# Soy & Heart Health

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**AN ESTIMATED 16 MILLION AMERICANS** (8.7 million men and 7.3 million women) were affected in 2005 by coronary heart disease (CHD), which includes heart attack and angina pectoris. In 2004, the most recent year for which statistics are available, approximately 451,000 Americans died of CHD. This represents about 20 percent of all deaths in the United States, making CHD the number one killer of Americans.[1]

## FDA-Approved Health Claim for Soy:

*25 grams of soy protein per day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.*

The number of deaths from CHD is divided approximately evenly among men and women, although the average age of a person having a first heart attack is 64.5 for men and 70.4 for women. It is estimated that in 2008, 770,000 Americans will have a new coronary attack, 430,000 will suffer a recurrent attack, and an additional 190,000 will have a "silent" first heart attack.[2]

Despite these grim statistics, CHD death rates decreased by a remarkable 59 percent between 1950 and 1999, and by 33 percent between 1994 and 2004. While much of this is due to improved medical treatment, the etiology of CHD is determined to a great extent by risk factors that can easily be modified through lifestyle changes.

An analysis of three large prospective cohort studies found that about 90 percent of CHD patients have prior exposure to at least one of the following risk factors:[3]

- *High total blood cholesterol levels (≥240 mg/dl or 6.22 mmol/l) or current treatment with cholesterol-lowering drugs*
- *Hypertension (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg) or current treatment with blood pressure-lowering drugs*
- *Current cigarette use*
- *Clinical report of diabetes*

It is clear that diet and nutrition choices can significantly impact the risk and incidence of CHD. Through several different mechanisms, soyfoods in particular may positively influence heart health.

## Effects of Soyfoods on Circulating Lipid Levels

Soyfoods have long been known as excellent sources of protein. In the past 15 years, the effect of this protein on blood cholesterol levels has attracted widespread research attention. The first rodent studies[4, 5] demonstrating soy protein's role in lowered cholesterol levels were published more than 60 years ago, and the first human clinical trial demonstrating this effect was published in 1967.[6] However, not until 1995 did the hypocholesterolemic effects of soy protein receive widespread recognition.

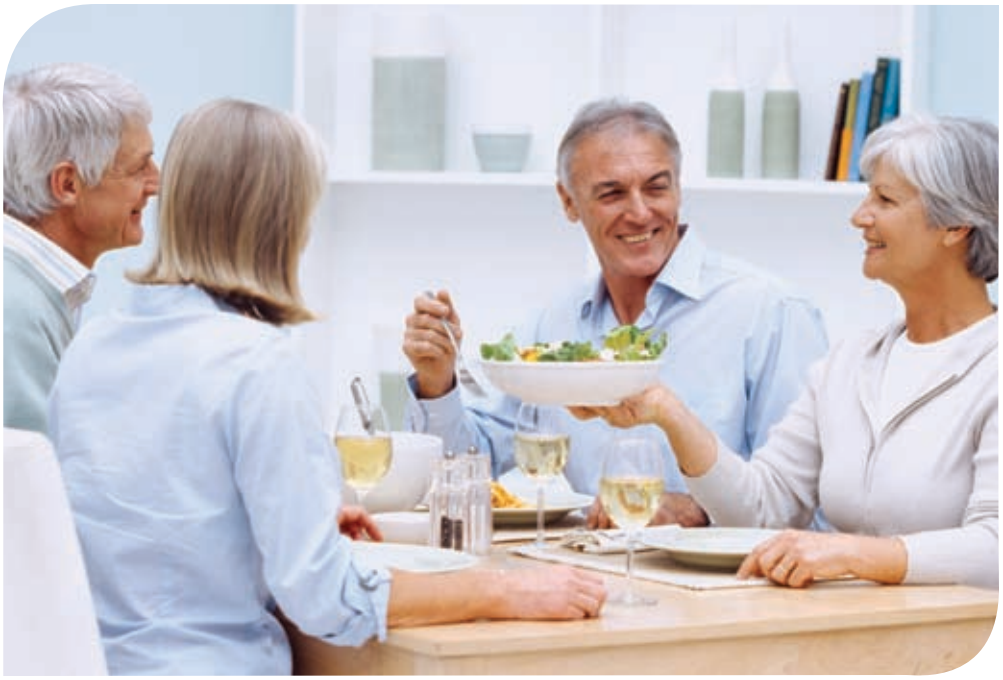
In that year, a meta-analysis of the clinical data, which included 38 different comparisons, found that soy protein reduced low density lipoprotein cholesterol (LDLC) by approximately 13 percent.[7] This reduction, which was independent of the fatty acid content of soyfoods, was greater than for any single non-pharmacological approach. In fact, at the time (before statins became widely available), this effect was essentially equal to that of the available cholesterol-lowering drugs.

The results of the 1995 meta-analysis prompted much investigation into the cholesterol-lowering effects of soy protein. Some of this research was directed at identifying the specific components and mechanisms responsible for cholesterol reduction, while others explored the responses of different subpopulations (e.g., normo- vs. hypercholesterolemic subjects, pre- vs. postmenopausal women) to soy protein. Some data suggest that cholesterol reduction is a result of peptides formed from the digestion of soy protein upregulating hepatic LDLC receptors.[8, 9] Researchers also continue to explore whether isoflavones in soybeans impact the efficacy of soy protein.[10]

At least 100 clinical trials investigating the hypocholesterolemic effects of soy protein have been conducted. However, the current estimates of the degree to which soy protein reduces LDLC are lower than initially thought. Substantial meta-analyses published between 2004 and 2007 (some of which included only trials published after 1995), including one by the American Heart

*Soyfoods may help reduce risk of coronary heart disease through several different mechanisms, including directly lowering blood cholesterol levels.*

*Recent research indicates that soy protein lowers LDL cholesterol by 3 to 5 percent. On a population level, each 1 percent decrease in LDL reduces CHD risk and/or mortality by 2 to 5 percent. Therefore, even a 3 percent reduction in LDL could lower risk for heart disease by as much as 15 percent.*



Association[11] and one by the federal Agency for Healthcare Research and Quality,[12] have concluded that soy protein lowers LDLC by 3 to 5 percent,[13] which is similar to the effects of soluble fiber.[14]

The reasons for the lowered estimates are not entirely known, although compared to earlier studies, the post-1995 trials involved subjects with lower baseline cholesterol levels and used somewhat lower amounts of soy protein. Also, many of the earliest studies were conducted in Italy and may have used less processed soy proteins. However, the extent to which each of these factors influences the cholesterol-lowering effects of soy is unclear.

*Soyfoods, which are typically low in saturated fat, can be used to reduce or replace other protein sources with higher saturated fat content.*

It is important to note that from a public health perspective, a 3 to 5 percent reduction in LDLC is quite meaningful. Over time, each 1 percent decrease in LDLC reduces CHD risk and/or mortality by as much as 2 to 5 percent.[15, 16] Therefore, even a 3 percent reduction in LDLC levels could lower risk for heart disease by as much as 15 percent. Furthermore, comprehensive dietary approaches to lowering cholesterol that have included soyfoods have resulted in reductions in LDLC ranging from 20 to 30 percent.[17]

The amount of soy protein needed to lower cholesterol is uncertain, although most trials have used at least 25 g/day, and for this reason, 25 g/day is generally considered to be the threshold intake required for cholesterol reduction. However, there is evidence suggesting that lower amounts are also effective.[18]

The advantage of incorporating soyfoods into heart-healthy diets extends beyond the direct effect of soy protein on cholesterol levels. Soyfoods, which are typically low in saturated fat, can be used to reduce or replace other protein sources with higher saturated fat content. Approximately 84 percent of the lipids in soybeans are unsaturated. Thus, substituting soyfoods for protein-rich foods higher in saturated fat will lead to a decrease in blood cholesterol levels as a result of both the reduction of saturated fat intake and the increase in polyunsaturated fat.[19]

Furthermore, although the predominant fatty acid in soybeans is the essential fatty acid linoleic acid, an omega-6 fatty acid, about 7 to 8 percent of lipids are in the form of the other essential fatty acid, alpha-linolenic acid (ALA), an omega-3 fatty acid.[19] Although ALA does not possess the same properties as the long-chain omega-3 fatty acids found in cold-water fish, evidence suggests that ALA does have direct coronary benefits.[20, 21]

Finally, meta-analyses have found that soy protein contributes to very modest increases (1 to 3 percent) in high-density-lipoprotein cholesterol (HDLC) and modest decreases (5 to 10 percent) in triglyceride levels. Each 1 percent or 1 mg increase in HDLC lowers CHD risk by 2 to 3 percent.[22, 23] Although there is debate about the value of triglyceride level as an independent predictor of CHD risk,[24] recent findings suggest that the role of fasting triglyceride levels in the etiology of CHD has been underestimated.[25, 26]

## Beyond Effects on Lipid Levels

Evidence from the epidemiologic literature suggests that soyfoods have additional coronary benefits independent of cholesterol levels. For example, even after controlling for a wide variety of CHD risk factors, a prospective study involving nearly 65,000 postmenopausal women from Shanghai found that soy protein intake was associated with a marked reduction in the risk of non-fatal myocardial infarction (relative risk = 0.14 for the highest vs. the lowest quartile of intake; P for trend = 0.001).[27]

A cross-sectional study involving 406 Chinese adults aged 40 to 65 years (134 males, 272 females), without confirmed relevant diseases,

found that soyfood intake was inversely related to bifurcation intima-media thickness (IMT), although the association was more apparent in men than women.[28]

Also, a prospective study involving 40,462 Japanese women (40 to 59 years old, without cardiovascular disease or cancer at baseline) found that when comparing those with frequent (≥5x/week) versus infrequent (≤2x/week) soy consumption, the multivariable hazard ratios were 0.64, 0.55, and 0.31 for risk of the incidence of cerebral infraction, myocardial infarction, and CHD mortality, respectively.[29]

It is highly unlikely that the cholesterol-lowering effects of soyfoods were primarily responsible for the effects observed in these three epidemiologic studies. Soy protein consumption in the upper intake categories was between 8 and 16 g/day, which is far less than the amounts used in the clinical trials demonstrating hypocholesterolemic effects of soy protein. Furthermore, the degree of protection was far greater than could be expected from a modest reduction in cholesterol.

Supporting these epidemiologic studies are various clinical studies that show soyfoods, soy protein, or soybean isoflavones favorably affect a number of biological measures that impact heart disease risk. Soybeans are essentially the only nutritionally-relevant source of isoflavones,[30] compounds which exert estrogen-like effects under certain experimental conditions.[31]

There is evidence that intervention with various soy products enhances endothelial function and systematic arterial compliance, inhibits LDLC-oxidation, increases LDL particle size and lowers blood pressure.[32] Although intriguing, the clinical trials have produced inconsistent findings and therefore no firm conclusions can be made at this time.

Recent data suggest that, at least in regard to the effects of isoflavones on inflammation, anti-inflammatory effects may only be observed in subjects at risk of CHD who have elevated levels of inflammatory markers.[33] The clinical studies in which the effects of different soy products on biological measures of CHD risk have been examined have involved subjects at both normal and elevated risk. Thus, the differences in baseline subject characteristics may account for some of the inconsistent clinical results overall.

*Heart disease is the leading cause of death for both men and women in the United States.*

## Practical Implications

Soy can make important contributions to heart-healthy diets in a number of ways, some of which may be unique to soy-based foods and beverages. In summary, these benefits include the following:

- *Soyfoods provide high-quality protein and most are relatively low in saturated fat.*
- *Soy protein directly lowers blood cholesterol levels. Although the effect is modest, it is important; further, soy protein can help make large reductions in cholesterol through dietary approaches more easily achievable.*
- *Soy protein produces modest elevations in HDL-cholesterol and modest decreases in triglycerides.*
- *Soyfoods contain ALA, an omega-3 fatty acid.*
- *Encouraging although speculative data suggest that soyfoods, soy protein and/or soy isoflavones may favorably affect a number of biological measures that impact heart disease risk, including endothelial function, systemic arterial compliance, LDL-cholesterol oxidation, LDL-cholesterol particle size and blood pressure.*

## Heart Healthy Sources of Soy Protein

| Soyfood | Serving size | Grams of soy protein |
|---|---|---|
| Soy bar | 1 bar | 14 |
| Soy burger | 1 patty | 13-14 |
| Soy pasta | ½ cup (cooked) | 13 |
| Soy breakfast patty | 2 patties | 11 |
| Soy nuts, roasted, unsalted | ¼ cup | 11 |
| Edamame | ½ cup | 11 |
| Tofu | ½ cup | 10 |
| Soy nut butter | 2 Tbsp | 7 |
| Soy chips | 1 bag | 7 |
| Soy cereal | 1 ¼ cup | 7 |
| Fortified soymilk | 1 cup | 6-7 |
| Soy yogurt, vanilla | 1 cup | 6 |
| Soy pudding | ½ cup | 6 |

## References


1. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2008;117:e25-146.
2. American Academy of Pediatrics. The prophylactic requirement and the toxicity of vitamin D. *Pediatrics* 1963;31:512-25.
3. Greenland P, Knoll MD, Stamler J, Neaton JD, Dyer AR, Garside DB, Wilson PW. Major risk factors as antecedents of fatal and nonfatal coronary heart disease events. *JAMA* 2003;290:891-7.
4. Meeker DR, Kesten D. Effect of high protein diets on experimental atherosclerosis of rabbits. *Arch Pathol* 1941;31:147-62.
5. Meeker DR, Kesten HD. Experimental atherosclerosis and high protein diets. *Proc Soc Exp Biol Med* 1940;45:543-5.
6. Hodges RE, Krehl WA, Stone DB, Lopez A. Dietary carbohydrates and low cholesterol diets: effects on serum lipids on man. *Am J Clin Nutr* 1967;20:198-208.
7. Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 1995;333:276-82.
8. Cho SJ, Juillerat MA, Lee CH. Cholesterol lowering mechanism of soybean protein hydrolysate. *J Agric Food Chem* 2007;55:10599-604.
9. Manzoni C, Duranti M, Eberini I, Scharnag H, Marz W, Castiglioni S, Lovati MR. Subcellular Localization of Soybean 7S Globulin in HepG2 Cells and LDL Receptor Up-Regulation by Its alpha' Constituent Subunit. *J Nutr* 2003;133:2149-55.
10. Zhuo XG, Melby MK, Watanabe S. Soy Isoflavone Intake Lowers Serum LDL Cholesterol: A Meta-Analysis of 8 Randomized Controlled Trials in Humans. *J Nutr* 2004;134:2395-400.
11. Sacks FM, Lichtenstein A, Van Horn L, Harris W, Kris-Etherton P, Winston M. Soy protein, isoflavones, and cardiovascular health: an American Heart Association Science Advisory for professionals from the Nutrition Committee. *Circulation* 2006;113:1034-44.
12. Balk E, Chung M, Chew P, Ip S, Raman G, Kuplenick B, Tatsioni A, Sun Y, Wolk B, DeVine D, Lua J. Effects of soy on health outcomes. Evidence report/technology assessment No. 126 (prepared by Tufts-New England Medical Center Evidence-based Practice Center under Contract No. 290-02-0022.) *AHRQ Publication No. 05-E024-2.* Rockville, MD Agency for Healthcare Research and Quality; July 2005.
13. Zhan S, Ho SC. Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile. *Am J Clin Nutr* 2005;81:397-408.
14. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. *Am J Clin Nutr* 1999;69:30-42.
15. Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? *BMJ* 1994;308:367-72.
16. Law MR, Wald NJ, Wu T, Hackshaw A, Bailey A. Systematic underestimation of association between serum cholesterol concentration and ischaemic heart disease in observational studies: data from the BUPA study. *BMJ* 1994;308:363-6.
17. Jenkins DJ, Kendall CW, Faulkner D, Vidgen E, Trautwein EA, Parker TL, Marchie A, Koumbridis G, Lapsley KG, Josse RG, Leiter LA, Connelly PW. A dietary portfolio approach to cholesterol reduction: combined effects of plant sterols, vegetable proteins, and viscous fibers in hypercholesterolemia. *Metabolism* 2002;51:1596-604.
18. Messina M. Potential public health implications of the hypocholesterolemic effects of soy protein. *Nutr* 2003;19:280-1.
19. Wu Z, Rodgers RP, Marshall AG. Characterization of vegetable oils: detailed compositional fingerprints derived from electrospray ionization fourier transform ion cyclotron resonance mass spectrometry. *J Agric Food Chem* 2004;52:5322-8.
20. Brouwer IA, Katan MB, Zock PL. Dietary alpha-linolenic acid is associated with reduced risk of fatal coronary heart disease, but increased prostate cancer risk: a meta-analysis. *J Nutr* 2004;134:919-22.
21. Holguin F, Tellez-Rojo MM, Lazo M, Mannino D, Schwartz J, Hernandez M, Romieu I. Cardiac autonomic changes associated with fish oil vs soy oil supplementation in the elderly. *Chest* 2005;127:1102-7.
22. Boden WE. High-density lipoprotein cholesterol as an independent risk factor in cardiovascular disease: assessing the data from Framingham to the Veterans Affairs High--Density Lipoprotein Intervention Trial. *Am J Cardiol* 2000;86:19L-22L.
23. Gotto AM, Jr. High-density lipoprotein cholesterol and triglycerides as therapeutic targets for preventing and treating coronary artery disease. *Am Heart J* 2002;144:S33-42.
24. Cullen P. Evidence that triglycerides are an independent coronary heart disease risk factor. *Am J Cardiol* 2000;86:943-9.
25. Bansal S, Buring JE, Rifai N, Mora S, Sacks FM, Ridker PM. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. *JAMA* 2007;298:309-16.
26. Nordestgaard BG, Benn M, Schnohr P, Tybjaerg-Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. *JAMA* 2007;298:299-308.
27. Zhang X, Shu XO, Gao YT, Yang G, Li Q, Li H, Jin F, Zheng W. Soy food consumption is associated with lower risk of coronary heart disease in Chinese women. *J Nutr* 2003;133:2874-8.
28. Zhang B, Chen YM, Huang LL, Zhou XX, Chen CG, Ye YB, Su YX. Greater habitual soyfood consumption is associated with decreased carotid intima-media thickness and better plasma lipids in Chinese middle-aged adults. *Atherosclerosis* 2007.
29. Kokubo Y, Iso H, Ishihara J, Okada K, Inoue M, Tsugane S. Association of dietary intake of soy, beans, and isoflavones with risk of cerebral and myocardial infarctions in Japanese populations: the Japan Public Health Center-based (JPHC) study cohort I. *Circulation* 2007;116:2553-62.
30. Franke AA, Custer LJ, Wang W, Shi CY. HPLC analysis of isoflavonoids and other phenolic agents from foods and from human fluids. *Proc Soc Exp Biol Med* 1998;217:263-73.
31. Kuiper GG, Lemmen JG, Carlsson B, Corton JC, Safe SH, van der Saag PT, van der Burg B, Gustafsson JA. Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta. *Endocrinology* 1998;139:4252-63.
32. Messina M, Lane B. Soy protein, soybean isoflavones, and coronary heart disease risk: Where do we stand? *Future Lipidology* 2007;2:55-74.
33. Fuchs D, Vafeiadou K, Hall WL, Daniel H, Williams CM, Schroot JH, Wenzel U. Proteomic biomarkers of peripheral blood mononuclear cells obtained from postmenopausal women undergoing an intervention with soy isoflavones. *Am J Clin Nutr* 2007;86:1369-75.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