

Improving Public Health, Reducing Health Care Costs: An Evidence-Based Study of Five Dietary Supplements

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Summary Report

Surveys of dietary intake and physical and laboratory data reveal that the typical American diet does not always provide a sufficient level of nutrients to support optimal health. Many clinicians also acknowledge that some Americans may need a vitamin and/or mineral or other supplement to meet specific nutrient needs.

Recent studies have also found health benefits associated with dietary supplements. For example, a Johns Hopkins study noted trauma patients who received vitamins E and C spent less time in Intensive Care Units and were “less likely to experience organ failure.” Progression of Alzheimer’s disease may be slowed by high doses of vitamins according to a Georgetown University pilot study with additional therapeutic trials underway. In a longitudinal study, high doses of vitamin supplements were beneficial to individuals with Age-related Macular Degeneration (AMD). A recent, limited Carolinas Medical Center study noted that adults with type-2 diabetes who take supplements reported fewer infections than those who did not take supplements.

The Lewin Group, Inc. was commissioned by the Dietary Supplement Education Alliance (DSEA) to conduct an evidence-based study of five dietary supplements that could potentially improve users’ health. The purpose of this study is threefold: (1) to critically review the research evidence for each supplement, (2) to develop estimates of the potential health care expenditure savings that could result from daily use of two of the supplements, and (3) for supplements where there is emerging evidence, to suggest areas of future research that would fill existing knowledge gaps. Supplements covered in this study include (1) **calcium (with Vitamin D)**, (2) **folic acid**, (3) **omega-3 fatty acids**, (4) **glucosamine**, and (5) **saw palmetto**.

Lewin was asked to develop estimates of potential cost savings that could result from daily use of only those supplements for which the highest standard of evidence exists at this time, and for which the Food and Drug Administration (FDA) has approved health claims. Cost estimates were developed for calcium (with Vitamin D) and folic acid, for which there is significant scientific agreement as to the improvement in health status and subsequent health expenditure reduction. Conservative estimates of savings were developed for specific relevant outcomes: for calcium, estimates of savings for avoided hip fractures among over age-65 were developed. For folic acid, estimates of savings from avoided incidences of babies being born with neural tube defects (NTD) were developed, keeping in mind that not all NTDs are nutritionally related.

Key Study Findings

- **Calcium:** Using a Congressional Budget Office (CBO-type) cost accounting methodology, the estimate of the five-year (2005-2009) net savings in hospital, nursing facility, and physician expenditures resulting from a reduction in the occurrence of hip fractures among the over age-65 population through daily intake of 1200 mgs. of calcium with Vitamin D is \$13.9 billion. Approximately 734,000 hip fractures could be avoided across the five years. Over one third of adults age-65 and over experience falls each year. Among injuries from falls, hip fractures cause the greatest number of deaths and lead to

the most severe health problems. Hip fractures also tend to be the most costly because in addition to requiring an in-hospital surgical procedure to repair the hip, nearly 50% of the operations result in a prolonged stay in a nursing home that can range from a few weeks to more than a hundred days or even longer. Up to 25% of community dwelling older adults who sustain hip fractures remain institutionalized for a whole year.

- **Folic Acid:** The total lifetime cost of a baby with Neural Tube Defect (NTD) in 2004 is roughly \$532,000, including direct medical costs, therapies and equipment, and special education. Out of about 4 million live births annually, NTDs occur in one of every 1,000 pregnancies in the U.S. Of 64 million American women who are of childbearing age, if just 10.8 million additional women began taking 400 mcg. of folic acid on a daily basis periconceptionally, approximately 600 babies would be born without NTDs, saving as much as \$326 million as a result. Over five years, taking into account the very low cost of the supplement, \$1.3 billion in lifetime costs could potentially be saved. Longstanding and extensive research with supporting conclusions led the US Public Health Service, Institute of Medicine, and Food and Drug Administration to establish recommendations and public health policies relating to folic acid intake and food fortification.
- **Omega-3 fatty acids:** Recent studies have suggested that omega-3 fatty acids have beneficial effects on cardiovascular disease (CVD). Furthermore, FDA recently announced a qualified health claim for EPA and DHA omega-3 fatty acids. CVD accounted for 38.5 percent of all deaths in the U.S. in 2001, including about 150,000 individuals who are under the age of 65. The cost of CVD in 2004 is estimated to be \$368.4 billion. The research literature also contains many promising studies of varying quality concerning the health benefits of omega-3 fatty acids for a wide number of chronic conditions (e.g., depression, renal disease, rheumatoid arthritis, and asthma) and additional research is warranted to verify these preliminary findings.

Our review found consistent evidence that omega-3 fatty acids help reduce deaths from CVD. In addition, there are studies demonstrating that omega-3 fatty acids may help lower blood pressure, may reduce the risk of re-blockage after an angioplasty, may increase exercise capacity in people with coronary arteriosclerosis, and may reduce the risk associated with irregular heartbeats. Most evidence for the health effects of omega-3 fatty acids in the general population (primary prevention studies) is from cohort studies conducted worldwide, whereas the bulk of the evidence for secondary prevention is from RCTs of limited duration. The data for secondary prevention mostly derives from one very large study, however data on women are limited in this study. The specific effects on different CVD outcomes (especially MI and stroke) are uncertain. In March 2004, the Agency for Healthcare Research and Quality (AHRQ) released a systematic review of the literature to assess the benefits of omega-3 fatty acids on CVD outcomes. AHRQ found that studies of omega-3 fatty acids were heterogeneous in that they examined different forms of omega-3 fatty acids, including dietary and supplemental fish oil, and varying combinations of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and alpha-linolenic acid (LNA) from plant sources. Also, studies tended to report on the different outcomes inconsistently. AHRQ concluded that focused and well- designed multicenter RCTs are now needed to validate earlier promising results and fill in any knowledge gaps. Our recommendation is to pursue these investigations in order to further advance the knowledge base concerning the health benefits of omega-3 fatty acids.

- Glucosamine:** Glucosamine has been shown to have anti-inflammatory effects and is believed to repair and maintain cartilage. To date, however, clinical studies on glucosamine have not conclusively demonstrated reductions in health service utilization that result from these clinical benefits. In order to further advance the science, the National Institutes of Health's *National Center for Complimentary and Alternative Medicine* (NCCAM) is now supporting two randomized double-blind studies of glucosamine. The first is a placebo control, parallel assignment efficacy study to examine whether glucosamine can improve joint function and/or reduce symptoms of knee osteoarthritis. The Glucosamine/ Chondroitin Arthritis Intervention Trial (GAIT) is in Phase III and is due to run another year. The other study is a pharmacokinetic study designed to examine the way glucosamine is absorbed and distributed throughout the body and is currently recruiting patients. Osteoarthritis is the most common musculoskeletal disease in the world, and its actual cause remains unknown. In 1999, approximately 10 million adults reported being diagnosed with osteoarthritis. Additionally, over 5 million adults reported having knee joint pain, swelling, and stiffness; about 25 percent of those with osteoarthritis reported having all three knee joint symptoms. Traditional treatments, most often anti-inflammatory drugs and pain relievers, produce variable results and may cause significant toxicity. The use of complementary and alternative therapies in the treatment of osteoarthritis has become more widespread, and particular interest has focused on glucosamine.
- Saw Palmetto:** Preliminary findings from our review of randomized clinical trials of the effects of saw palmetto for alleviating the symptoms of benign prostatic hyperplasia (BPH) indicate that use of the herb yields slight to moderate improvement in symptoms for men with this chronic urinary syndrome. A recently released review of clinical trials of the herb also found that saw palmetto reduces the symptoms of BPH, increases urinary flow, improves the quality of life and is well tolerated, and may be considered a viable first-line therapy for treating lower urinary tract symptoms associated with BPH. Additionally, at this time there are no known safety hazards or contraindications to using saw palmetto with other medications. BPH is the most common morbid medical condition in men and is responsible for some urinary symptoms in most men over the age of 50. BPH is generally treated with alpha-adrenergic blocking agents, finasteride, surgical interventions, or no specific therapy ("watchful waiting"). Currently the National Center for Complementary and Alternative Medicine (NCCAM) is conducting a randomized, double-blind, placebo controlled clinical trial of the safety and efficacy of saw palmetto, with careful attention to the methodological deficiencies of prior studies (e.g., the influence of confounding variables on observed outcomes.)

Analysts at The Lewin Group conducted extensive English-language searches on the internet and in print journals for relevant information on each supplement. Examples of resources used include MedLine, PubMed, Institute of Medicine, the Cochrane Library, the NHS Economic Evaluation Database, and National Institute of Health's (NIH) Osteoporosis and Related Bone Disease's National Resource Center. Telephone conversations were also conducted with researchers at NIH and with published economists at the Centers for Disease Control (CDC) in order to be sure that the latest research was identified and incorporated into the review.

Structured protocols were used to locate materials and evaluate their quality, paying considerable attention to issues of both internal and external validity. In our assessment of the quality of the research and the strength of the existing evidence, the underlying criterion was “the extent to which all aspects of the study’s design and conduct can be shown to protect against systematic bias, nonsystematic bias, and inferential error.” We found that the research literature is in various stages of development for each of the five supplements, ranging from robust bodies of clinical trials, meta-analyses, and well controlled cohort studies (as in the case of calcium and folic acid) to emerging bodies of research that are less conclusive and contain clinical trials of varying quality.

Figure 1 below shows the conceptual framework for the study. Cost estimates were developed of the potential health care expenditure savings that could result from daily use of calcium (with Vitamin D) and folic acid. For each of these supplements we attempted to determine if each of three casual links existed:

1. Does the supplement produce a physiological effect as shown by a change in biological markers? and if so;
2. Does this physiological effect create a change in health status? and if so;
3. Is this change in health status associated with a decrease in health care expenditures? (e.g., avoided hospitalizations and/or nursing home stays, and avoided instances of birth defects).
4. Methodological rigor is greatest for the meta analysis and randomized controlled trial (RCT). While various observational study designs can detect associations between variables (e.g., a change in one variable is linked to a change in the value of the other), RCTs are the “gold standard” for demonstrating causation, though they may not be applicable in every instance. One benefit of using an evidence-based medicine classification of studies is that it allows the reader to gauge the quality of the available literature. In such a review, more weight and credibility is given to designs that control for systematic and unsystematic bias. For this study, we used only the highest standard of evidence to support the development of the cost models for calcium and folic acid. Additionally, experts in the respective fields reviewed the models and provided input.
5. **Calcium (with Vitamin D):** There is considerable rigorous evidence supporting the effect of calcium on reducing bone loss and/or osteoporosis among post-menopausal women, especially when taken with vitamin D. There is also considerable evidence supporting the association of reduced bone loss and reduced fractures, with the best evidence supporting a reduction in hip fractures. Finally, there is considerable evidence supporting a reduction not only in the cost of the hospitalization to repair the hip, but also the post-acute stay for some proportion of patients in a skilled nursing facility. Additionally, physician surgical fees were determined using the Medicare physician fee schedule. The parameters used in the cost model are built upon the evidence found in the literature for each association.
6. Using a Congressional Budget Office (CBO) cost accounting approach, gross and net costs to a Medicare-like payer were determined for a five-year period (2005 – 2009). The current five-year cost of hip fracture among the country’s seniors is \$39 billion. Potential savings could be achieved through a reduction in hospitalizations, nursing facility stays, and physician surgical fees for some number of avoided hip fractures. We found that out

of approximately 320,000 hip fractures each year, approximately 138,000 hip fractures could be avoided in 2004 through daily use of calcium with Vitamin D. The five-year estimated cost offset (or savings) associated with avoided hospitalization for hip fracture is approximately \$6.7 billion. The five-year estimated savings associated with avoided skilled nursing facility admissions for extended post-acute rehabilitation is approximately \$8.6 billion, and approximately \$1 billion could be saved in physician surgical fees. Taking into account the cost of the supplement, we estimate a five year cost savings of **\$13.9 billion**.

7. **Folic acid:** Scientists now concur that the occurrence of neural tube defects (NTDs) is reduced if women consume folic acid or a folic acid-containing supplement before they become pregnant, and continue to do so in the early stages of pregnancy. It is both surprising and tragic given the strength of the evidence of folic acid's role in reducing birth defects (coupled with the low purchase price of the supplement) that not every woman of childbearing age is taking folic acid on a routine basis.
8. However, despite the overwhelming evidence demonstrating that NTDs could be reduced by 50 percent and national policies about the benefits of folic acid use, the number of babies born with NTDs has not declined to the extent expected. A recent Gallup poll found that a large number of women of child-bearing age reported knowing about the benefits of folic acid but are not themselves taking it. As a public health intervention, daily intake of folic acid costs little, and can result in very large savings as babies are born without NTD. Therefore, when prioritizing the allocation of resources devoted to favorable health interventions, it seems that folic acid is worthy of attention.
9. A targeted communication intervention that disseminates information through public awareness campaigns, coupled with an increase in the number of health care providers advising women between the ages of fifteen and 45 to take a folic acid supplement regardless of their intentions to conceive a child could produce startling results. Unpublished data from a 2002 Porter Novelli International survey reports that 88 percent of female participants indicated that they would take a folic acid supplement if their physician recommended it; only 37 percent of the women's physicians actually recommended supplemental folic acid during their pregnancy. We suspect that many women may not have realized that the prenatal vitamins they were given often contain folic acid, however, once a woman discovers she is pregnant, it is usually too late to prevent the occurrence of NTD.
10. Using a similar cost accounting approach to that used for calcium (with Vitamin D), gross and net costs to a payer were determined for a five-year period (2005 – 2009). Currently, approximately 4000 babies are born with NTDs, each with an estimated lifetime cost in 2005 of \$543,000 in direct medical expenses, varying types of therapy and equipment and special education costs. Potential savings could be achieved through a reduction in the incidence of NTDs through more women of childbearing age taking folic acid on a daily basis preconceptionally and through their pregnancies. If 10.8 million women began taking 400 mcg. of folic acid on a daily basis, approximately 600 babies would be born without NTDs, savings of as much as \$326 million as a result. Over five years, taking into account the very low cost of the supplement and the fact that not all NTDs are nutritionally related, **\$1.3 billion** could potentially be saved.
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Conclusion

In this study, we conducted extensive literature reviews in order to assess the consistency, validity, and impact of current research on each of five dietary supplements and to estimate the potential impact on health care expenditures for two of these, calcium and folic acid. We also suggested areas of further research to fill existing gaps in our current knowledge of the other three supplements.

The literature related to the health effects of each of the dietary supplements is at different stages of maturation in terms of its sophistication and statistical power. For calcium and folic acid, the body of research is extensive, spanning over 30 years. The more recent studies address concerns raised in earlier studies and represent significant scientific agreement concerning the improvements in health status associated with these supplements. In these two instances, the consensus is that findings from the studies reviewed reflect sufficient consistency, validity, and impact, and that informed use of these supplements will provide significant health benefits. Studies on the other three supplements have been conducted over a shorter period of time, and in some cases, fewer exist. Among existing studies, sample sizes are often too small to demonstrate significant clinical impact. As such, the cumulative effect of checks and counter-checks which provide consistency and validity to a body of scientific research is yet to be achieved.

In the case of omega-3 fatty-acids, the literature, though not yet completely definitive, suggests numerous benefits related to maintenance of cardiovascular health and prevention of health disease. Recently the FDA announced a qualified health claim for EPA and DHA omega-3 fatty acids. As indicated by AHRQ, however, well-designed multicenter RCTs are needed to confirm the observed effect of omega-3 fatty acids on CVD outcomes. Additionally, we recommend that research address questions about the effect of omega-3 fatty acids on CVD outcomes in specific subpopulations or individuals with chronic diseases (e.g., diabetes).

For saw palmetto and glucosamine, the literature is more emergent in nature and much less consistent. Nevertheless, research findings continue to be promising and there are preliminary indications that saw palmetto provides quality-of-life benefits related to symptomatic relief of benign prostatic hyperplasia and that glucosamine produces anti-inflammatory effects. Large government-funded studies are now underway which should provide more definitive results and add to the body of scientific knowledge on the use of these supplements for purposes that are more related to reductions in health service utilizations, and thus to cost savings.

The overall conclusion of this study is that in certain instances, supplements are an inexpensive and safe way to improve health status and reduce health care expenditures. In these cases, the role of public policy to support their use is unambiguous. In other instances, although the available evidence is less definitive, it warrants attention from health care providers and their patients, as well as continued investment of public financing for additional research. As the research literature evolves and matures, more will be known about each of the supplements considered in this analysis, as well as supplements that will be studied in the future.

http://www.naturalproductsinfo.org/index.php?src=gendocs&ref=lewin_1_conclusion&category=Lewin