very important. Among the patterns of lifestyle to reduce cardiovascular disease nutrition plays an important role (7,8). In recent years, numerous research studies on different food groups and their effect on the prevention of cardiovascular diseases and related mechanisms have been carried out(9,10).

Recent obtained evidence suggests beneficial effects of some food groups, including fruits, vegetables, legumes, nuts, whole grains, low-fat dairy products and fish is the prevention of cardiovascular disease (11). Given the importance of nutrition in health and prevention of cardiovascular disease, in this study, using a variety of different sources of information, the relation between consumption of various food groups with prevention of cardiovascular disease was investigated.

Methods

In this simple review study using databases pubmed, pubmed central, scopus, web of science and keywords of cardiovascular disease, nutrition, food groups, diet and food consumption patterns, evidence of new and updated in relation to the role of the different food groups in the prevention of cardiovascular disease were studied.

Results

of 123 papers found in the database, 55 article investigated the role and relevance of different food groups with cardiovascular disease and other unrelated articles to the subject of this study and other investigations regarding to various foodstuffs and protective role in other diseases except cardiovascular diseases had been excluded. The results of the study showed that specific food groups affect the risk of cardiovascular disease through coordination and interaction of important elements of food and bioactive

phytochemicals elements that are classified in other parts of this study.

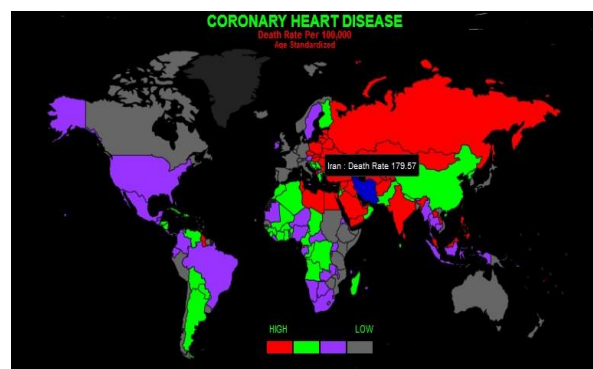


Figure 1. Mortality rate due to coronary heart disease in the world and Iran (2016) (12)

Fruits and vegetables: because of many global changes and dissimilarity of fruits effect with vegetables and the likely reaction of compounds in food when cooking vegetables, assessment of effects of vegetables and fruits on is extremely complex. However consumption of fruits and vegetables reduces cardiovascular disease risk based on obtained evidence (13). The recommended plants regimes for health are based on high consumption of fruits and vegetables. Recent reports obtained from extensive prospective review and meta-analysis seems convincing in a considerable extent (14,15).

Data from 10,000 Norwegian men followed by medical cares during four decades suggests that people who consume vegetables, more fruits and seeds have a 10.8% lower risk of fatal disease and 20% lower risk of stroke in comparison with people who consume low amounts of this material (16). These surveys emphasized consumption of berries, low caloric fruits and rich in polyphenols in the Northern European diet in the prevention of cardiovascular disease. For stroke, the results of a meta-analysis of 20 observational study suggests a protective effect of vegetarian food with a linear dose-response relationship as well as a 32 percent risk reduction of stroke by increasing the amount of daily vegetables consumption (17).

The results of another meta-analysis study carried out on overall mortality and mortality due to cardiovascular disease and its relationship with the consumption of fruits and vegetables in 16 long-term reviews indicates a reduced natural mortality and mortality due to cardiovascular disease with more daily intake of these substances (15). One reason for this observation is that plant foods have low sodium

and high potassium that can reduce blood pressure (18). However, other risk factors for cardiovascular disease are not known.

It seems that the effects of plant foods as fruits and vegetables on health are generally a result of their high fiber, antioxidants and minerals other than sodium. These features is a result of their overall consumption more than 5 servings per day (19,20).

Grains: grains such as nuts and cereal (dried beans, peas, lentils and soybeans) are foods rich in nutrients and high energy, which contain abundant nutrients. although grains are not rich in the fat, but they are rich in protein and complex carbohydrates, fiber, minerals except sodium and micronutrients such as folate and phytochemicals such as saponins (glycosylated triterpene with feature of lowering cholesterol) and polyphenolic compounds that their beneficial effects on health are known (21).

A conducted meta-analysis on 5 prospective cohort study has shown that consumption of grains is inversely associated with the incidence of cardiovascular disease, whereas has no significant relationship with incidence of diabetes (22). Epidemiological observations demonstrated that consumption of beans has a beneficial effect in weight loss and smaller waist circumference and systolic blood pressure (23, 20).

Other studies indicated other beneficial effects on reducing risk factors for cardiovascular disease such as lipids, glucose and blood pressure as a result of the consumption of grains (25,26). Data obtained in different studies suggested that decreased circulating blood glucose and insulin is as a result of grain consumption that was associated with absorption of carbohydrates and better control of sugar. In general, long-term use of cereals is recommended in the diet of diabetic patients (27,28).

Although mild hypotensive effect of the consumption of bean was recently approved, but there are some controversies between opinions. In these investigations the dose of cereals consumption was between 46 to 150 grams per day, which have not been reported no overweight. The results of these studies indicate the importance of whole grains eating in diet to protect against cardiovascular disease (29).

Nuts (peanuts): nuts and peanuts similar to other grain foods are rich in nutrients. Although most of these materials are derived from fat, their fatty acids are especially polyunsaturated fatty acids in the form of oleic acid, round and polyunsaturated, including linoleic acid (18: 2n-6) and alpha-linoleic acid (ALA,

C18: 3N-3), N-3 fatty acids. Peanuts are rich in complex carbohydrates and fiber, protein, tocopherols, polyphenols and minerals without sodium (30). The term of seed is used for tree seeds such as almonds, walnuts, hazelnuts, pistachios and peanuts. Although they are plant but have nutrient characteristics similar to tree seeds.

Many long-term studies on the incidence of cardiovascular disease and its relationship with the frequency of consumption of seeds (nuts) (including peanuts and peanut butter) have been reported. Research on the protective effects of nut consumption on lethal and nonlethal cardiovascular diseases indicated and approved an inverse relationship of grain intake with fatal cardiovascular disease and grain consumption for a period of four weeks with nonlethal cardiovascular diseases (consumption equivalent to 28.4 g). The dose-response relationship between consumption of seeds (nuts) and the reduction of cardiovascular disease has been observed in all studies (31,32). Some group studies also suggest a link between nut consumption and lower serum levels of bio-markers of inflammation (22).

Studies have shown that an average consumption of 67 grams of different nuts reduces cholesterol as an average decrease of 4/7% of LDL cholesterol, which is dependent on the nut (33). Diet rich in nuts will also reduce triglycerides. Other research studies show the beneficial effects of a diet rich in nuts on the performance of oxidation, inflammation and function of the arteries (30). In another study, consumption of diets rich in grains per day can reduce cardiovascular disease by 30% and in the midst of all this, 49 percent reduction of heart attacks can be observed (11).

The early evidence approved the cardiovascular protection as a result of use of seeds. Based on these results, America Heart Association (AHA) suggests diet high in grains as an important strategy in reducing the risk of heart attack for the primary prevention cardiovascular diseases (34).

Since nuts are foods rich in fat, these high-energy materials are often fattening. However, there is no epidemiological evidence in this regard and reports on group reviews indicates an inverse relationship between nut consumption and body mass index (BMI) or overweight over time (35, 36).

Other studies also show that increased consumption of nuts can reduce the risk of metabolic syndrome and therefor can lead to less obesity. Lack of overweight after taking the seeds are largely related to the effects of high satiation (37, 38).

Dairy products: Dairy products contain important nutrients in the diet such as carbohydrates, protein, calcium, potassium and micro-nutrients such as vitamin D (39, 40).

Dairy fat containing saturated fatty acids, which in the past was believed to be harmful. Therefore, the dietary guidelines generally recommended low fatty products. But recent evidence from observational studies suggests that milk or dairy products does not increase the risk of cardiovascular disease and regardless of the amount of fat may reduce the risk of cardiovascular disease (41, 42).

In an analysis of 17 studies, milk consumption was not associated with risk of cardiovascular disease or stroke, but overall a slight negative correlation with the risk of cardiovascular disease was observed. Also there was no relationship between the consumption of low-fat and high-fat dairy products or dairy products with cardiovascular disease (42).

Even high-fat dairy products presumably have high level of fatty acids, did not increase the risk of cardiovascular disease and the recent evidence regarding the consumption of saturated fatty acids and risk of cardiovascular disease confirmed this subject. However, weak protective effect against cardiovascular disease may be due to the effect of lowering blood pressure that in prospective studies has been observed (43, 44).

It is believed that inhibition of angiotensin-converting enzyme by peptides derived from milk proteins (casein and whey protein) play an important role in the antihypertensive effect. There are other evidence suggest that dairy products have beneficial effects on metabolic syndrome and many types of diabetes that are mainly due to the consumption of low-fat dairy products and yogurt, and was associated with reduction of overweight and obesity (45). Also, high-fat dairy products such as cheese has no negative effects on blood lipids that are predicted based on the amount of saturated fat.

Recent experiments on different kinds of dairy foods for more information on their effects on blood lipids in similar fat of dairy intake indicates that hard cheese has a lesser enhancing effect of LDL cholesterol than butter or milk (44). In one study, eating 143 grams of cheese per day with 27% fat, did not increase LDL cholesterol from baseline and also decreased its value compared with 47 grams of butter consumption per day (46). The high calcium content of milk increases the fat excretion in the feces and the

fermentation process and leads to prebiotics effects in the colon that have been proposed as useful mechanisms due to the lack of effect on enhancing the cholesterol (42).

New assessments of the effects of milk and its derived products on the risk of cardiovascular disease and on the intermediate indexes, changes our vision and attitude towards neutral or even beneficial effect regardless of the fat content. Altogether dairy products are important nutrients that have a significant role in better quality of diet for most of the population.

Fish: There are many evidence regarding the cardioprotective of fatty acids with polyunsaturated n-3 long chain (LCn3PUFA), mainly acids eicosapentaenoic (C20: 5n3, EPA) and docosahexaenoic acid (C22: 6n3, DHA) (47). The main source of these fatty acids is seafood. LCn3PUFA are found plentiful in fatty fish (herring, salmon, tuna, sardines), whereas in low-fat fish (such as cod), they are in the liver that is a natural source of fish oil.

Effects of LCn3PUFA on plasma lipids and vascular activity were seen at pharmaceutical doses and just higher than 3g per day. Cardiac effects, especially protection against sudden cardiac death due to antiarrhythmic effects can be seen in the regular intake of 250 mg per day (48). This amount of consumption is easily achieved by at least two servings of fish preferably fatty fish a week (49). There are some evidence indicating significant relationship of regular consumption of fish, against ischemic stroke. Increased consumption of two servings of fish per week was associated with 4% decreased risk of cardiovascular disease (50, 51).

Another meta-analysis of 17 prospective studies in groups with no history of cardiovascular disease compared those with the lowest intake and those consumed one serving of fish per week, demonstrated a 16% reduction in the risk of fatal heart attack (52). In a study of dose-response from eight prospective study showed that consumption of 100 grams of fish per week was associated with a 5% reduction in acute coronary syndrome. These data reinforce advantages and benefits of fish consumption (53).

Meat products: According to increasing impact of the expected total cholesterol and LDL cholesterol, saturated fatty acids in red meat, the main source of protein and fat, dietary recommendations for health always include restrictions on the consumption of red meat or recommend replacing it with white meat (chicken), which is much lower in fat (54). But the

evidence from recent epidemiological studies shows a weak direct relationship between the unprocessed red meat consumption with risk of stroke, diabetes, or deaths from cardiovascular diseases, whereas consumption of processed meat such as sausage certainly are associated with harmful consequences of cardiovascular mortality (55). The main reason for these differences in the health effects between processed and unprocessed meat is that processed meat is prepared via salt handling, processing or smoked and has higher sodium content and also contain harmful additives such as nitrites, nitrates and nitrosamines (56, 57).

In addition to the impact on vascular health, red meat has a little effect on levels of lipids, blood pressure or body weight (58). Overall, current evidence suggests that moderate consumption of red meat is not considered as a risk factor for cardiovascular disease or diabetes.

Discussion

Several decades of research on the impact of healthy food and nutritional intervention on various diseases have provided many excellent and high-quality evidence about the power of foods and diet in influencing cardiovascular outcomes. According to the results of this study overall, diets rich in fruits and vegetables due to high fiber content, antioxidants and minerals other than sodium along with specific food groups, such as beans, nuts, fish and fermented low fat dairy products are appropriate in the prevention of cardiovascular disease and should probably be an important part of a healthy lifestyle.

In addition, the results of our study indicated that moderate consumption of red meat is not considered as a risk factor for cardiovascular disease or diabetes, whereas consumption of processed meat such as sausages definitely is associated with harmful cardiovascular outcomes and mortality.

References

- Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *New Eng J Med*. 2000;343(1):16-22.
- Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364(9438):937-52.
- Karkhah A, Saadi M, Nouri HR. In silico analyses of heat shock protein 60 and calreticulin to designing a novel vaccine shifting immune response toward T helper 2 in atherosclerosis. *Comput Biol Chem*. 2017;67:244-54.
- Esmailzadeh S, Ghanbari Andarieh M, Ghadimi R, Agajani Delavar M. Body mass index and gonadotropin hormones (LH & FSH) associate with clinical symptoms among women with polycystic ovary syndrome. *Global journal of health science*. 2015;7(2):101.
- Ghadimi R, Ashrafian Amiri H, Nasrollahpour Shirvani SD. Anthropometric Indices Associated With Serum Biomarkers Of Cardiometabolic Disorders In 25-60 Years Old Couples. 2016;15(5): 230-338.
- Ghadimi R, Kamrani MS, Zarghami A, Darzi AA. The role of nutrition in educational and spiritual development of human beings: Quranic perspective. 2013;15(1) 34-9.
- Akesson A, Larsson SC, Discacciati A, Wolk A. Low-risk diet and lifestyle habits in the primary prevention of myocardial infarction in men: a population-based prospective cohort study. *J Am Coll Cardiol*. 2014;64(13):1299-306.
- Karkhah A, Amani J. A potent multivalent vaccine for modulation of immune system in atherosclerosis: an in silico approach. *Clin Exp Vaccine Res*. 2016;5(1):50-9.
- Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, et al. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation*. 2006;114(1):82-96.
- Mozaffarian D, Appel LJ, Van Horn L. Components of a cardioprotective diet. *Circulation*. 2011;123(24):2870-91.
- Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Aros F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *New Eng J Med*. 2013;368(14):1279-90.
- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. heart disease and stroke statistics-2016 update: A report from the American heart association. *Circulation*. 2016;133(4):38-360.
- Dauchet L, Amouyel P, Hercberg S, Dallongeville J. Fruit and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies. *J Nutrition*. 2006;136(10):2588-93.
- Larsson SC, Virtamo J, Wolk A. Total and specific fruit and vegetable consumption and risk of stroke: a prospective study. *Atherosclerosis*. 2013;227(1):147-52.
- Wang X, Ouyang Y, Liu J, Zhu M, Zhao G, Bao W, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. *BMJ*. 2014;349:g4490.
- Hjartaker A, Knudsen MD, Tretli S, Weiderpass E. Consumption of berries, fruits and vegetables and mortality among 10,000 Norwegian men followed for four decades. *Eur J Nut*. 2015;54(4):599-608.
- Hu D, Huang J, Wang Y, Zhang D, Qu Y. Fruits and vegetables consumption and risk of stroke: a meta-analysis of prospective cohort studies. *Stroke*. 2014;45(6):1613-9.
- Karkhah A, Zabihi E, Ebrahimtabar F, Babajani Roshan T. Can allergic disorders decrease the risk of thromboembolic events in atherosclerosis? an evidence-based review. *Inter Biologic Biomed J*. 2016;2(3):91-7.[InPersian].
- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *New Eng J Med*. 1997;336(16):1117-24.
- Karkhah A. Destructive effect of quinone-containing compounds on cytochrome P450: Arbutin as a double-edged sword. *Casp J Intern Med*. 2016;7(4):300-1.[In Persian].
- Ros E, Hu FB. Consumption of plant seeds and cardiovascular health: epidemiological and clinical trial evidence. *Circulation*. 2013;128(5):553-65.
- Afshin A, Micha R, Khatibzadeh S, Mozaffarian D. Consumption of nuts and legumes and risk of incident ischemic heart disease, stroke, and diabetes: a systematic review and meta-analysis. *Am J Clin Nut*. 2014;100(1):278-88.

23. Mattei J, Hu FB, Campos H. A higher ratio of beans to white rice is associated with lower cardiometabolic risk factors in Costa Rican adults. *Am J Clin Nut.* 2011;94(3):869-76.
24. Papanikolaou Y, Fulgoni VL, 3rd. Bean consumption is associated with greater nutrient intake, reduced systolic blood pressure, lower body weight, and a smaller waist circumference in adults: results from the National Health and Nutrition Examination Survey 1999-2002. *J Am Coll Nut.* 2008;27(5):569-76.
25. Anderson JW, Major AW. Pulses and lipaemia, short- and long-term effect: potential in the prevention of cardiovascular disease. *Br J Nut.* 2002;88(3):263-71.
26. Bazzano LA, Thompson AM, Tees MT, Nguyen CH, Winham DM. Non-soy legume consumption lowers cholesterol levels: a meta-analysis of randomized controlled trials. *Nutr Metab Cardiovasc Dis.* 2011;21(2):94-103.
27. Sievenpiper JL, Kendall CW, Esfahani A, Wong JM, Carleton AJ, Jiang HY, et al. Effect of non-oil-seed pulses on glycaemic control: a systematic review and meta-analysis of randomised controlled experimental trials in people with and without diabetes. *Diabetologia.* 2009;52(8):1479-95.
28. Bayani MA, Karkhah A, Hoseini SR, Qarouei R, Nouroodini HQ, Bijani A, et al. The relationship between type 2 diabetes mellitus and osteoporosis in elderly people: a cross-sectional study. *Inter Bio Biomed J.* 2016;2(1):39-46. [In Persian].
29. Jayalath VH, de Souza RJ, Sievenpiper JL, Ha V, Chiavaroli L, Mirrahimi A, et al. Effect of dietary pulses on blood pressure: a systematic review and meta-analysis of controlled feeding trials. *Am J Hyper.* 2014;27(1):56-64.
30. Ros E. Health benefits of nut consumption. *Nut.* 2010;2(7):652-82.
31. Luo C, Zhang Y, Ding Y, Shan Z, Chen S, Yu M, et al. Nut consumption and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: a systematic review and meta-analysis. *Am J Clin Nut.* 2014;100(1):256-69.
32. Zhou D, Yu H, He F, Reilly KH, Zhang J, Li S, et al. Nut consumption in relation to cardiovascular disease risk and type 2 diabetes: a systematic review and meta-analysis of prospective studies. *Am J Clin Nut.* 2014;100(1):270-7.
33. Sabate J, Oda K, Ros E. Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials. *Arch Inter Med.* 2010;170(9):821-7.
34. Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the american heart association/american stroke association. *Stroke.* 2014;45(12):3754-832.
35. Bes-Rastrollo M, Wedick NM, Martinez-Gonzalez MA, Li TY, Sampson L, Hu FB. Prospective study of nut consumption, long-term weight change, and obesity risk in women. *Am J clin Nut.* 2009;89(6):1913-9.
36. Ibarrola-Jurado N, Bullo M, Guasch-Ferre M, Ros E, Martinez-Gonzalez MA, Corella D, et al. Cross-sectional assessment of nut consumption and obesity, metabolic syndrome and other cardiometabolic risk factors: the PREDIMED study. *PloS one.* 2013;8(2): 57367.
37. Salas-Salvado J, Fernandez-Ballart J, Ros E, Martinez-Gonzalez MA, Fito M, Estruch R, et al. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. *Arch Int Med.* 2008;168(22):2449-58.
38. Babio N, Toledo E, Estruch R, Ros E, Martinez-Gonzalez MA, Castaner O, et al. Mediterranean diets and metabolic syndrome status in the PREDIMED randomized trial. *Canada Med Associat J.* 2014;186(17):649-57.
39. Akbari R, Adelani B, Ghadimi R. Serum vitamin D in hypertensive patients versus healthy controls is there an association?. *Caspian J Int Med.* 2016;7(3):168-72.
40. Ghadimi R, Esmailzadeh S, Firoozpour M, Ahmadi A. Does vitamin D status correlate with clinical and biochemical features of polycystic ovary syndrome in high school girls?. *Casp J Int Med.* 2014;5(4):202-8.
41. Gibson RA, Makrides M, Smithers LG, Voevodin M, Sinclair AJ. The effect of dairy foods on CHD: a systematic review of prospective cohort studies. *Br J Nut.* 2009;102(9):1267-75.
42. Soedamah-Muthu SS, Ding EL, Al-Delaimy WK, Hu FB, Engberink MF, Willett WC, et al. Milk and dairy consumption and incidence of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. *Am J Clin Nut.* 2011;93(1):158-71.
43. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *Am J Clin Nut.* 2010;91(3):535-46.
44. German JB, Gibson RA, Krauss RM, Nestel P, Lamarche B, van Staveren WA, et al. A reappraisal of the impact of dairy foods and milk fat on cardiovascular disease risk. *Eur J Nut.* 2009;48(4):191-203.

45. Tong X, Dong JY, Wu ZW, Li W, Qin LQ. Dairy consumption and risk of type 2 diabetes mellitus: a meta-analysis of cohort studies. *Eur J Clin Nut.* 2011;65(9):1027-31.
46. Hjerpsted J, Leedo E, Tholstrup T. Cheese intake in large amounts lowers LDL-cholesterol concentrations compared with butter intake of equal fat content. *Am J Clin Nut.* 2011;94(6):1479-84.
47. De Caterina R. n-3 fatty acids in cardiovascular disease. *New Eng J Med.* 2011;364(25):2439-50.
48. McLennan PL. Cardiac physiology and clinical efficacy of dietary fish oil clarified through cellular mechanisms of omega-3 polyunsaturated fatty acids. *Eur Journal App Physiol.* 2014;114(7):1333-56.
49. Kris-Etherton PM, Harris WS, Appel LJ. Omega-3 fatty acids and cardiovascular disease: new recommendations from the American Heart Association. *Arterioscl Thromb Vasc Biol.* 2003;23(2):151-2.
50. Xun P, Qin B, Song Y, Nakamura Y, Kurth T, Yaemsiri S, et al. Fish consumption and risk of stroke and its subtypes: accumulative evidence from a meta-analysis of prospective cohort studies. *Eur J Clin Nut.* 2012;66(11):1199-207.
51. Chowdhury R, Stevens S, Gorman D, Pan A, Warnakula S, Chowdhury S, et al. Association between fish consumption, long chain omega 3 fatty acids, and risk of cerebrovascular disease: systematic review and meta-analysis. *BMJ.* 2012;345:e6698.
52. Zheng J, Huang T, Yu Y, Hu X, Yang B, Li D. Fish consumption and CHD mortality: an updated meta-analysis of seventeen cohort studies. *Pub Health Nut.* 2012;15(4):725-37.
53. Leung Yinko SS, Stark KD, Thanassoulis G, Pilote L. Fish consumption and acute coronary syndrome: a meta-analysis. *Am J Med.* 2014;127(9):848-57.
54. Micha R, Wallace SK, Mozaffarian D. Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. *Circulation.* 2010;121(21):2271-83.
55. Pan A, Sun Q, Bernstein AM, Schulze MB, Manson JE, Willett WC, et al. Red meat consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. *Am J Clin Nut.* 2011;94(4):1088-96.
56. Rohrmann S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, et al. Meat consumption and mortality--results from the European prospective investigation into cancer and nutrition. *BMC Med.* 2013;11:63.
57. Micha R, Michas G, Lajous M, Mozaffarian D. Processing of meats and cardiovascular risk: time to focus on preservatives. *BMC medicine.* 2013;11:136.
58. Li D, Siriamornpun S, Wahlqvist ML, Mann NJ, Sinclair AJ. Lean meat and heart health. *Asia Pac J Clin Nut.* 2005;14(2):113-9.