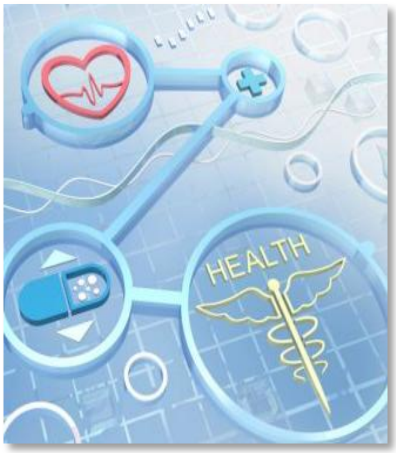
LDL-CHOLESTEROL REDUCTION AND CHD-COST SAVINGS THROUGH PHYTOSTEROL AND PSYLLIUM DIETARY FIBER USAGE



Reducing an individual's LDL cholesterol level will help to reduce his or her odds of experiencing a costly CHD event.

Prevalence and Social Consequences

Hypercholesterolemia is defined as the occurrence of higher concentrations of low-density lipoprotein (LDL) cholesterol and lower concentrations of functional HDL cholesterol, which is correlated to a higher risk of coronary heart disease because of the promotion of plaque development in arteries. Basically, when too much LDL cholesterol accumulates in arteries, it can cause blockage and increase the risk of a heart attack or stroke (American Heart Association, 2012). According to the CDC, more than 13% of all U.S. adults have high cholesterol (Centers for Disease Control and Prevention, 2012). Over the last several decades, progress has been made in dyslipidemia treatment in both increased awareness and treatment development. Current treatment guidelines dictate that LDL cholesterol should be the primary target of therapy.

It is expected that any intervention, including dietary supplementation, that is shown to reduce a person's LDL cholesterol level will also help to reduce the odds of experiencing a costly CHD event. According to the National Institutes of Health, it is estimated that a 1% reduction in LDL-cholesterol level, on average, reduces risk for hard CHD events (myocardial infarction and CHD death) by approximately 1% (Grundy, et al., 2004). Furthermore, according to research conducted by the Cholesterol Treatment Trialists' (CTT) Collaboration in 2010, the risk reduction of a major vascular event (coronary death, MI, coronary revascularization, or stroke) was 15% to 22% per year, given an LDL reduction of 0.51 mmol/L to 1.07 mmol/L (Baigent, et al., 2010). This corresponds to a mean risk reduction of 28% to 21% per 1.0 mmol/L reduction in LDL, or a relative risk reduction of 0.74% to 1.56% given a 1 mg/dL reduction in LDL-cholesterol levels. Thus, Frost & Sullivan deduces that a 1.2 mg/dL reduction in serum LDL-cholesterol reduces the risk of CHD by 1% (Baigent, et al., 2010).

In this chapter, a review of the scientific literature related to phytosterol and psyllium dietary fiber intake and its possible effect on reducing LDL cholesterol levels is provided. This CEBM approach-based literature review is used to determine the expected effect on reducing the chance of experiencing a costly CHD event, and the possible net cost saving is calculated.

The consumption of phytosterols, which are structurally related to cholesterol found in animals, has been shown to help hinder cholesterol absorption in the digestive tract.

Phytosterols

Literature Review

Plants contain compounds called phytosterols that are structurally related to cholesterol found in animals (Cleveland Clinic, 2011). Phytosterols are present in high concentrations in vegetable oils and nuts, although other plant sources contribute to their total dietary intake. There are many distinct phytosterols, of which beta-sitosterol and campesterol are among the most abundant. Normal dietary intake of phytosterols ranges from 0.15 to 0.45 g per day (Ostlund, 2002). Phytosterol consumption has been known to lower cholesterol levels, and evidence points to a mechanism in which phytosterols hinder cholesterol absorption in the digestive tract. Because of the connection to reducing cholesterol levels, the FDA allows health claims for consumption of phytosterols as part of a diet that may reduce the risk of heart disease. The National Cholesterol Education Programs (NCEP) recommends that the daily intake for phytosterols—at levels that confer a CHD event avoidance benefit through cholesterol reduction—is 2 g per day (Cleveland Clinic, 2011).

To quantify the possible effect of phytosterol consumption on the occurrence of a CHD event, a rigorous search was conducted that focused on identifying published studies quantifying the effect of phytosterol supplementation on blood levels of LDL cholesterol. The goal was to collect a set of studies that were representative of the state of scientific literature known today regarding phytosterol's efficacy. First, the team searched for studies that tested for a direct causal relationship between intake of the dietary supplement and the relative risk of a disease event was conducted, but none were identified. Thus, the research team reviewed studies that tested for a causal relationship between supplement intake and the level of a biomarker, which is correlated to the relative risk of a disease event. The research team sought to include studies that were similar in terms of study and methodology protocol to control observable variance. Studies were not selected on the basis of the magnitude or direction or statistical significance of the reported findings.

In all, 42 studies matched keyword combinations such as "phytosterol"; "coronary heart disease" or "cardiovascular disease"; and "risk reduction." The search was conducted between February 1 and March 31, 2013. Of the reported study methods, randomized controlled trials (including sequential and crossover studies) were preferred because they are designed to directly test for a cause-and-effect relationship between supplementation and outcome. Nine RCT studies were identified as being representative of the literature. The included studies indirectly tested for the relationship between dietary supplement intake and the risk of a CHD-attributed disease event through the LDL-cholesterol biomarker.

All nine studies included subjects who had hypercholesterolemia. The RCTs compared a treatment group that received daily phytosterol supplement with a placebo group. In the sequential studies, all subjects received daily phytosterol supplement for a period either before or after a period taking only placebo. In the crossover studies, the subjects took either phytosterols or placebo for a period, followed by a washout period; then, they switched to the opposite product. In all studies, phytosterol supplementation or placebo was given for 2 to 6 weeks, depending on the study. Four of the studies are referenced and discussed in the text below, and references are given for the other five in the footnotes to Figure 4.1.

Figure 4.1—Phytosterols Literature Review: Description of the Qualified Studies

Author	Year	Event definition		Study description and primary event outcome
		Sterol ester	Free sterol equivalent	
Acuff	2007	1.3 g	0.8 g	Study Type - RCT; Population - Hyper-cholesterol-emic; Outcome - Plasma LDL
Maki et al.,	2012		1.8 g	Study Type - RCT; Population - Hyper-cholesterol-emic; Outcome - Plasma LDL
McPherson[16]	2005		1.26 g	Study Type - RCT; Population - ; Outcome - LDL-cholesterol
Lau	2005		1.8 g	Study Type - RCT; Population - Type 2 diabetic, and non-diabetic; Outcome - LDL-cholesterol
Carr	2009	3.0 g		Study Type - RCT; Population - Normal adults; Outcome - LDL-cholesterol
De Graaf[17]	2002		1.8 g	Study Type - RCT; Population - Hyper-cholesterol-emic; Outcome - Plasma total cholesterol
Hallikainen[18]	2002		2.0 g	Study Type - Treatment only; Population - Mildly hyper-cholesterol-emic; Outcome - Serum LDL cholesterol
Mussner[19]	2002		1.82 g	Study Type - RCT; Population - Mildly hyper-cholesterol-emic; Outcome - Total cholesterol
Nestel[20]	2001		2.4 g	Study Type - RCT; Population - Hyper-cholesterol-emic; Outcome - LDL-cholesterol

Note: All figures are rounded. Source: Frost & Sullivan

16 McPherson, Ostlund, Goldberg, Bateman, Schimmoeller, & CA, 2005

17 De Graaf, et al., 2002

18 Hallikainen, Sarkkinen, Wester, & Uusitupa, 2002

19 Mussner, Parhofer, Von Bergmann, Schwandt, Broedl, & Otto, 2002

20 Nestel, Cehun, Pomeroy, Abbey, & Weldon, 2001

Among the nine studies analyzed was that of Maki et al., (2012) (Maki et al., 2012). This was a randomized, crossover study that enrolled 32 U.S. subjects who were hypercholesterolemic. The subjects first received a placebo for five weeks, followed by either placebo or phytosterol for six weeks, and then crossed over to the opposite product for six weeks. Phytosterol was given as 1.8 g per day in tablet form. Plasma lipid profiles were measured at the end of each treatment period. The analysis showed that compared with the placebo, the average LDL-cholesterol concentration after six weeks of phytosterol supplementation decreased by a statistically significant 4.9%, equivalent to an average reduction of 7.6 mg/dL (0.19 mmol/L).

Another study analyzed was that of Carr et al., (2009) which was a randomized, parallel, placebo-controlled study that enrolled 32 U.S. subjects, 24 of whom were hypercholesterolemic, while the remainder were normocholesterolemic (Carr, Krogstrand, Schlegel, & Fernandez, 2009). Each day for four weeks, the subjects took either 3 g of phytosterol (in ester form) or a placebo. Plasma lipid profiles were measured at the end of the treatment period. Analysis showed that, compared with the placebo group, the average LDL-cholesterol concentration after four weeks of phytosterol supplementation decreased by a statistically significant 11%, equivalent to a reduction of 16 mg/dL (0.41 mmol/L).

Acuff et al., (2007) conducted a placebo-controlled sequential study on 16 U.S. subjects who were hypercholesterolemic, with a four-week placebo phase followed by a two-week washout period, and then a four-week treatment phase (Acuff, Cai, Dong, & Bell, 2007). Phytosterol (in ester form) was given as a capsule at a dose of 1.3 g per day, equivalent to 0.8 g per day of free phytosterol. At the end of the treatment period, LDL cholesterol in the phytosterol group decreased on average by a statistically significant 4% (6.1 mg/dL, 0.16 mmol/L) compared with the placebo group.

Lau et al., (2005) studied phytosterol supplementation in a randomized, crossover, placebo-controlled trial in Canada that consisted of two 21-day treatment (placebo or supplement) periods that were separated by a 28-day washout period (Lau, Journoud, & Jones, 2005). Twenty hypercholesterolemic subjects took part, 15 of whom were diabetic. Phytosterols were given as 1.8 g per day mixed with margarine and served on toast. An analysis of lipid profiles at the end of the treatment periods showed that for the non-diabetic subjects, LDL cholesterol was reduced by an average of 15.1% (24 mg/dL, 0.62 mmol/L) after phytosterol compared with placebo consumption. For diabetic subjects, the reduction in LDL was 26.8%.

Figure 4.2—Phytosterols Literature Review: Description of the Qualified Studies—Summary of Findings

Author	Total sample (N)	Change in LDL cholesterol mg/dL (absolute outcome reduction)	Change in LDL cholesterol mmol/L (absolute outcome reduction)	Study weights (based on sample size variance)
Acuff	16	6.1	0.1576	6.2%
Maki	32	7.6	0.1970	12.5%
McPherson	52	10.4	0.2687	20.2%
Lau	29	24.4	0.6300	5.4%
Carr	32	16.3	0.4200	6.2%
De Graaf	70	19.0	0.4900	12.1%
Hallikainen	11	18.2	0.4700	4.3%
Mussner	63	10.0	0.2584	24.5%
Nestel	22	25.2	0.6500	8.6%
Average	29	13.4*	0.3935*	

* Weighted Average

Note: All figures are rounded. Source: Frost & Sullivan

An average of 283,389 events per year could be avoided from 2013 to 2020, which is nearly 2.3 million accumulated avoided events over the same period if all U.S. adults over the age of 55 diagnosed with CHD were to use phytosterol dietary supplements at protective levels.

Empirical Results

The research team had to deduce the level of phytosterol's efficacy through an assessment of its effect on a relevant biomarker known to have a casual relationship with a given subject's relative risk of experiencing a CHD event. Specifically, reported study outcomes included plasma or serum concentrations of LDL cholesterol and other lipids before, during, and at the end of the treatment or placebo periods. The research team linked these outcomes to health care utilization based on evidence that the observed reduction in LDL cholesterol would decrease the risk of CHD. Thus, the research team derived the expected CHD risk reduction metric given the reduction in LDL cholesterol levels based on the work of the Cholesterol Treatment Trialists' (CTT) Collaboration in 2010, where a 1.2 mg/dL reduction in serum LDL-cholesterol reduces the risk of CHD by 1% (Baigent, et al., 2010).

Thus, the expected relative risk reduction of a CHD-related medical event, given the use of phytosterol dietary supplements at preventive daily intake levels among the target population, was 11.2% based on the review of the scientific literature. This expected risk reduction metric assumes a 1% reduction in relative risk for every 1.2 mg/dL reduction in LDL cholesterol levels. To calculate the NNT, an event rate of 16% was used because this is the expected level of risk of a CHD event among the adult population over the age of 55 (National Health and Nutrition Examination Survey, 2013). Using the CEBM approach (Center for Evidence Based Medicine, 2012) to calculate NNT, this implies that the total number of people who must be treated with phytosterols to avoid one CHD event is 65. In other words, if 65 people adopted a phytosterols regimen at protective levels as a means to reduce their LDL cholesterol levels, one avoided CHD event could be realized. Given this calculated NNT, an annual average of 283,389 avoided events from 2013 to 2020 and 2,267,111 cumulative avoided events over that period could be expected.

An average of $4.23 billion per year and a cumulative savings of $34.00 billion from 2013 to 2020 in avoidable hospital utilization costs is potentially realizable if all U.S. adults over the age of 55 diagnosed with CHD were to use phytosterol dietary supplements at protective levels.

Figure 4.3—Phytosterols Literature Review: Summary Results—CEBM Approach

Metric	Measure
Weighted relative risk reduction (weighted for sample size variance) (RRR)	11.2%
CHD event rate (ER)	16%
Number of people needed to treat to avoid one CHD event (NNT), people	65
Average number of events avoided annually if everybody in the target population* used phytosterols at protective levels, 2013–2020, people	283,389
Cumulative number of events avoided if everybody in the target population* used phytosterols at protective levels, 2013–2020, people	2,267,111

*Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

Using the same annual average cost per person for a CHD-related event ($16,690), the total potentially avoidable hospital utilization cost for all U.S. adults over the age of 55 diagnosed with CHD given the use of the phytosterols at preventive daily intake levels would average $4.2 billion per year—a cumulative total savings of $34.0 billion from 2013 to 2020 to health care cost payers.

A review of retail products on the market showed that the consumer cost of a daily dose (2 grams) of phytosterols is roughly $0.15. The annual expected cost of phytosterols for the target population would average slightly more than $54.48 per person, for a total of $872.7 million per year—a cumulative cost of nearly $7.0 billion in supplement expenditures from 2013 to 2020.

Based on the finding that the total cost savings derived from avoided CHD events for the target population given the use of phytosterols was, on average, $4.2 billion (nearly $34.0 billion cumulatively during the forecast period), the net cost savings derived from the daily use of phytosterols, after accounting for the cost of supplementation, would average $3.3 billion per year—nearly $26.6 billion cumulatively. In terms of the calculated cost-benefit ratio, $4.87 in avoided health care expenditures could be realized per $1 spent on phytosterol supplementation. See Figures 8.9 to 8.12 in the appendix for a detailed reporting of the empirical results.

Figure 4.4—Phytosterols Cost Analysis: Summary Results—Cost of Dietary Supplementation of the Target Population, 2013–2020

Metric	Measure
Median cost of phytosterol supplementation at protective levels, 2013	$0.15
Expected annual median cost of phytosterol supplementation at protective levels, 2013	$54.48
Average annual cost of phytosterol dietary supplementation of the target population*, 2013–2020	$872.7 M
Cumulative cost of phytosterol dietary supplementation of the target population* , 2013–2020	$6.98 B

*Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

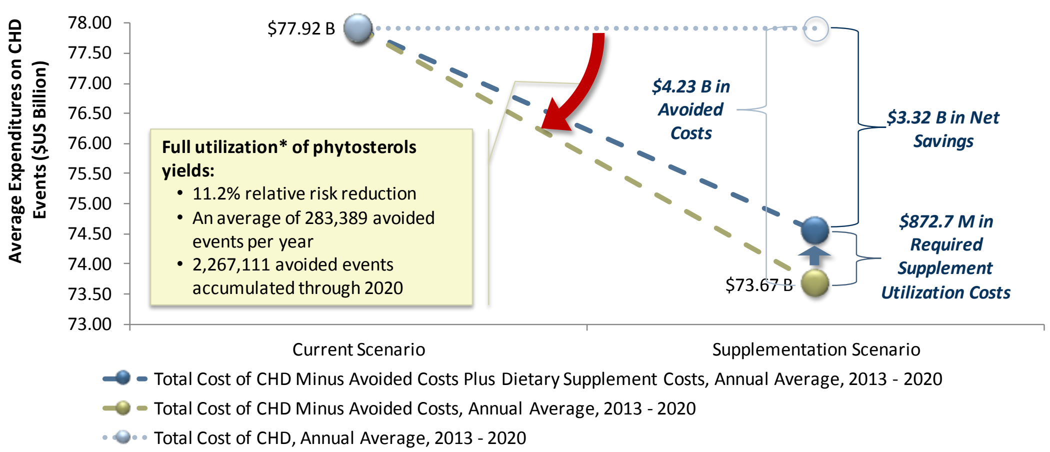
Figure 4.5—Phytosterols Cost Analysis: Summary Results—Avoided Hospital Utilization Expenditures* due to Dietary Supplement Intervention, 2013–2020

Metric	Measure
Average annual avoided hospital utilization expenditures related to CHD if incidence is reduced through phytosterol supplements, 2013–2020	$4.23 B
Cumulative avoided hospital utilization expenditures related to CHD if incidence is reduced through phytosterol supplements, 2013–2020	$34.00 B
Average annual hospital utilization expenditures for CHD-related events if incidence is reduced through phytosterol supplements, 2013–2020	$73.67 B
Cumulative expenditures on CHD-related events if incidence is reduced though phytosterol supplements, 2013–2020	$589.33 B

*Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

$26.56 billion in cumulative net CHD-attributed cost savings from 2013 to 2020 is potentially realizable if the entire target population were to use phytosterol dietary supplements at protective intake levels.

Figure 4.6—Phytosterols Cost Analysis: Net Health Care Cost Savings* Summary Results, 2013–2020



* Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

Figure 4.7—Phytosterols Cost Analysis: Summary Results—Net Cost Savings* due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2013–2020

Metric	Measure
Average net potential direct savings per year from avoided CHD hospital utilization events due to phytosterol dietary supplement intervention, 2013–2020	$3.32 B
Cumulative net potential direct savings from avoided CHD hospital utilization events due to phytosterol dietary supplement intervention, 2013–2020	$26.56 B
Net benefit cost ratio, $ per one dollar spent on dietary supplement	$4.87

*Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

It is expected that less than 0.2% of adults over the age of 55 are already regular users of phytosterol dietary supplements, suggesting that nearly all of the potential net cost health care savings have yet to be realized.

This cost-benefit analysis makes the assumption that in the supplementation scenario all U.S. adults over the age of 55 with CHD use phytosterol/stanols supplements at protective levels from a base of zero usage among this population segment. In other words, the calculated net savings is the total potential net savings. However, only 0.2% of adults over the age of 55 are regular users of phytosterol dietary supplements, according to the 2012 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs. (Ipsos Public Affairs, 2012).[21] This suggests that nearly all of the expected $3.3 billion in potential net savings has yet to be realized, thus, it is expected that there are significant cost savings yet be realized through the increased usage of phytosterol dietary supplements among the high-risk target population.

Figure 4.8—Phytosterols Cost Analysis: Summary Results—Net Cost Savings* Yet to be Realized due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2013–2020

Metric	Measure
Percentage of adults over the age of 55 who are regular users of phytosterol dietary supplements, 2012	0.15%
Average number of CHD events avoided annually among the target population* yet to regularly use phytosterol, 2013–2020	282,950
Cumulative number of CHD events avoided among the target population* yet to regularly use phytosterol, 2013–2020	2,263,602
Average net direct savings per year from avoided CHD hospital utilization events due to phytosterol dietary supplement intervention yet to be realized, 2013–2020	$3.31 B
Cumulative net direct savings from avoided CHD hospital utilization events due to phytosterol dietary supplement intervention yet to be realized, 2013–2020	$26.52 B

*Among all U.S. adults over the age of 55 with CHD

Source: Note: All figures are rounded. Source: Ipsos Public Affairs and Frost & Sullivan

21 It is not known what percentage of this target population also suffers from CHD, but for the purposes of this analysis, Frost & Sullivan has made the assumption that approximately the same percentage (0.2%) of adults over the age of 55 with CHD also are regular users of phytosterol dietary supplements. Also for the purposes of this analysis, as the Ipsos survey did not ask dosage, Frost & Sullivan has made the assumption that regular users in this target population are highly likely to be consuming enough phytosterol to provide a protective effect. More research is required to test these assumptions.

Psyllium Dietary Fiber

Literature Review

Dietary fiber includes soluble and insoluble fiber from plant foods. The composition of fiber depends on its source. The type and amount of fiber consumed has many effects on the physiology of digestion. For example, the intestinal absorption of bile acids, along with the cholesterol that they carry, is slowed by the presence of soluble fiber in the intestine. Certain soluble fibers, such as beta-glucans and arabinoxylans, are more effective at lowering cholesterol than other types of fiber.

Psyllium dietary fiber has been found to help lower cholesterol by inhibiting cholesterol absorption in the intestine.

Psyllium dietary fiber, for example, is a common soluble fiber and has traditionally been used as a gentle bulk forming laxative (University of Maryland Medical Center, 2013). Sourced from the Plantago ovata herb, psyllium dietary fiber is most commonly grown in India and its husks have been found to help lower cholesterol (University of Maryland Medical Center, 2013).

The Institute of Medicine (IOM) of the National Academy of Sciences (NAS) recommends that women consume 25 g of dietary fiber per day and men consume 38 g per day based on an optimal diet formula stating that at least 14 g of fiber is needed for every 1,000 calories (Institute of Medicine, 2006). There is no established UL for total fiber. According to the IOM report, "[a]lthough occasional adverse gastrointestinal symptoms are observed when consuming some of the isolated or synthetic fibers, serious chronic adverse effects have not been observed. A UL was not set for dietary fiber or functional fiber. Because of the bulky nature of fibers, excess consumption is likely to be self-limited" (Institute of Medicine, 2006).

As in the case of the phytosterols analysis, a rigorous search was conducted that focused on identifying published studies quantifying the effect of psyllium dietary fiber supplementation on blood levels of LDL cholesterol. The objective was to identify a set of studies that represented the state of scientific literature on the subject of psyllium dietary fiber and its link to CHD risk. In this analysis, studies that were reviewed tested for a causal relationship between psyllium dietary fiber intake and the level of a biomarker that is correlated to the relative risk of a disease event because no studies that tested for the direct relationship were identified. The research team included only studies similar in methodology protocol in an attempt to control for observable variance. Studies were not selected on the basis of the magnitude, direction or statistical significance of the reported findings.

Specifically, 102 studies matched the keyword combinations of "fiber"; "coronary heart disease" or "cardiovascular disease"; and "risk reduction." The search was conducted between February 1 and March 31, 2013. The preferred studies were randomized, controlled trials. For the sake of closer comparison, the research team sought to analyze studies using the same type of fiber supplement. Four RCT studies were identified as being representative of the literature on psyllium dietary fiber. The included studies indirectly tested for the relationship between psyllium fiber intake and the risk of a CHD-attributed disease event through the LDL-cholesterol biomarker. The four RCTs tested psyllium fiber supplementation in hypercholesterolemic individuals. In all studies, the supplement was consumed for between 40 days and 26 weeks, and the blood lipids (including LDL cholesterol) were measured and compared for treatment and control subjects.

Figure 4.9—Psyllium Dietary Fiber Literature Review: Description of the Qualified Studies

Author	Year	Daily treatment dose (g)	Study description
Anderson	2000	10.2	Study Type - RCT; Population - Hyper-cholesterolemic; Fiber Supplement Type—Psyllium
Anderson	1991	10.2	Study Type - RCT; Population - Hyper-cholesterolemic; Fiber Supplement Type—Psyllium
Anderson	1999	10.2	Study Type - RCT; Population - Diabetic and Hyper-cholesterolemic; Fiber Supplement Type—Psyllium
Everson	1992	15.0	Study Type - RCT; Population - Hyper-cholesterolemic; Fiber Supplement Type—Psyllium

Note: All figures are rounded. Source: Frost & Sullivan

Anderson et al., (1991) studied 52 hypercholesterolemic U.S. subjects (Anderson, Floore, Geil, O'Neal, & Balm, 1991). All subjects first completed a cholesterol-lowering diet over a period of eight weeks. They maintained the diet while they were randomly assigned to supplement with either psyllium fiber (10.2 g/day) or placebo. After eight weeks of consuming the supplement, LDL cholesterol levels of the psyllium group had declined by 17 mg/dL (0.45 mmol/L) compared with the placebo, a statistically significant difference.

Everson et al., (1992) studied 20 U.S. men with mild hypercholesterolemia (Everson, Daggy, McKinley, & Story, 1992). In a randomized crossover design, the subjects received a 40-day course of psyllium fiber supplement (15 g/day) or placebo, followed a washout period of 11 days, and then crossed over to the other treatment. The psyllium fiber treatment resulted in a significant 10 mg/dL (0.26 mmol/L) decrease in LDL cholesterol compared with the placebo.

In a study of 29 U.S. men who had both hypercholesterolemia and diabetes, Anderson et al., (1999) randomly assigned either psyllium (10.2 g/day) or a placebo after a two-week period of dietary stabilization (Anderson, Allgood, Turner, Oeltgen, & Daggy, 1999). After eight weeks of treatment, serum lipids and other markers were measured. Relative to the placebo group, the LDL-cholesterol concentration in the psyllium group had declined by an average of 17.8 mg/dL (0.46 mmol/L). The difference did not achieve significance.

Finally, in a multicenter study in the U.S., Anderson et al., (2000) recruited 248 subjects with hypercholesterolemia (Anderson, et al., 2000). Subjects were put on a cholesterol-lowering diet for an initial eight-week period, and then randomly assigned to receive psyllium fiber or a placebo supplement. After 26 weeks, the average LDL-cholesterol concentration declined by 10.4 mg/dL (0.27 mmol/L) in the psyllium group compared with the placebo group. The difference was statistically significant.

Figure 4.10—Psyllium Dietary Fiber Literature Review: Description of the Qualified Studies—Summary of Findings

Author	Total sample (N)	Change in LDL cholesterol mg/dL (absolute outcome reduction)	Change in LDL cholesterol mmol/L (absolute outcome reduction)	Study weights based on sample size variance
Anderson	248	10.45	0.2700	76.4%
Anderson	52	17.42	0.4500	10.1%
Anderson	29	17.80	0.4600	5.8%
Everson	40**	10.00	0.2584	7.8%
Average	92	13.9	0.3596	

* Weighted Average
**Crossover study

Note: All figures are rounded. Source: Frost & Sullivan

<u>Empirical Results</u>

Because the set of qualified studies examined the link between the use of psyllium fiber and the reduction in LDL cholesterol, the research team followed the same approach as the one adopted for the phytosterol literature review and assumed that 1.2 mg/dL reduction in serum LDL cholesterol reduces the risk of CHD by 1% based on the work of the CTT Collaboration (Baigent, et al., 2010). The research team then indirectly arrived at a relative risk of CHD from dietary fiber supplementation to apply to its economic analysis.

The expected relative risk reduction of a CHD-related medical event, given the daily use of psyllium dietary fiber at preventive daily intake levels among all people over the age of 55 diagnosed with CHD, was 11.5%. As in the phytosterol analysis, an event rate of 16% was adopted because 16% of the adult population over the age of 55 is at a high risk of experiencing a CHD-related event. Using the CEBM approach to calculate NNT, this suggests that 63 people need to be treated with psyllium dietary fiber to avoid one CHD event. Given this deduced NNT, an annual average of 292,165 avoided events from 2013 to 2020—2,337,318 cumulative avoided events could be realized.

An average of 292,165 avoided events per year from 2013 to 2020 or over 2.3 million accumulated avoided events over the same period if all U.S. adults over the age of 55 diagnosed with CHD were to use psyllium dietary fiber at protective intake levels.

Figure 4.11—Psyllium Dietary Fiber Literature Review: Summary Results—CEBM Approach

Metric	Measure
Weighted relative risk reduction (weighted for inter-study variance) (RRR)	11.5%
Event rate (ER)	16%
Number of people needed to treat to avoid one CHD event (NNT), people	63
Average number of CHD events avoided annually if everybody in the target population* used phytosterols, 2013–2020, people	292,165
Cumulative number of CHD events avoided if everybody in the target population* used phytosterols, 2013–2020, people	2,337,318

*Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

In terms of avoided direct health care expenditure, a potential total cost savings among all U.S. adults over the age of 55 diagnosed with CHD given the use of the psyllium dietary fiber at preventive daily intake levels would be an average annual total savings of $4.2 billion per year and cumulative savings of $34.0 billion from 2013 to 2020, assuming an annual average cost per person experiencing a CHD-related event at $16,690.

Based on the reviewed studies, all patients underwent a preliminary dietary program to help standardize daily intakes of dietary fiber and other macro- and micronutrient intake levels, in order to help control for that possible variance. Thus, all patients in the psyllium fiber treatment groups are assumed to have been consuming comparable levels of dietary fiber prior to treatment. In addition, the U.S. Food and Drug Administration allows companies to claim on their product labels that intake of 7 g or more per day of psyllium soluble fiber may reduce the risk of CHD (U.S. Food & Drug Administration, 2012). Based on the qualified studies, the expected dose size for psyllium fiber was in the range of 10.2 to 15.0 g of psyllium fiber per day. For the purposes of this study, Frost & Sullivan assumed a conservative daily dose of psyllium fiber of 10 g was sufficient to realize its expected health-conferring benefits.

Based on the review of best-selling psyllium dietary fiber retail products in brick-and-mortar, online, and mail-order retail establishments, the cost of a daily dose of 10 g of psyllium dietary fiber is just over $0.30 per day. Based on this cost, the annual expected cost of psyllium fiber for all U.S. adults over the age of 55 would be just over $111.31 per person—more than $1.9 billion per year on average for the total sub-population, and more than $15.2 billion cumulatively from 2013 to 2020.

Figure 4.12—Psyllium Dietary Fiber Cost Analysis: Summary Results—Cost of Dietary Supplementation of the Target Population*, 2013–2020

Metric	Measure
Median cost of psyllium dietary fiber at protective levels, 2013	$0.30
Expected annual median cost of psyllium dietary fiber at protective levels, 2013	$111.31
Average annual cost of psyllium dietary fiber supplementation of the target population*, 2013–2020	$1.90 B
Cumulative cost of psyllium dietary fiber supplementation of the target population*, 2013–2020	$15.20 B

*Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

Figure 4.13—Psyllium Dietary Fiber Cost Analysis: Summary Results—Avoided Hospital Utilization Expenditures* due to Dietary Supplement Intervention, 2013–2020

Metric	Measure
Average annual avoided hospital utilization expenditures related to CHD if incidence is reduced through the use of psyllium dietary fiber, 2013–2020	$4.38 B
Cumulative avoided hospital utilization expenditures related to CHD if incidence is reduced through the use of psyllium dietary fiber, 2013–2020	$35.05 B
Average annual hospital utilization expenditures for CHD-related events among all U.S. adults over the age of 55 if incidence of events is reduced though the use of psyllium dietary fiber, 2013–2020	$73.53 B
Cumulative hospital utilization expenditures for CHD-related events among all U.S. adults over the age of 55 if incidence of events is reduced though the use of psyllium dietary fiber, 2013–2020	$588.28 B

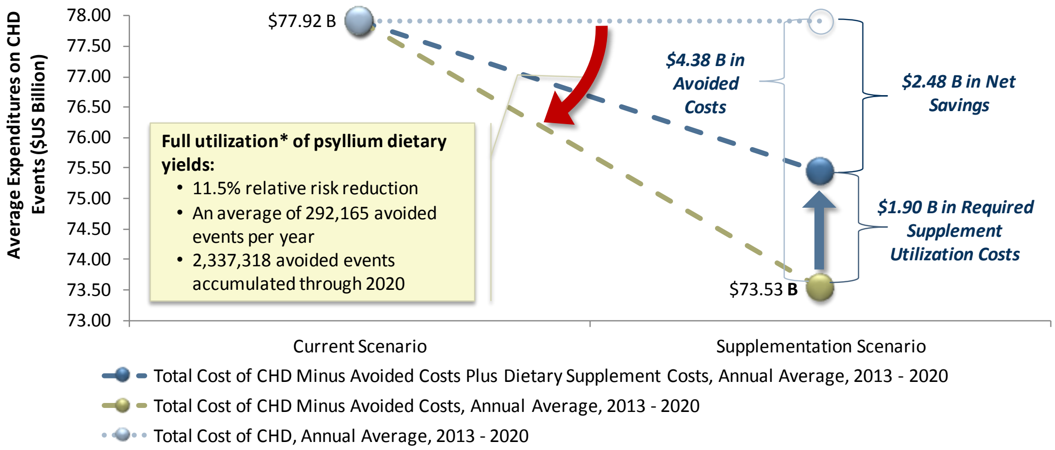
*Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

Given the total cost savings derived from avoided CHD events for the target population based on the use of psyllium dietary fibers, the net savings in direct expenditures after accounting for the cost of psyllium dietary fiber supplementation would average $2.5 billion per year, and more than $19.9 billion cumulatively from 2013 to 2020. In terms of the calculated cost benefit ratio, $2.31 in avoided health care expenditures could be realized per $1 spent on psyllium dietary fiber supplementation. See Figures 8.13 to 8.16 in the Appendix for a detailed reporting of the empirical results.

An average annual total savings of $4.38 billion per year and a cumulative savings of $35.05 billion from 2013 to 2020 is potentially realizable if all U.S. adults over the age of 55 diagnosed with CHD were to use protective levels of psyllium fiber.

Nearly $20 billion in cumulative net CHD-attributed cost savings from 2013 to 2020 is potentially realizable if the entire target population were to use psyllium dietary fiber at protective levels.

Figure 4.14—Psyllium Dietary Fiber Cost Analysis: Net Health Care Cost Savings* Summary Results, 2013–2020



* Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

Figure 4.15—Psyllium Dietary Fiber Cost Analysis: Summary Results—Net Cost Savings* due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2013–2020

Metric	Measure
Average net potential direct savings per year from avoided CHD hospital utilization events if incidence is reduced through the use of psyllium dietary fiber, 2013–2020	$2.48 B
Cumulative net potential direct savings from avoided CHD hospital utilization events if incidence is reduced through the use of psyllium dietary fiber, 2013–2020	$19.85 B
Net benefit cost ratio, $ per one dollar spent on dietary supplement	$2.31

* Among all U.S. adults over the age of 55 with CHD
Note: All figures are rounded. Source: Frost & Sullivan

This cost-benefit analysis assumes that in the supplementation scenario all U.S. adults over the age of 55 with CHD used psyllium dietary fiber at protective levels from a base of zero usage among this population segment. In other words, the calculated net savings is the total potential net savings. However, because a share of adults over the age of 55 regular use psyllium dietary fiber, this segment of the target population already has a reduced risk of experiencing a costly CHD event and is already realizing its risk-reducing benefits.

According to the 2012 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs, 8% of adults over the age of 55 in the United States are regular users of fiber supplements (Ipsos Public Affairs, 2012).[22] This implies that the remainder—92%—has yet to realize the benefits of regular use of dietary fiber, including psyllium fiber. Because avoided expenditures and net cost savings are a direct function of the total number of people in the target population using psyllium dietary fiber, the calculation of avoided health care expenditures and net cost savings yet to be realized is simply a proportional adjustment of the total potential avoided expenditures and net cost savings.

It is expected that there are significant potential cost savings yet to be realized valued at nearly $18 billion in cumulative net CHD-attributed cost savings if all current non-regular users in the high-risk target population were to fully utilize psyllium dietary fiber.

Knowing this, it is expected that $199.6 million of the $2.48 billion in net potential direct savings per year from avoided CHD hospital utilization events because of psyllium dietary fiber intervention is already realized in the total expected CHD costs. This equates to an average of 268,647 avoidable events per year yet to be realized because of underutilization of psyllium dietary fiber. This corresponds to an average of $2.28 million per year in net savings yet to be realized because of underutilization of psyllium dietary fiber—nearly $18.25 billion in cumulative net savings from 2013 to 2020. Thus, it is expected that there are significant cost savings yet be realized through the increased usage of psyllium dietary fiber among the high-risk target population.

Figure 4.16—Psyllium Dietary Fiber Cost Analysis: Summary Results—Net Cost Savings* Yet to be Realized due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2013–2020

Metric	Measure
Percentage of target population* who are regular users of psyllium dietary fiber, 2012	8.0%
Average number of CHD hospital utilization events avoided annually among the target population* yet to regularly use psyllium dietary fiber, 2013–2020	268,647
Cumulative number of CHD hospital utilization events avoided among the target population* yet to regularly use psyllium dietary fiber, 2013–2020	2,149,175
Average net direct savings per year from avoided CHD hospital utilization events due to psyllium dietary fiber intervention yet to be realized, 2013–2020	$2.28 B
Cumulative net direct savings from avoided CHD hospital utilization events due to psyllium dietary fiber intervention yet to be realized, 2013–2020	$18.25 B

* Among all U.S. adults over the age of 55 with CHD
Source: Note: All figures are rounded. Source: Ipsos Public Affairs and Frost & Sullivan

22 It is not known what percentage of this target population also suffers from CHD, but for the purposes of this analysis, Frost & Sullivan has made the assumption that approximately the same percentage (8%) of adults over the age of 55 with CHD also are regular users of fiber dietary supplements. The Ipsos survey did not ask specifically about the type of fiber supplements being taken. Even in the unlikely event that all the fiber supplements were psyllium products, that would leave 92% of the population yet to achieve the benefit of psyllium fiber supplementation. Also for the purposes of this analysis, as the Ipsos survey did not ask dosage, Frost & Sullivan has made the assumption that regular users in this target population are highly likely to be consuming enough fiber to provide a protective effect. More research is required to test these assumptions.

There are significant health care cost savings to be realized if there was a concerted effort to identify high CHD risk populations and motivate them to adopt a dietary supplement regime as a means to help control escalating costs associated with preventable disease events.

Conclusion

Phytosterols and psyllium dietary fiber could confer significant potential cost savings for all U.S. adults over the age of 55 with diagnosed CHD. A significant amount of scientific research has already been conducted involving phytosterols and psyllium dietary fiber, and there is an indication that these supplements produce a likely positive impact on disease risk reduction. However, more scientific research should be undertaken to test this hypothesis in order to avoid the use of indirect means to calculate the expected number needed to be treated to avoid one CHD event. The potential cost saving derived from the use of phytosterol and psyllium dietary fiber supplements at preventive daily intake levels is expected to be significant because of the direct link to lowering LDL cholesterol levels. It is because of this direct link that the postulation was made that there would be consequential impact on reducing the risk of experiencing a CHD event.

Overall and independent of the exact figures calculated in this analysis, what has been demonstrated in this analysis is that there are likely significant health care cost savings to be realized through a concerted effort to identify high CHD risk populations and motivate them to use phytosterol and psyllium dietary fiber supplements as a means to help control escalating social costs associated with rising disease-incidence rates for preventable diseases. There are many ways to identify and motivate high CHD risk people to use effective dietary supplements, including the use of new technologies that identify high-risk populations before they experience costly acute treatment events; the use of incentives for consumers, health care professionals, and other key stakeholders to address the antecedents of disease as opposed to the utilization of acute treatment services; and increased general education. Only then can a smarter approach that utilizes certain dietary supplements that have been shown scientifically to help reduce the risk of experiencing a costly disease event among high disease-risk population groups be effective at controlling potential health care costs.

THE USE OF CHROMIUM PICOLINATE AND ITS EFFECT ON THE RISK OF DIABETES-ATTRIBUTED CORONARY HEART DISEASE

The total health care expenditure on managing and treating diabetes-attributed CHD among diabetics over the age of 55 with CHD will be an average of $33 billion per year from 2013 to 2020.

Prevalence and Social Consequences

Type 2 diabetes mellitus (type 2 diabetes) is the most common form of diabetes in the United States; 90 to 95% of diabetes patients suffer from type 2 diabetes. The total health care cost of diabetes in 2012 in the United States was about $245 billion, of which $176 billion was attributed to direct medical costs and $69 billion in reduced productivity, according to the American Diabetes Association (American Diabetes Association, 2011). Regarding direct medical costs, nearly 60% of total expenditures are related to hospitalizations. Type 2 diabetes is a chronic disease marked by high levels of glucose in the blood. It is most common in patients that are over the age of 55, have a high-density lipoprotein (HDL) cholesterol of less than 35 mg/dL or triglyceride level of greater than 250 mg/dL, and/or have high blood pressure. The primary means to inhibit complications related to type 2 diabetes are diet and exercise. However, if diet and exercise do not help a person maintain normal glucose levels, physicians may have to prescribe medication.

In 2012, it was estimated that more than 17 million U.S. adults over the age of 55 suffered from diabetes (American Diabetes Association, 2011). Men are slightly more likely to have diabetes than women, and non-Hispanic blacks have higher prevalence rates compared with non-Hispanic whites, Asian Americans, and Hispanics. Within this group, nearly 7 million adults over the age of 55 have also been diagnosed with CHD, and nearly 2 million of these people suffer from a CHD event annually[23]. This suggests that total expenditures on direct medical costs associated with diabetes-attributed CHD events were $26.4 billion in 2012.

23 Based on the Frost & Sullivan analysis of the National Health and Nutrition Examination Survey (National Health and Nutrition Examination Survey, 2010)