



2017

Optimizing Heart Failure Outcomes Through Diet: A Review

Farley B. Neasman III

Follow this and additional works at: <https://mds.marshall.edu/mjm>



Part of the [Cardiovascular Diseases Commons](#), [Community Health and Preventive Medicine Commons](#), [Medical Biochemistry Commons](#), [Medical Nutrition Commons](#), and the [Nutritional and Metabolic Diseases Commons](#)

Recommended Citation

Neasman, Farley B. III (2017) "Optimizing Heart Failure Outcomes Through Diet: A Review," *Marshall Journal of Medicine*: Vol. 3: Iss. 3, Article 8.

DOI: <http://dx.doi.org/10.18590/mjm.2017.vol3.iss3.8>

Available at: <https://mds.marshall.edu/mjm/vol3/iss3/8>

DOI: <http://dx.doi.org/10.18590/mjm.2017.vol3.iss3.8>

Author Footnote: Acknowledgements: Robert Touchon, MD MPH, and Ellen Thompson MD

Open Access | 

References with DOI

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 2013;62(16):e147-e239. doi:10.1016/j.jacc.2013.05.019.
2. Azad N, Lemay G. Management of chronic heart failure in the older population. *Journal of Geriatric Cardiology*. 11.4 (2014): 329.
3. Roger VL. Epidemiology of heart failure. *Circulation Research*. 113.6 (2013): 646-659. <https://doi.org/10.1161/circresaha.113.300268>
4. <http://news.heart.org/heart-failure-numbers-to-increase-by-nearly-40-percent-in-next-15-years/>
5. Mozzafarian D, Benjamin EJ, Go AS, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation*. 2016;133:e38-e360.
6. Curtis LH, Whellan DJ, Hammill BG, Hernandez AF, Anstrom KJ, Shea AM, Schulman KA. Incidence and prevalence of heart failure in elderly persons, 1994-2003. *Archives of Internal Medicine*. 168.4 (2008): 418-424. <https://doi.org/10.1001/archinternmed.2007.80>
7. Hardy DR. The booming dynamics of aging: From awareness to action. Report of the 2005 White House Conference on Aging. 2005.
8. www.cms.gov
9. Heidenreich PA, Trogdon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, et al. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation*. 2011;123(8):933–44. <https://doi.org/10.1161/cir.0b013e31820a55f5>
10. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the united states a policy statement from the American Heart Association. *Circulation: Heart Failure*. 6.3 (2013): 606-619. <https://doi.org/10.1161/hhf.0b013e318291329a>
11. Kannel WB, Belanger AJ. Epidemiology of heart failure. *American Heart Journal*. 121.3 (1991): 951-957.
12. He J, Ogden LG, Bazzano IA, Vupputuri S, Loria C, Whelton PK. Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. *Archives of Internal Medicine*. 161.7 (2001): 996-1002. <https://doi.org/10.1001/archinte.161.7.996>
13. Kannel WB, Castelli WP, Gordon T, McNamara PM. Serum cholesterol, lipoproteins, and the risk of coronary heart disease: the Framingham Study. *Annals of Internal Medicine*. 74.1 (1971): 1-12. <https://doi.org/10.7326/0003-4819-74-1-1>
14. Paulus WJ, Tschöpe C. A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. *Journal of the American College of Cardiology*. 62.4 (2013): 263-271.
15. Yancy, Clyde W., et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice

Guidelines and the Heart Failure Society of America. *Journal of the American College of Cardiology*. (2016). <https://doi.org/10.1161/cir.000000000000435>

16. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *Jama*. 311.5 (2014): 507-520. <https://doi.org/10.1001/jama.2013.284427>

17. <http://www.idf.org/treatment-algorithm-people-type-2-diabetes>

18. Jensen, Michael D., et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Journal of the American College of Cardiology*. 63.25_PA (2014). <https://doi.org/10.1161/01.cir.0000437739.71477.ee>

19. Panel, National Cholesterol Education Program NCEP Expert. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation*. 106.25 (2002): 3143.

20. Roberts CK, Vaziri ND, Barnard RJ. Effect of diet and exercise intervention on blood pressure, insulin, oxidative stress, and nitric oxide availability. *Circulation*. 106.20 (2002): 2530-2532. <https://doi.org/10.1097/00005768-200205001-00059>

21. Svetkey LP, Simons-Morton D, Vollmer WM, Appel LJ, Conlin PR, Ryan DH, Ard J, Kennedy BM. Effects of dietary patterns on blood pressure: subgroup analysis of the Dietary Approaches to Stop Hypertension (DASH) randomized clinical trial. *Archives of Internal Medicine*. 159.3 (1999): 285-293. <https://doi.org/10.1001/archinte.159.3.285>

22. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, Hu ZX, Lin J, Xiao JZ, Cao HB, Liu PA, Jiang XG, Jiang YY, Wang JP, Zheng H, Zhang H, Bennett PH, Howard BV. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care*. 20.4 (1997): 537-544. <https://doi.org/10.2337/diacare.20.4.537>

23. Eriksson KF, Lindgärde F. Prevention of Type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmö feasibility study. *Diabetologia*. 34.12 (1991): 891-898. <https://doi.org/10.1007/bf00400196>

24. Leon AS, Sanchez OA. Response of blood lipids to exercise training alone or combined with dietary intervention. *Medicine and science in sports and exercise*. 33.6; SUPP (2001): S502-S515. <https://doi.org/10.1097/00005768-200106001-00021>

25. Kelley GA, Kelley KS. Effects of diet, aerobic exercise, or both on non-HDL-C in adults: a meta-analysis of randomized controlled trials. *Cholesterol*. 2012 (2012). <https://doi.org/10.1155/2012/840935>

26. Rathore SS, Masoudi FA, Wang Y, Curtis JP, Foody JM, Havranek EP, Krumholz HM. Socioeconomic status, treatment, and outcomes among elderly patients hospitalized with heart failure: findings from the National Heart Failure Project. *American Heart Journal*. 152.2 (2006): 371-378. <https://doi.org/10.1016/j.ahj.2005.12.002>

27. US Department of Health and Human Services, and US Department of Health and Human Services. *Physical activity guidelines for Americans*. (2008).

28. Eckel RH, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a

report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 63.25_PA (2014). <https://doi.org/10.1161/01.cir.0000437740.48606.d1>

29. Ward BW, et al. Early release of selected estimates based on data from the January–March 2013 National Health Interview Survey. National Center for Health Statistics (2013).

30. CDC.gov. Health, United States, 2015, table 53.

31. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. *Jama*. 311.8 (2014): 806–814. <https://doi.org/10.1097/01.sa.0000451505.72517.a5>

32. Miller WC, Koceja DM, Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *International Journal of Obesity*. 21.10 (1997): 941–947. <https://doi.org/10.1038/sj.ijo.0800499>

33. Halton TL, Willett WC, Liu S, Manson JE, Stampfer MJ, Hu FB. Potato and french fry consumption and risk of type 2 diabetes in women. *The American Journal of Clinical Nutrition*. 83.2 (2006): 284–290.

34. Carrera-Bastos P, Fontes-Villalba M, O’Keefe JH, Lindeberg S, Cordain L. The western diet and lifestyle and diseases of civilization. *Research Reports in Clinical Cardiology*. 2 (2011): 15–35. <https://doi.org/10.2147/rrcc.s16919>

35. Galland L. Diet and inflammation. *Nutrition in Clinical Practice*. 25.6 (2010): 634–640.

36. Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, Hu FB. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. *The American Journal of Clinical Nutrition*. 80.4 (2004): 1029–1035.

37. <https://www.nhlbi.nih.gov/health/health-topics/topics/dash>

38. Salehi-Abargouei A, Maghsoudi Z, Shirani F, Azadbakht L. Effects of Dietary Approaches to Stop Hypertension (DASH)-style diet on fatal or nonfatal cardiovascular diseases—incidence: a systematic review and meta-analysis on observational prospective studies. *Nutrition*. 29.4 (2013): 611–618. <https://doi.org/10.1016/j.nut.2012.12.018>

39. Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. *Journal of the American College of Cardiology*. 57.11 (2011): 1299–1313. <https://doi.org/10.1016/j.jacc.2010.09.073>

40. Sofi F, et al. Adherence to Mediterranean diet and health status: meta-analysis. *BMJ*. 337 (2008): a1344. <https://doi.org/10.1136/bmj.a1344>

41. Schwingshackl L, Missbach B, König J, Hoffmann G. Adherence to a Mediterranean diet and risk of diabetes: a systematic review and meta-analysis. *Public Health Nutrition*. 18.07 (2015): 1292–1299. <https://doi.org/10.1017/s1368980014001542>

42. Craig WJ, Mangels AR. Position of the American Dietetic Association: vegetarian diets. *Journal of the American Dietetic Association* 109.7 (2009): 1266–1282. <https://doi.org/10.1016/j.jada.2009.05.027>

43. Ornish D, Brown SE, Scherwitz LW, Billings JH, Armstrong WT, Ports TA, McLanahan SM, Kirkeeide RL, Brand RJ, Gould KL. Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. *The Lancet*. 336.8708 (1990): 129–133. <https://doi.org/10.1017/cbo9780511759048.038>

-
44. Esselstyn CB Jr, Gendy G, Doyle J, Golubic M, Roizen MF. A way to reverse CAD? *Journal of Family Practice*. 63.7 (2014): 356-364.
45. Sacks FM, Castelli WP, Donner A, Kass EH. Plasma lipids and lipoproteins in vegetarians and controls. *New England Journal of Medicine* 292.22 (1975): 1148-1151. <https://doi.org/10.1056/nejm197505292922203>
46. Fisher M, Levine PH, Weiner B, Ockene IS, Johnson B, Johnson MH, Natale AM, Vaudreuil CH, Hoogasian J. The effect of vegetarian diets on plasma lipid and platelet levels. *Archives of Internal Medicine*. 146.6 (1986): 1193-1197. <https://doi.org/10.1001/archinte.146.6.1193>
47. Key TJ, Fraser GE, Thorogood M, Appleby PN, Beral V, Reeves G, et al. Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies. *The American Journal of Clinical Nutrition*. 70.3 (1999): 516s-524s.
48. Clarke R, Shipley M, Armitage J, Collins R, Harris W. Plasma phospholipid fatty acids and CHD in older men: Whitehall study of London civil servants. *British Journal of Nutrition*. 102.2 (2009): 279. <https://doi.org/10.1017/s0007114508143562>
49. Lennie TA, et al. Dietary fat intake and proinflammatory cytokine levels in patients with heart failure. *Journal of Cardiac Failure*. 11.8 (2005): 613-618. <https://doi.org/10.1016/j.cardfail.2005.06.434>
50. Mozaffarian D, Pischon T, Hankinson SE, Rifai N, Joshipura K, Willett WC, Rimm EB. Dietary intake of trans fatty acids and systemic inflammation in women. *The American Journal of Clinical Nutrition*. 79.4 (2004): 606-612.
51. Mozaffarian D, Aro A, Willett WC. Health effects of trans-fatty acids: experimental and observational evidence. *European Journal of Clinical Nutrition*. 63 (2009): S5-S21. <https://doi.org/10.1038/sj.ejcn.1602973>
52. Riediger ND, Othman RA, Suh M, Moghadasian MH. A systemic review of the roles of n-3 fatty acids in health and disease. *Journal of the American Dietetic Association*. 109.4 (2009): 668-679. <https://doi.org/10.1016/j.jada.2008.12.022>
53. Micallef MA, Munro IA, Garg ML. An inverse relationship between plasma n-3 fatty acids and C-reactive protein in healthy individuals. *European Journal of Clinical Nutrition*. 63.9 (2009): 1154-1156. <https://doi.org/10.1038/ejcn.2009.20>
54. Farzaneh-Far R, Harris WS, Garg S, Na B, Whooley MA. Inverse association of erythrocyte n-3 fatty acid levels with inflammatory biomarkers in patients with stable coronary artery disease: The Heart and Soul Study. *Atherosclerosis*. 205.2 (2009): 538-543. <https://doi.org/10.1016/j.atherosclerosis.2008.12.013>
55. Bonanome A, Pagnan A, Biffanti S, Opportuno A, Sorgato F, Dorella M, Maiorino M, Ursini F. Effect of dietary monounsaturated and polyunsaturated fatty acids on the susceptibility of plasma low density lipoproteins to oxidative modification. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 12.4 (1992): 529-533. <https://doi.org/10.1161/01.atv.12.4.529>
56. Cholesterol, Beyond. Modifications of low-density lipoprotein that increase its atherogenicity Steinberg. 915-24.
57. Tsimikas S, Brilakis ES, Miller ER, McConnell JP, Lennon RJ, Kornman KS, Witztum JL, Berger PB. Oxidized phospholipids, Lp (a) lipoprotein, and coronary artery disease. *New England Journal of Medicine* 353.1 (2005): 46-57.

-
58. Tsutsui T, et al. Plasma oxidized low-density lipoprotein as a prognostic predictor in patients with chronic congestive heart failure. *Journal of the American College of Cardiology*. 39.6 (2002): 957-962. [https://doi.org/10.1016/s0735-1097\(02\)01721-7](https://doi.org/10.1016/s0735-1097(02)01721-7)
59. Sabaté J, Ang Y. Nuts and health outcomes: new epidemiologic evidence. *The American Journal of Clinical Nutrition* 89.5 (2009): 1643S-1648S. <https://doi.org/10.3945/ajcn.2009.26736q>
60. Bes-Rastrollo M, Wedick NM, Martínez-González MA, Li TY, Sampson L, Hu FB. Prospective study of nut consumption, long-term weight change, and obesity risk in women. *The American Journal of Clinical Nutrition*. 89.6 (2009): 1913-1919. <https://doi.org/10.3945/ajcn.2008.27276>
61. Martínez-González MA, Bes-Rastrollo M. Nut consumption, weight gain and obesity: Epidemiological evidence. *Nutrition, Metabolism and Cardiovascular Diseases* 21 (2011): S40-S45. <https://doi.org/10.1016/j.numecd.2010.11.005>
62. Ros E, Nunez I, Perez-Heras A, Serra M, Gilabert R, Casals E, Deulofeu R. A walnut diet improves endothelial function in hypercholesterolemic subjects a randomized crossover trial. *Circulation*. 109.13 (2004): 1609-1614. <https://doi.org/10.1016/j.accreview.2004.06.062>
63. Ma Y, Njike VY, Millet J, Dutta S, Doughty K, Treu JA, Katz DL. Effects of Walnut Consumption on Endothelial Function in Type 2 Diabetic Subjects: A randomized controlled crossover trial. *Diabetes Care* 33.2 (2010): 227-232. <https://doi.org/10.2337/dc09-1156>
64. Hu FB. Plant-based foods and prevention of cardiovascular disease: an overview. *The American Journal of Clinical Nutrition* 78.3 (2003): 544S-551S.
65. Sari I, Baltaci Y, Bagci C, Davutoglu V, Erel O, Celik H, Ozer O, Aksoy N, Aksoy M. Effect of pistachio diet on lipid parameters, endothelial function, inflammation, and oxidative status: a prospective study. *Nutrition*. 26.4 (2010): 399-404. <https://doi.org/10.1016/j.nut.2009.05.023>
66. Spiller GA, Jenkins DJ, Cragen LN, Gates JE, Bosello O, Berra K, Rudd C, Stevenson M, Superko R. Effect of a diet high in monounsaturated fat from almonds on plasma cholesterol and lipoproteins. *Journal of the American College of Nutrition*. 11.2 (1992): 126-130.
67. Abbey M, Noakes M, Belling GB, Nestel PJ. Partial replacement of saturated fatty acids with almonds or walnuts lowers total plasma cholesterol and low-density-lipoprotein cholesterol. *The American Journal of Clinical Nutrition*. 59.5 (1994): 995-999.
68. Mukuddem-Petersen J, Oosthuizen W, Jerling JC. A systematic review of the effects of nuts on blood lipid profiles in humans. *The Journal of Nutrition*. 135.9 (2005): 2082-2089.
69. Kris-Etherton PM, Pearson TA, Wan Y, Hargrove RL, Moriarty K, Fishell V, Etherton TD. High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. *The American Journal of Clinical Nutrition* . 70.6 (1999): 1009-1015.
70. Kelly JH, Sabaté J. Nuts and coronary heart disease: an epidemiological perspective. *British Journal of Nutrition*. 96.S2 (2006): S61-S67. <https://doi.org/10.1017/bjn20061865>
71. Kris-Etherton PM, Zhao G, Binkoski AE, Coval SM, Etherton TD. The effects of nuts on coronary heart disease risk. *Nutrition Reviews*. 59.4 (2001): 103-111. <https://doi.org/10.1111/j.1753-4887.2001.tb06996.x>
72. Sabaté J. Nut consumption, vegetarian diets, ischemic heart disease risk, and all-cause mortality: evidence from epidemiologic studies. *The American Journal of Clinical Nutrition*. 70.3 (1999): 500s-503s.

-
73. Bao Y, Han J, Hu FB, Giovannucci EL, Stampfer MJ, Willett WC, Fuchs CS. Association of nut consumption with total and cause-specific mortality. *New England Journal of Medicine*. 369.21 (2013): 2001-2011. <https://doi.org/10.1056/nejmoa1307352>
74. Guasch-Ferré M, Bullo M, Martinez-Gonzalez MA, Ros E, Corella D, Estruch R, et al. Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. *BMC Medicine*. 11.1 (2013): 1. <https://doi.org/10.1186/1741-7015-11-164>
75. Craig WJ, Mangels A R. Position of the American Dietetic Association: vegetarian diets. *Journal of the American Dietetic Association*. 109.7 (2009): 1266-1282. <https://doi.org/10.1016/j.jada.2009.05.027>
76. Luu HN, Blot WJ, Xiang YB, Cai H, Hargreaves MK, Li H, et al. Prospective evaluation of the association of nut/peanut consumption with total and cause-specific mortality. *JAMA Internal Medicine*. 175.5 (2015): 755-766. <https://doi.org/10.1001/jamainternmed.2014.8347>

Optimizing Heart Failure Through Diet

Farley B. Neasman III¹

Author Affiliations:

1. Joan C. Edwards School of Medicine, Marshall University, Huntington, West Virginia

The author has no financial disclosures to declare and no conflicts of interest to report.

Corresponding Author:

Farley B. Neasman III
Marshall University Joan C. Edwards School of Medicine
Huntington, West Virginia
Email: farley3@gmail.com

Abstract

Heart failure is a growing epidemic that will add significant monetary and human costs to an already overtaxed health-care system. Though promising new medications have recently been approved, this complex condition is largely preventable through aggressive risk factor modification, with diet being shown to have a greater effect than exercise. An underrated component of a healthy diet is the simple addition of nuts – the anti-inflammatory fatty acids, healthy proteins, and general availability have been shown to improve survival and reduce the primary risk factors contributing to heart failure, making the addition of nuts and legumes to the diet an attractive, cost-effective tool to promote cardiovascular well-being.

Keywords

heart failure, diet, nuts, legumes, fatty acids, risk factor modification

Introduction

Heart failure, defined as a “complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood”¹, is the most common reason for hospitalization in patients over 65 years of age² and has reached epidemic proportions. In 2013, the prevalence was estimated to be 5.8 million in the US and 23 million worldwide³, with an incidence of 870,000 new cases in the US in 2015⁴ and a 5 year mortality of 50%.⁵ Heart failure increases in incidence with age, affecting nearly 20 per 1000 persons aged 65-69 and rising sharply to more than 80 per 1000 among those older than 85⁶ – this is particularly concerning given that 20% of Americans are expected to be over age 65 by 2050.⁷ In 2012 as part of the Affordable Care Act, the Readmission Reduction Program was put into effect, imposing financial penalties on hospital systems with higher than average 30 day readmission rates for various conditions – this has helped to decrease the 30 day readmission for heart failure from 25% in 2009 to approximately 21.9% in 2016.⁸ However, the more than \$30 billion cost of treating heart failure – including hospitalizations, medications, and lost wages – is only expected to rise.⁹ In fact, with an expected increase in heart failure prevalence to more than 8 million in the US, the total cost is projected to more than double, from over \$30 billion currently to \$70 billion by 2030.¹⁰

Risk Factors

Heart failure is defined by the ACC/AHA stages (Stage A = risk factors, Stage B = structural heart disease, Stage C and D = structural heart disease with previous or current symptoms) and the NYHA functional classes (Class I = no functional limitations, Class II = slight limitation; ordinary physical activity results in symptoms, Class III = marked limitation in physical activity but comfortable at rest, Class IV = symptoms at rest).¹ Hypertension and coronary artery disease have been recognized as the most important risk factors since the early 1990s¹¹, with others including valvular heart disease, physical inactivity, male gender, lower levels of education, cigarette smoking, overweight, and diabetes.¹² Roughly half of heart failure cases are considered HFrEF (heart failure with reduced ejection fraction), with EF<40% - mostly due to myocardial infarction by way of coronary artery disease – with the other half referred to as heart HFpEF (heart failure with preserved ejection fraction), with EF>50%¹, a heterogeneous umbrella term under which are subsumed various disparate pathologies. Though there is considerable overlap

between the two entities, particularly with regard to symptomatology and diastolic dysfunction, risk factors for HFpEF lean towards older age, female gender, atrial fibrillation, and hyperlipidemia (in addition to obesity, CAD, and DM), with hypertension being the greatest risk factor.¹ Dyslipidemia has been recognized as a major risk factor for CAD and therefore HFpEF since evaluation of the original Framingham data¹³ though its role in HFpEF is thought to be more complex, contributing to an inflammatory milieu in the setting of systemic and endothelial inflammation wrought by hypertension, diabetes, and obesity, the resultant reduction in nitric oxide bioavailability and molecular derangements, all culminating in ventricular stiffness.¹⁴

Pharmacological Treatment

Current nonsurgical treatment for stage B and C HFrEF, including evidence-based beta blockade, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), aldosterone receptor inhibitors, and diuresis for symptoms¹ have recently been updated to include combination angiotensin receptor blockers and neprilysin inhibition (ARNI) and ivabradine, for further rate control.¹⁵ Pharmacological recommendations for HFpEF are much less robust, limited to blood pressure control, diuresis for symptomatic relief, and a potential role for ARBs in reducing hospitalizations.¹ To date, unlike HFrEF, there are no HFpEF-specific medications to improve mortality. Thus, a greater focus is being placed not only on the prevention of heart failure in general, but on the amelioration of contributing conditions. In heart failure stage A (patients at risk but without structural disease or symptoms), treatment of hypertension and lipid disorders receives an IA recommendation, with treatment of obesity and diabetes receiving an IC recommendation.¹

Lifestyle Modification

Therapeutic lifestyle interventions are the cornerstone of treatment for the primary risk factors for heart failure – hypertension, type 2 diabetes, obesity, and dyslipidemia.¹⁶⁻¹⁹ In one study, systolic and diastolic blood pressure improved by 20 and 8 points respectively, through diet and exercise²⁰, and in another, dietary changes alone were found to be an effective treatment for hypertension.²¹ Diet and exercise were associated with a 42% reduction in the risk of developing type 2 diabetes²², and a 50% remission in diabetes after 6 years.²³ One meta-analysis reported a 5.8-25% increase in HDL with varying results on LDL due to diet and exercise²⁴, while another reported a maximum improvement in LDL of 18 points (mean of 8.5 points) due to diet alone, that increased to a maximum of 21.7 point (mean of 11) when exercise was added.²⁵ It goes without saying that diet and exercise are the mainstays of treatment for obesity. It also goes without saying that aggressive lifestyle management of the primary risk factors for heart failure would reduce its incidence, prevalence, morbidity, and mortality – particularly for patients of lower socioeconomic status, who not only have higher heart failure readmissions, but have higher mortality.²⁶

Physical Activity

The Physical Activity Guidelines for Americans recommend moderately intense aerobic activity for at least 2.5 hours weekly, vigorous aerobic activity for 1 hour and 15 minutes (or a combination) in addition to strength training²⁷, and the ACC/AHA Guidelines on Lifestyle Management to Reduce Cardiovascular Risk recommend 3-4 weekly 40 minute sessions of moderate-vigorous activity.²⁸ While it is estimated that 18% of Americans over age 18 meet the

aerobic and strength training recommendation, nearly 50% of US adults meet the aerobic recommendations.²⁹ However, with nearly 33.5% of adults being hypertensive, 12.6% with diabetes, 12.1% with high serum cholesterol³⁰, and nearly 33% obese³¹, it would be overly simplistic to assume that these numbers could be brought to zero by perfect compliance with the exercise recommendations. Many of the patients who would benefit the most are unable to exercise due to the comorbidities of their illnesses. Nevertheless, diet carries the lion's share of weight loss – a meta-analysis concluded that on average, study participants were able to reduce their weight by 10.7kg through diet alone, 2.9kg through exercise alone, and 11kg with diet and exercise.³²

Diet

Decades of research have produced an abundance of information linking isolated macronutrients and eating patterns to various health outcomes and associated serum markers. The western diet is characterized by higher intake of processed grains, eggs, salt, high fat dairy, red and processed meats, sweets, white potatoes, French fries, and sugar sweetened beverages³³ and has been associated with CAD, obesity, hypertension, hyperlipidemia and type 2 diabetes³⁴ by way of systemic inflammatory marker such as tumor necrosis factor (TNF)- α , interleukin (IL)-6, and high-sensitivity C-reactive protein (hsCRP).³⁵ Markers of endothelial dysfunction – E-selectin, soluble intercellular adhesion molecule (sICAM)-1 and soluble vascular cell adhesion molecule (sVCAM)-1 – are also associated with the western diet.³⁶

In contrast, various dietary patterns have been consistently associated with lower levels of inflammatory markers and improved health outcomes. The National Institute of Health sponsored Dietary Approaches to Stop Hypertension (DASH) diet is based on 2000 calories daily and recommends 6-8 daily servings of grains, 6 or fewer servings of meats, fish, and poultry, 4-5 servings of fruits, 4-5 servings of vegetables, 2-3 servings of low fat or fat free dairy, 2-3 servings of fats and oils, 4-5 weekly servings of nuts, seeds, dry beans, and peas, and 5 or fewer weekly servings of sweets. Importantly, sodium is restricted to 2300 mg at most.³⁷ A meta-analysis showed the DASH diet to contribute a 20% reduction in the risk of cardiovascular disease, 19% reduction in risk of coronary heart disease, 19% reduction in risk of stroke, and a 29% reduction in risk of heart failure.³⁸

The Mediterranean diet is characterized by the historical dietary pattern in the Mediterranean region and includes daily consumption of whole grains, vegetables, fruits, low fat dairy, monounsaturated fatty acids in the form of olive oil (the primary source for α -linolenic acid / ALA, an essential polyunsaturated fatty acid (PUFA), and moderate daily consumption of wine with meals, with weekly consumption of fish, poultry, nuts and legumes, and minimization of red meat.³⁹ It has been associated with a 9% reduction in cardiovascular disease mortality and a 9% reduction in overall mortality⁴⁰, a -0.69 log hazard ratio for metabolic syndrome (in addition to improving waist circumference, HDL, and BP)³⁹, and a 19% reduction in risk of diabetes.⁴¹

Vegetarian diets, which eschew meat, fish, poultry, eggs, and dairy, have been determined by the American Dietetic Association to be healthful, complete, and useful in the treatment and prevention of disease in all stages of life (including pregnancy and infancy, and at all energy levels. Compared with nonvegetarians, vegetarians have lower cholesterol levels, BMI, cholesterol, rates of diabetes and cancer, and rates of death from CAD.⁴² Two case series showed that vegetarian diets are associated with improvement in angiographically determined coronary

artery disease.^{43,44} Vegetarians have been shown to have significantly lower cholesterol levels than nonvegetarians^{45,46}, as well as up to 24% lower risk of death from coronary artery disease.⁴⁷

Dietary Fatty Acids

The association of fatty acids and health, particularly pertaining to coronary artery disease and heart failure, cannot be understated, given their association with serum inflammatory markers.³⁵ In one study, dietary fatty acids strongly correlated with levels of CRP, total cholesterol, apolipoprotein B, and LDL, and PUFA levels were inversely related to CRP – the highest quartile of saturated fatty acid (SFA) intake was associated with a twofold greater risk of CHD, and the opposite difference was seen with PUFA (but not MUFA).⁴⁸ A study of compensated HFrEF patients on optimal medical therapy revealed higher TNF- α levels and lower event free survival in patients with higher intake of SFA and trans fatty acids (TFA), while patients who consumed diets higher in omega-3 and other polyunsaturated fats had lower levels of TNF receptors.⁴⁹ Data from the Harvard Nurses' Health Study revealed that (TFA) intake was associated with elevated levels of soluble TNF receptors 1 and 2 – also, TFA intake was associated with CRP in women with elevated BMI.⁵⁰ TFA levels positively correlate with elevated LDL, lower HDL, elevated IL-6, CRP, and TNF- α , even when compared to SFA. When 2% of energy from SFA, carbohydrate, MUFA, and PUFA were isocalorically replaced with TFA, risk of myocardial infarction or death due to cardiovascular causes increased 20, 24, 27, and 32%, respectively.⁵¹ Specifically, omega-3 (n-3 polyunsaturated) fatty acids are associated with lower levels of inflammatory markers, and may even have anti-arrhythmic effects, thought to be due to their effect on cardiac membranes.⁵² The N-3 fatty acids eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA) are inversely associated with levels of CRP in healthy subjects⁵³, and EPA and docosahexaenoic acid (DHA) are inversely associated with levels of CRP and IL-6 in patients with stable coronary artery disease.⁵⁴ The association of fatty acids with cardiovascular health is further complicated by susceptibility to oxidative damage. Diets rich in MUFA showed increased resistance to oxidation, whereas PUFA are more prone to oxidation – a quality which extends to the PUFA moieties of LDL.^{55,56} Oxidized LDL is highly associated with coronary artery stenosis⁵⁷, negatively correlates with ejection fraction, and is a predictor of mortality in heart failure.⁵⁸

Dietary Nut Intake

Nuts are one of the most readily available sources of beneficial fatty acids, and ample research exists showing their association with health and longevity. A diet including nut consumption has been shown to be associated with decreased risk of obesity and weight gain⁵⁹, and higher levels of nut intake were associated with weight loss.^{60,61} Walnuts - rich in antioxidants and ALA (n-3 fatty acid) -improved endothelial function as evidenced by reduction in sICAM-1 in hyperlipidemic patients⁶² and flow mediated dilatation in diabetics.⁶³ Improvement in endothelium dependent vasodilation may be due to the presence of arginine in nuts, and its role in nitric oxide biosynthesis.⁶⁴ Diets including nuts have been found to improve lipid profiles⁶⁵⁻⁶⁹, decrease risk of coronary heart disease⁷⁰⁻⁷¹,and reduce all-cause mortality.⁷²⁻⁷⁵ A 2015 review found that nut intake was inversely related to mortality among a cohort of over 206,000 African American and Chinese men and women, many from a lower socio-economic status. The increase in survival in all ethnic groups was due to improvement in ischemic heart disease associated with peanut intake – peanuts are ubiquitous and inexpensive, and thus were determined to be an ideal dietary option to reduce cardiovascular risk.⁷⁶

Conclusion

As stated above, heart failure is a fast-growing medical and financial crisis. While new therapies will inevitably be developed, the focus on prevention and lifestyle modifications cannot be overstated. Small nutritional changes may be associated with greater compliance than large dietary overhaul, and can lay the groundwork for sustainable improvement. The incorporation of nuts into a heart-healthy diet is one such change that, though it may be small, has undeniably significant health benefits, and may reduce heart failure incidence, prevalence, morbidity, and mortality.

References

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 2013;62(16):e147-e239. doi:10.1016/j.jacc.2013.05.019.
2. Azad N, Lemay G. Management of chronic heart failure in the older population. *Journal of Geriatric Cardiology*. 11.4 (2014): 329.
3. Roger VL. Epidemiology of heart failure. *Circulation Research*. 113.6 (2013): 646-659.
4. <http://news.heart.org/heart-failure-numbers-to-increase-by-nearly-40-percent-in-next-15-years/>
5. Mozaffarian D, Benjamin EJ, Go AS, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation*. 2016;133:e38-e360.
6. Curtis LH, Whellan DJ, Hammill BG, Hernandez AF, Anstrom KJ, Shea AM, Schulman KA. Incidence and prevalence of heart failure in elderly persons, 1994-2003. *Archives of Internal Medicine*. 168.4 (2008): 418-424.
7. Hardy DR. The booming dynamics of aging: From awareness to action. Report of the 2005 White House Conference on Aging. 2005.
8. www.cms.gov
9. Heidenreich PA, Trogdon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, et al. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation*. 2011;123(8):933-44.
10. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the united states a policy statement from the American Heart Association. *Circulation: Heart Failure*. 6.3 (2013): 606-619.
11. Kannel WB, Belanger AJ. Epidemiology of heart failure. *American Heart Journal*. 121.3 (1991): 951-957.
12. He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. *Archives of Internal Medicine*. 161.7 (2001): 996-1002.
13. Kannel WB, Castelli WP, Gordon T, McNamara PM. Serum cholesterol, lipoproteins, and the risk of coronary heart disease: the Framingham Study. *Annals of Internal Medicine*. 74.1 (1971): 1-12.
14. Paulus WJ, Tschöpe C. A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. *Journal of the American College of Cardiology*. 62.4 (2013): 263-271.
15. Yancy, Clyde W., et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Journal of the American College of Cardiology*. (2016).
16. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *Jama*. 311.5 (2014): 507-520.

17. <http://www.idf.org/treatment-algorithm-people-type-2-diabetes>
18. Jensen, Michael D., et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Journal of the American College of Cardiology*. 63.25_PA (2014).
19. Panel, National Cholesterol Education Program NCEP Expert. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation*. 106.25 (2002): 3143.
20. Roberts CK, Vaziri ND, Barnard RJ. Effect of diet and exercise intervention on blood pressure, insulin, oxidative stress, and nitric oxide availability. *Circulation*. 106.20 (2002): 2530-2532.
21. Svetkey LP, Simons-Morton D, Vollmer WM, Appel LJ, Conlin PR, Ryan DH, Ard J, Kennedy BM. Effects of dietary patterns on blood pressure: subgroup analysis of the Dietary Approaches to Stop Hypertension (DASH) randomized clinical trial. *Archives of Internal Medicine*. 159.3 (1999): 285-293.
22. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, Hu ZX, Lin J, Xiao JZ, Cao HB, Liu PA, Jiang XG, Jiang YY, Wang JP, Zheng H, Zhang H, Bennett PH, Howard BV. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care*. 20.4 (1997): 537-544.
23. Eriksson KF, Lindgärde F. Prevention of Type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmö feasibility study. *Diabetologia*. 34.12 (1991): 891-898.
24. Leon AS, Sanchez OA. Response of blood lipids to exercise training alone or combined with dietary intervention. *Medicine and science in sports and exercise*. 33.6; SUPP (2001): S502-S515.
25. Kelley GA, Kelley KS. Effects of diet, aerobic exercise, or both on non-HDL-C in adults: a meta-analysis of randomized controlled trials. *Cholesterol*. 2012 (2012).
26. Rathore SS, Masoudi FA, Wang Y, Curtis JP, Foody JM, Havranek EP, Krumholz HM. Socioeconomic status, treatment, and outcomes among elderly patients hospitalized with heart failure: findings from the National Heart Failure Project. *American Heart Journal*. 152.2 (2006): 371-378.
27. US Department of Health and Human Services, and US Department of Health and Human Services. *Physical activity guidelines for Americans*. (2008).
28. Eckel RH, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 63.25_PA (2014).
29. Ward BW, et al. Early release of selected estimates based on data from the January–March 2013 National Health Interview Survey. *National Center for Health Statistics* (2013).
30. CDC.gov. *Health, United States, 2015, table 53*.
31. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. *Jama*. 311.8 (2014): 806-814.
32. Miller WC, Koceja DM, Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *International Journal of Obesity*. 21.10 (1997): 941-947.
33. Halton TL, Willett WC, Liu S, Manson JE, Stampfer MJ, Hu FB. Potato and french fry consumption and risk of type 2 diabetes in women. *The American Journal of Clinical Nutrition*. 83.2 (2006): 284-290.
34. Carrera-Bastos P, Fontes-Villalba M, O’Keefe JH, Lindeberg S, Cordain L. The western diet and lifestyle and diseases of civilization. *Research Reports in Clinical Cardiology*. 2 (2011): 15-35.

35. Galland L. Diet and inflammation. *Nutrition in Clinical Practice*. 25.6 (2010): 634-640.
36. Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, Hu FB. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. *The American Journal of Clinical Nutrition*. 80.4 (2004): 1029-1035.
37. <https://www.nhlbi.nih.gov/health/health-topics/topics/dash>
38. Salehi-Abargouei A, Maghsoudi Z, Shirani F, Azadbakht L. Effects of Dietary Approaches to Stop Hypertension (DASH)-style diet on fatal or nonfatal cardiovascular diseases—incidence: a systematic review and meta-analysis on observational prospective studies. *Nutrition*. 29.4 (2013): 611-618.
39. Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. *Journal of the American College of Cardiology*. 57.11 (2011): 1299-1313.
40. Sofi F, et al. Adherence to Mediterranean diet and health status: meta-analysis. *BMJ*. 337 (2008): a1344.
41. Schwingshackl L, Missbach B, König J, Hoffmann G. Adherence to a Mediterranean diet and risk of diabetes: a systematic review and meta-analysis. *Public Health Nutrition*. 18.07 (2015): 1292-1299.
42. Craig WJ, Mangels AR. Position of the American Dietetic Association: vegetarian diets. *Journal of the American Dietetic Association* 109.7 (2009): 1266-1282.
43. Ornish D, Brown SE, Scherwitz LW, Billings JH, Armstrong WT, Ports TA, McLanahan SM, Kirkeeide RL, Brand RJ, Gould KL. Can lifestyle changes reverse coronary heart disease? *The Lifestyle Heart Trial*. *The Lancet*. 336.8708 (1990): 129-133.
44. Esselstyn CB Jr, Gendy G, Doyle J, Golubic M, Roizen MF. A way to reverse CAD? *Journal of Family Practice*. 63.7 (2014): 356-364.
45. Sacks FM, Castelli WP, Donner A, Kass EH. Plasma lipids and lipoproteins in vegetarians and controls. *New England Journal of Medicine* 292.22 (1975): 1148-1151.
46. Fisher M, Levine PH, Weiner B, Ockene IS, Johnson B, Johnson MH, Natale AM, Vaudreuil CH, Hoogasian J. The effect of vegetarian diets on plasma lipid and platelet levels. *Archives of Internal Medicine*. 146.6 (1986): 1193-1197.
47. Key TJ, Fraser GE, Thorogood M, Appleby PN, Beral V, Reeves G, et al. Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies. *The American Journal of Clinical Nutrition*. 70.3 (1999): 516s-524s.
48. Clarke R, Shipley M, Armitage J, Collins R, Harris W. Plasma phospholipid fatty acids and CHD in older men: Whitehall study of London civil servants. *British Journal of Nutrition*. 102.2 (2009): 279.
49. Lennie TA, et al. Dietary fat intake and proinflammatory cytokine levels in patients with heart failure. *Journal of Cardiac Failure*. 11.8 (2005): 613-618.
50. Mozaffarian D, Pischon T, Hankinson SE, Rifai N, Joshipura K, Willett WC, Rimm EB. Dietary intake of trans fatty acids and systemic inflammation in women. *The American Journal of Clinical Nutrition*. 79.4 (2004): 606-612.
51. Mozaffarian D, Aro A, Willett WC. Health effects of trans-fatty acids: experimental and observational evidence. *European Journal of Clinical Nutrition*. 63 (2009): S5-S21.
52. Riediger ND, Othman RA, Suh M, Moghadasian MH. A systemic review of the roles of n-3 fatty acids in health and disease. *Journal of the American Dietetic Association*. 109.4 (2009): 668-679.

53. Micallef MA, Munro IA, Garg ML. An inverse relationship between plasma n-3 fatty acids and C-reactive protein in healthy individuals. *European Journal of Clinical Nutrition*. 63.9 (2009): 1154-1156.
54. Farzaneh-Far R, Harris WS, Garg S, Na B, Whooley MA. Inverse association of erythrocyte n-3 fatty acid levels with inflammatory biomarkers in patients with stable coronary artery disease: The Heart and Soul Study. *Atherosclerosis*. 205.2 (2009): 538-543.
55. Bonanome A, Pagnan A, Biffanti S, Opportuno A, Sorgato F, Dorella M, Maiorino M, Ursini F. Effect of dietary monounsaturated and polyunsaturated fatty acids on the susceptibility of plasma low density lipoproteins to oxidative modification. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 12.4 (1992): 529-533.
56. Cholesterol, Beyond. Modifications of low-density lipoprotein that increase its atherogenicity Steinberg. 915-24.
57. Tsimikas S, Brilakis ES, Miller ER, McConnell JP, Lennon RJ, Kornman KS, Witztum JL, Berger PB. Oxidized phospholipids, Lp (a) lipoprotein, and coronary artery disease. *New England Journal of Medicine* 353.1 (2005): 46-57.
58. Tsutsui T, et al. Plasma oxidized low-density lipoprotein as a prognostic predictor in patients with chronic congestive heart failure. *Journal of the American College of Cardiology*. 39.6 (2002): 957-962.
59. Sabaté J, Ang Y. Nuts and health outcomes: new epidemiologic evidence. *The American Journal of Clinical Nutrition* 89.5 (2009): 1643S-1648S.
60. 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. *The American Journal of Clinical Nutrition*. 89.6 (2009): 1913-1919.
61. Martínez-González MA, Bes-Rastrollo M. "Nut consumption, weight gain and obesity: Epidemiological evidence. *Nutrition, Metabolism and Cardiovascular Diseases* 21 (2011): S40-S45.
62. Ros E, Nunez I, Perez-Heras A, Serra M, Gilabert R, Casals E, Deulofeu R. A walnut diet improves endothelial function in hypercholesterolemic subjects a randomized crossover trial. *Circulation*. 109.13 (2004): 1609-1614.
63. Ma Y, Njike VY, Millet J, Dutta S, Doughty K, Treu JA, Katz DL. Effects of Walnut Consumption on Endothelial Function in Type 2 Diabetic Subjects: A randomized controlled crossover trial. *Diabetes Care* 33.2 (2010): 227-232.
64. Hu FB. Plant-based foods and prevention of cardiovascular disease: an overview. *The American Journal of Clinical Nutrition* 78.3 (2003): 544S-551S.
65. Sari I, Baltaci Y, Bagci C, Davutoglu V, Erel O, Celik H, Ozer O, Aksoy N, Aksoy M. Effect of pistachio diet on lipid parameters, endothelial function, inflammation, and oxidative status: a prospective study. *Nutrition*. 26.4 (2010): 399-404.
66. Spiller GA, Jenkins DJ, Cragen LN, Gates JE, Bosello O, Berra K, Rudd C, Stevenson M, Superko R. Effect of a diet high in monounsaturated fat from almonds on plasma cholesterol and lipoproteins. *Journal of the American College of Nutrition*. 11.2 (1992): 126-130.
67. Abbey M, Noakes M, Belling GB, Nestel PJ. Partial replacement of saturated fatty acids with almonds or walnuts lowers total plasma cholesterol and low-density-lipoprotein cholesterol. *The American Journal of Clinical Nutrition*. 59.5 (1994): 995-999.
68. Mukuddem-Petersen J, Oosthuizen W, Jerling JC. A systematic review of the effects of nuts on blood lipid profiles in humans. *The Journal of Nutrition*. 135.9 (2005): 2082-2089.

69. Kris-Etherton PM, Pearson TA, Wan Y, Hargrove RL, Moriarty K, Fishell V, Etherton TD. High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. *The American Journal of Clinical Nutrition* . 70.6 (1999): 1009-1015.
70. Kelly JH, Sabaté J. Nuts and coronary heart disease: an epidemiological perspective. *British Journal of Nutrition*. 96.S2 (2006): S61-S67.
71. Kris-Etherton PM, Zhao G, Binkoski AE, Coval SM, Etherton TD. The effects of nuts on coronary heart disease risk. *Nutrition Reviews*. 59.4 (2001): 103-111.
72. Sabaté J. Nut consumption, vegetarian diets, ischemic heart disease risk, and all-cause mortality: evidence from epidemiologic studies. *The American Journal of Clinical Nutrition*. 70.3 (1999): 500s-503s.
73. Bao Y, Han J, Hu FB, Giovannucci EL, Stampfer MJ, Willett WC, Fuchs CS. Association of nut consumption with total and cause-specific mortality. *New England Journal of Medicine*. 369.21 (2013): 2001-2011.
74. Guasch-Ferré M, Bullo M, Martinez-Gonzalez MA, Ros E, Corella D, Estruch R, et al. Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. *BMC Medicine*. 11.1 (2013): 1.
75. Craig WJ, Mangels A R. Position of the American Dietetic Association: vegetarian diets. *Journal of the American Dietetic Association*. 109.7 (2009): 1266-1282.
76. Luu HN, Blot WJ, Xiang YB, Cai H, Hargreaves MK, Li H, et al. Prospective evaluation of the association of nut/peanut consumption with total and cause-specific mortality. *JAMA Internal Medicine*. 175.5 (2015): 755-766.