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Title: Health Economics and Nutrition: A Review of Published Evidence

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Abstract: The relationship between nutrition and health-economic outcomes is important at both the individual and societal levels. Not only do nutritional choices made by individuals affect their health condition, thus influencing productivity and economic contribution to society, but also nutrition interventions carried out by the state have the potential to affect economic output in significant ways. This paper reviews studies of nutrition interventions where health-related economic implications of the intervention have been addressed. Results of the search strategy have been categorized into three areas: economic studies of micronutrient deficiencies and malnutrition; economic studies of dietary improvements; and economic studies of functional foods. It is found that although a significant number of studies have calculated the health-economic impacts of nutrition interventions, approaches and methodologies are sometimes ad hoc in nature and vary widely in quality. Development of an encompassing economic framework to evaluate costs and benefits from such interventions is a potentially fruitful area for future research.

Key Words: nutrition economics, malnutrition, micronutrient deficiencies, dietary improvements, functional foods
INTRODUCTION

The relationship between nutrition and health is well documented and associations between various nutrient impacts and nutritional interventions have been widely reported. The addition or removal of specific components into or from an individual’s diet can result in significant health improvements with the potential to result in non-trivial economic benefits. There is growing interest in the economics of nutrition, which broadly can be thought of as the process of researching and characterising health and economic outcomes following nutrition interventions and nutrition recommendations for the benefit of society. Assessing the health and economic impact of food consumption patterns or specific changes in nutritional behaviour on health and disease is highly relevant, for a number of reasons. For example, such assessments have the potential to play an important role in the development of nutrition recommendations and could also inform regulatory processes related to nutrition labelling and health claims.

One way in which the efficacy of a nutrition intervention can be evaluated is by examining the changes in costs and outcomes it causes. This could include measures of utility, reflecting the preference that an individual (or society as a whole) might have for a particular health state. It has been shown that when faced with a choice regarding a specific change in nutrition, if a rational individual stands to gain more in utility than the disutility associated with their personal cost of making the change, they are expected to choose a course of action that maximizes their expected utility. The consequences of individual nutrition choices can then be aggregated to determine the impact on populations. A variety of metrics exist for measuring the health-economic impacts of nutrition at the macro level, including changes in the direct costs of treating health conditions that could be improved with nutrition interventions; improvements in productivity resulting from decreases in morbidity and
premature mortality; generalized monetized estimates of adjusted life years; and condition-
specific willingness to pay (WTP) estimates of gains in utility from improved health states.

A nutrition intervention can be evaluated at the macroeconomic level in terms of
potential gains and losses to society as both indirect and societal costs. When the total costs of
a nutrition intervention are less than the prospective benefits, there is a potential gain in
societal welfare from the intervention. Such potential welfare gains do not require every
single member of society to benefit; rather, they require only that the total potential gains
outweigh the total potential losses. However, on a personal basis, a quantifiable benefit or
incentive must be foreseen to make a change in nutrition behaviour attractive. The typical
methods used to evaluate these types of potential welfare gains at the micro-level include
cost-minimisation analysis (CMA), cost-benefit analysis (CBA), cost-effectiveness analysis
(CEA), and cost-utility analysis (CUA). It is critical that the value of an intervention, as well
as the costs, be known in order to calculate whether a net benefit exists.3 One study discussed
methods for evaluating the economic benefits associated with improved health resulting from
changes in diet and exercise 4; other work has endeavoured to link the microeconomic aspects
of health economics with the welfare related macro aspects by developing a welfare-theoretic
model predicated upon the individual utility function.5 An exploration of the health economics
of preventative nutrition, outlining the economic burden of numerous nutrition-related health
problems, has also been carried out.6 This review will identify existing research which
characterizes health and economic outcomes in nutrition for the benefit of society.

Given increasing pressure on health care budgets, the development of food and
functional food products along with nutritional therapeutic modalities is facing new
challenges. The assessment of the value-for-money of nutrition interventions should be a
common goal for regulatory authorities, public health policy makers and the scientific
community. To date little research has been undertaken with respect to identifying the
economic aspects associated with nutrition interventions or programs and their health
benefits. The objective of this review paper is therefore to conduct a systematic review of the
existing literature to properly contextualize the current state of the field, with the hope that
improved understanding of relevant methods and findings will facilitate the development of
an encompassing evaluation framework with the flexibility to be applicable to a wide array of
interventions.

METHODS

A multidisciplinary expert workshop was held to elucidate the scope of the relationship
between nutrition and health while identifying key issues that should be considered when
proposing new studies of the economic consequences of nutrition interventions and policies.¹
During that workshop, a subset of the current evaluation methods used in health economics
and pharmacoeconomics was reported to be not completely suitable for the evaluation of the
socioeconomic impact of nutritional habits in general, and of specific nutrition interventions
in particular. At that workshop the term “nutrition economics” was coined to refer to a
specific sub-field within health economics, highlighting the need to identify existing studies in
order to facilitate the further development of adapted methodologies. With the findings of this
workshop in mind, a strategy for a comprehensive systematic literature review was
formulated.

Search Strategy

The databases in Table 1 were queried with the search strategies and critical assessment as
specified. The initial key words were defined based on the thesaurus of the databases being
searched by a skilled information specialist; biomedical databases were queried for economic
and nutritional terms and economic databases were queried for nutrition terms. Figure 1
provides a flowchart summarizing the search process. It should be noted that searches for
specific nutrients were not undertaken; although this is acknowledged as a factor that has the
potential to limit the scope of this review, it is believed that the search strategy employed did
reveal the preponderance of literature given that studies on specific nutrients were likely to be
detected by using broad nutritional terms.

Targeted attempts to search out “grey” literature beyond the documents contained in
the databases named in Table 1 were made with Google Scholar, a tool which uses Google to
search the internet for peer-reviewed papers, theses, books and articles from academic
publishers, societies, preprint repositories, universities and other scholarly organizations.

Sciuris, a tool which searches MEDLINE citations, ScienceDirect ejournal articles, patents,
technical reports and scholarly web pages, was also used in attempt to find “grey” literature,
as was the AgEcon Search database. A significant body of research was found to exist in the
“grey” literature for economic studies on micronutrient interventions. This literature, largely
comprised of reports from various non-governmental organizations (NGOs), was not included
in the present report because it was of varying quality, for instance containing non systematic
reviews or epidemiological studies of small populations, and was in many cases out of date
compared to the published scientific literature. Nevertheless, “grey” literature with a focus on
other economic nutrition relationships was included if it met the inclusion criteria.

Inclusion and exclusion criteria according to Patients Intervention Comparison Outcomes
(PICO) Question

Titles and abstracts of the studies returned by the search were reviewed independently by two
researchers against the following inclusion and exclusion criteria:

Patients – since nutrition interventions have the capacity to benefit wide cross-sections of the
population, all studies done on human subjects were considered for inclusion. Studies carried
out on animals or those that attempted to extrapolate from animal subjects were excluded.

Intervention – all studies concerning a change in diet (either the addition of a healthy
substance or the removal of unhealthy substance) were eligible for inclusion. Studies on
nutrition interventions where the effect (efficacy or effectiveness) had not been established before, either through randomized controlled trials (RCTs), observational comparative studies (cohort or case-control) or at least pre/post observational studies, were not included. Studies dealing with enteral nutrition were not considered, as this is a special nutrition application in hospital surroundings and often under medical supervision or during medical procedure, rather than a food pattern or change in diet. Also, studies in which the treatment was a medical product or otherwise not considered food were not included.

Comparison – economic research often relies on simulation models or “natural experiments.” As a result, relevant comparisons can include a simulated or observed section of the population which has not received a nutrition intervention or is receiving a different type of treatment, or historical comparisons in which economic parameters before or after an intervention are evaluated.

Outcome – studies reporting a quantifiable change in health outcomes, which may result in changes to the direct or indirect costs associated with the change in health status due to the nutrition intervention, were included. Studies in which other measurable economic parameters related to nutrition, and relevant to the socio-economic environment, were calculated also merited consideration for inclusion. Studies not involving any economic aspect of health outcomes from a nutrition intervention were excluded. The references and citations of all relevant articles were cross-checked for additional relevant studies with only English-language written studies being reviewed.

A special mention of how studies of obesity, a complex medical condition which can be affected by nutrition as well as by other lifestyle and environmental factors, were addressed within this review may be necessary. Obesity management interventions were included if there was a clear food-related nutritional component to the intervention as well as measurement of an identifiable health outcome. For example, a change in body mass index
(BMI) or body weight is likely to reduce the risk factor for a number of chronic diseases; however, if the link to a related health disease such as diabetes or coronary heart disease was not established in the paper, then the study was not included. Though the economics of obesity is an important and interesting topic, a complete investigation of it would be beyond the scope of this review, and related research has already been reviewed elsewhere. A final issue with respect to methodology pertains to how this review approaches evaluations of major nutrition programs. The United States Department of Agriculture (USDA) has a number of large and important nutrition programs including the WIC (Women, Infants and Children) and SNAP (Special Nutrition Assistance Program, formerly the food stamp program). These programs are important and a considerable number of evaluations of their general efficacy along with economic efficiency have been conducted. However, the USDA itself urges extreme caution in interpreting conclusions from studies of these programs for a variety of reasons. Accordingly, such studies were not included in this review.

RESULTS

The initial search of the databases listed in Table 1 resulted in over 13,000 returns. Many of the returns were excluded because their focus was not upon human nutrition or because they were editorial comments not consisting of attempts to quantify the health-economic effects of a nutrition intervention. A preliminary review of search findings suggested categorization of the literature into three areas: 1) research examining the economics of food fortification and dietary change to improve micronutrient intake and malnutrition; 2) research relating to economic improvements as a result of healthier diets; and 3) research aimed at studying the economic aspects of foods which can provide a health benefit beyond normal nutrition, referring mainly to functional foods. A discussion of studies falling into each of these three areas is found in the following sections.

1) Economic Studies of Micronutrient Deficiencies and Malnutrition
Studies examining various economic aspects of micronutrient deficiencies and malnutrition are summarized in Table 2. Twenty-six studies were included; seven were cost-effectiveness analyses, two were cost-benefit analyses and two were RCTs; others varied from simulation models to systematic reviews of RCTs. As Table 2 shows, micronutrient deficiencies in the low and middle income world are the most commonly studied areas with respect to economic studies of nutrition interventions. While these deficiencies can have tremendous economic costs, their treatment, specifically through improving the nutrient content of food, has been demonstrated to be very cost effective. Studies included in this section comprise the existing research on the economic consequences of food improvements devised to correct micronutrient deficiencies including fortification of staple foods with vitamin A, iron, iodine, zinc, and folate, as well as policies aimed at increasing consumption of foods naturally high in these minerals.

To date the most comprehensive study pertaining to the economics of micronutrient food interventions identified the feasibility and cost-effectiveness of 122 food fortification strategies in 48 countries. Addressing the criticism that the cost estimates of previous studies are out of date, not sufficiently detailed, and lack rigour, the authors estimate the CEA of micronutrient fortified foods in those countries building upon an existing model. Notable in that paper is the detailed and transparent description of the methods used in cost-effectiveness calculations. The results of their analysis are reported in the cost per disability adjusted life year (DALY) saved, which provides a single index whereby the morbidity and mortality to a particular disease can be measured. For micronutrient interventions, the cost per DALY saved is considered to be the best available method to quantify the economic benefits of the intervention.

Folate (also known as vitamin B9 or folic acid, a nutrient essential for human development) deficiency is notable in that it has also afflicted the populations of developed countries. Folate deficiencies often result in neural tube defects (NTD), which occur at a very
early stage of development; increased consumption of folate during pregnancy can reduce the risk for NTD. The cost effectiveness of folate fortification has been studied extensively.\textsuperscript{20-23} An interesting aspect of the economic consequences of NTDs is the difficulty associated with measuring adverse health consequences that occur very early in life—a large part of the economic benefit of folate fortifications is the increased future productivity of newborns who do not become afflicted by a NTD. Since the assumptions around future earnings and the discount rate can influence these results significantly, appropriate estimation methods should be used.

A relatively new strategy for dealing with micronutrient deficiencies is biofortification, a method of breeding plants resulting in their being naturally high in micronutrients. The benefit-cost ratio for investments in plant breeding for crops designed to reduce anaemia has been found to be high.\textsuperscript{27} A few authors have considered the economic underpinnings of biofortification\textsuperscript{28,29}; one particular study calculated found high levels of cost-effectiveness for rice bio-fortified with Vitamin A.\textsuperscript{30} In general, when a food is fortified or biofortified with micronutrients it has a lower cost structure than would an equivalent but separate supplementation program. Economic studies of biofortification applications in countries including India, Australia, New Zealand, and Uganda have been carried out.\textsuperscript{30-34} Another method of adding micronutrients to food is through genetic modification of a crop in such a manner that the edible portion of the harvested grain is high in a specific micronutrient by design. The economics of both genetically enhanced micronutrient rich rice and mustard have both been studied.\textsuperscript{26,35,36} These programs are, for the most part, the same in that the portion of the population receiving the micronutrient enhanced food should become healthier, potentially leading to a valuable economic benefit. Researchers carried out a study of home fortification with zinc in Pakistan and found that a reduction in diarrhoea and improvement in
haemoglobin concentrations led to a reduction in child mortality, higher earnings and increased IQ scores.\textsuperscript{37}

The literature on improving basic nutrition by alleviating protein and energy malnutrition (PEM) is somewhat limited. Correcting PEM in the developing world has the potential to improve a number of health conditions which can have a considerable economic impact. Some research has shown that PEM can play a major role in susceptibility to infectious diseases such as HIV/AIDS, tuberculosis, and malaria.\textsuperscript{38} The Copenhagen Consensus, a panel of eminent economists, ranked nutrition investments 2\textsuperscript{nd}, 5\textsuperscript{th}, 11\textsuperscript{th}, and 12\textsuperscript{th} among their recommendations to advance global welfare. The economic elements of malnutrition and associated manifestations could prove to be an interesting endeavour for future research.

2) Economic Studies of Dietary Improvements

Once the basic needs of human nutrition have been met by addressing core nutrients and mineral and micronutrient deficiencies, focus can be shifted to dealing with improving human health as part of a normal diet. Increasing consumption of nutrient-dense food or reducing consumption of unhealthy foods in the diet can lead to improvements in health, especially with respect to many chronic health conditions. Scientific research increasingly confirms that human diet can have a significant impact on disease, quality of life (QOL), and healthy longevity. Detrimental dietary patterns such as high intake of fat/saturated fat and low intake of calcium and fibre-containing foods such as whole grains, vegetables, and fruits can cause conditions that impair the quality of life and accelerate mortality. Diseases and health conditions identified as being good candidates for preventative nutrition strategies include: age-related macular degeneration (AMD), certain birth defects, cataracts, colon cancer, coronary heart disease (CHD), diabetes, hypertension, kidney stones, low birth weight, obesity, osteoporosis, pre-eclampsia, and stroke.\textsuperscript{39}
The review identified thirty studies relating to quantifiable health and economic benefits from dietary improvements (Table 3). While few assessments have been made to estimate the economic cost of poor or unbalanced diet, it has been conservatively estimated to be over $70 billion annually in the United States.\textsuperscript{40} This implies that if dietary improvements were made by all or a portion of the population, then a portion of these costs could be saved, resulting in an economic benefit to both public and private interests. One of the first attempts to put an economic value on nutrition interventions estimated the effect of reducing saturated fat on the incidence and cost of CHD in the United States.\textsuperscript{41} A key finding of this research was that a relatively small reduction in dietary saturated fat could result in annual savings of almost $13 billion. Another well-studied relationship in nutrition is the relationship between sodium and CHD; one study found that a 3g per day dietary salt reduction could result in $10 to $24 billion in health care savings.\textsuperscript{42} Other research into dietary reductions of calorie consumption in the American diet also showed that modest dietary changes could result in billions of dollars in savings in health care costs.\textsuperscript{43,44} Showing that the economic benefit of dietary improvement is not limited to the developed world, it has also been found that a voluntary reduction in salt intake is a cost effective method of reducing chronic disease in a number of low and middle income countries. Other research examined the effectiveness of two strategies to reduce sodium consumption, and found that a mean population reduction in sodium intake of 9.5% would lead to considerable reductions in both morbidity and disease costs.\textsuperscript{45,46} McCarron and Heaney examined the healthcare savings related to consumption of adequate dairy products and estimated savings from a reduction in obesity, hypertension, type 2 diabetes, osteoporosis, kidney stones, certain outcomes of pregnancy, and some cancers to be in excess of $200 billion over a 5 year period.\textsuperscript{47} Osteoporosis, characterized by reduced bone mineral density, has the potential to be improved by increased consumption of calcium
and vitamin D. While research demonstrating the cost-effectiveness of supplements as a
treatment for osteoporosis has been reported, it is surprising that similar studies were not
found for food fortifications or dietary changes to improve calcium and/or vitamin D intake
during the course of this review.

Obesity, a serious health condition seemingly at the opposite end of the spectrum from
the problem of malnutrition, is often seen in the less wealthy population. Studies have
demonstrated that obesity carries significant economic costs, estimating that the cost of
obesity in the United States is $99 billion and that the future cost of obesity in China will
climb to nearly 9% of their gross national product by 2025. A health technology
assessment reviewed the cost-effectiveness of pharmaceutical and surgical interventions and
conducted a Markov simulation to the cost-effectiveness of a low-fat diet combined with
exercise in an obese population, finding a relatively high cost per QALY gained. However,
the only disease reduction conceded was diabetes, making this particular estimate very
conservative. Policy decisions such as “junk” food taxes and food labelling requirements
designed to increase consumption of healthy foods and decrease the consumption of unhealthy
foods are another method with the potential to improve public health and as a result reduce
health care costs. Recent work modelled the impact of tax and incentive polices aimed at
increasing fruit and vegetable consumption in France, finding that some strategies were cost-
effective in increasing healthy food consumption while reducing the risk of death from cancer
and CHD. Another study examined four potential food taxation-subsidy alternatives and
found that all would be regressive from an economic standpoint; moreover the economic
burden of such taxes would be more harsh for the poor than for the rich. Nevertheless, the
authors found that a combination of taxes with subsidization of healthy foods would produce
overall population health gains. Similar research explored the potential effects of applying
the UK’s value-added tax to a broader range of foods, finding that the incidence of ischaemic
heart disease would decrease. However, consumers would have to spend more on food, implying that their incomes should be raised to compensate.\textsuperscript{53} This would be particularly true for those in lower income groups. A subsequent paper calculated the impacts from health, nutrition and economic perspectives of related measures in the UK, and concluded that such policies, while having the potential to improve health outcomes, could have the undesirable effect of actually reducing consumption of healthy foods.\textsuperscript{54} As an alternative to such “fat tax” policies, one study investigated the health and economic impacts of “thin subsidies” designed to encourage increased consumption of fruits and vegetables, and found that the cost per life saved of such a policy compared favourably to other existing programs in the US.\textsuperscript{55}

The potential savings resulting from the US’s \textit{Nutrition Labelling and Education Act} were calculated and it was determined that the expected subsequent reduction in body weight in some sections of the population could result in $63 to $166 billion, a saving greater than the cost of implementing the act.\textsuperscript{56} Further research found that limiting “junk” food marketing to children would be an extremely cost effective intervention tool for government.\textsuperscript{57} Governments also generally possess the ability to institute outright bans on consumptions of certain food types if there is a net benefit to doing so; one study concluded that the reduction in healthcare costs from banning trans fats in Canada would more than offset the food industry cost increases that the ban would cause.\textsuperscript{58} In general, most policy and educational efforts to improve health through nutrition have shown to be cost effective. Population wide policy interventions are likely to offer excellent value for money in the prevention of obesity through the health nutrition impact of improved labelling and a “junk” food tax.\textsuperscript{59}

There has been some research with respect to the potential role of education initiatives in generating positive nutrition outcomes; for example, Rajgopal et al examined the costs and benefits of the expanded food and nutrition education program run by the cooperative extension serve at Virginia Tech University.\textsuperscript{60} They found that participation in six to twelve
nutrition education lessons could result in healthcare savings due to the delay and/or avoidance of poor nutrition related chronic diseases. Similar results were found in Oregon, Iowa, and New York. The cost effectiveness of child nutrition education efforts in Peru has been studied; however, that research did not have a defined health benefit and did not meet the inclusion criteria for this review. The authors found that a targeted education program was cost-effective in reducing stunting and mortality. The cost-effectiveness of different “minimal contact” educational strategies to reduce serum cholesterol was assessed; it was found that short counselling sessions could be cost-effective in reducing cholesterol.

The so-called “Mediterranean diet” provides an intriguing example of a cost effective approach in reducing the cost of CHD at a micro level. However, defining Mediterranean diet in detail is difficult and interpretation of the published information depends on this. The Mediterranean diet involves eating primarily plant-based foods, such as fruits and vegetables, whole grains, legumes and nuts; replacing butter with healthy fats such as olive oil and canola oil; using herbs and spices to flavour foods; limiting red meat; and increasing fish and poultry consumption. Though the Mediterranean diet holds promise for improving the health of its consumers, food availability could limit its widespread adoption. Two studies have examined similar dietary modifications involving increased consumption of fruit and vegetables, which are believed to reduce the incidence of some types of cancer and, as a result, yield cost savings.

The cost effectiveness of a number of nutrition interventions including the Mediterranean diet, intensive lifestyle change, a reduced fat diet, various nutritional counselling strategies, and extensive educational efforts have been examined, and it was found that all ten of the nutritional interventions investigated were cost effective. It was also noted that nutrition intervention can constitute a highly efficient component of a strategy to reduce the burden of disease. An ongoing research project is focusing on examining the
economic and health impacts of the *Programme for Complementary Food in Older People in Chile*. This program aims to increase the health and economic situation of the specified group, and is notable as a proactive approach in addressing changes in the demographic characteristics of the population using nutrition as a tool to deal with the economic and health demands of an aging society. A study of blood serum cholesterol reduction resulting from the implementation of Swedish guidelines for non-pharmalogical treatment of hypercholesterolaemia found that both low-and-medium intensity strategies reduced cholesterol by only a small amount; per-subject treatment costs were five times higher in the medium-intensity group.

It may be reasonable to conclude that interventions aimed at positive dietary changes are cost-effective through a reduction in the burden of chronic diseases which can be prevented through healthier nutrition, as well as production losses avoided through a healthier workforce. The economic benefits of encouraging and educating the public on improving food habits will be a profitable aid for policymakers dealing with the increasing health- and economic burden of healthcare.

3) Economic Studies of Functional Foods

Little research has focused on researching and characterizing the health and economic outcomes of functional foods; as a result the search revealed only seven studies (Table 4). Two were cost-effectiveness studies, two were cost of illness analyses, and three were other heterogeneous studies. There is a natural evolution from pursuing adequate nutrition via increasing micronutrient consumption using food as a means to improve health beyond basic nutrition. Food scientists and nutrition researchers are continuously devising new functional foods, loosely defined as food products designed to provide health benefits beyond basic nutrition. Consumption of these foods has the potential to improve human health; in turn this health improvement has the potential to provide economic benefits.
The earliest example of an economic benefit arising from the use of a functional food was a study of the cost-effectiveness of grain fortified with cyanocobalamin and folic acid. Folic acid is normally considered a vitamin; however, the benefit focused upon in the study was a lowering of plasma homocysteine levels for the prevention of CHD. This goes beyond basic nutrition, making the fortified grain in this study more of a functional food. The authors found this particular fortification could be cost-effective and have a major benefit on populations' health for primary and secondary prevention of CHD, but noted that further research may be required to confirm that homocysteine-lowering therapy decreases CHD event rates.

Research on the relationship between cholesterol and CHD has led to a number of studies focusing on the ability of functional foods to lower serum cholesterol and hence reduce the incidence and costs of CHD. Plant sterol and stanol addition in foods, which have been shown to inhibit cholesterol absorption, have been studied particularly extensively. The cost-effectiveness of plant sterol and stanol enriched margarines and dairy products has been demonstrated as efficient in reducing cholesterol and CHD related costs. A recent study found that significant healthcare savings should result from introduction of plant sterol enriched functional foods to the Canadian market.

Additional research on the economic benefits of functional foods with the potential to reduce the incidence of CHD includes an examination of the economic benefit of trans-fat free canola oil. Research found that such a product would result in significant economic benefits to Canadian society. Other research employed a simulation model to calculate the cost effectiveness of omega-3 fatty acids in the reduction of CHD and found supplementation would result in fewer fatal myocardial infarctions and was cost-effective in treating CHD. An important aspect of omega-3 fatty acids not covered by that study was the ancillary health
benefits such as the prevention of cancer and other neurological diseases; further research is needed to fill this gap.

Flax is considered by many to be a functional food ingredient because it is rich in alpha-linolenic acid (ALA), an omega-3 fatty acid. Because of this property, flax consumption has the potential to reduce the incidence of diseases such as CHD, diabetes, cancer, kidney disease, and Alzheimer’s disease. The reduction in healthcare costs that could result from increased flax consumption in Canada has been estimated to be between one and three billion dollars annually. It is noteworthy that clinical research and limited economic analysis indicate the potential for functional foods to be cost effective across a more diversified area of health concerns; some examples include antioxidants and eye disease; cancer and omega-3 fatty acids and antioxidants; Alzheimer’s disease and omega-3 fatty acids; conjugated linoleic acid and obesity; probiotic/prebiotics and bowel diseases and diarrhea; and prevention of atopic dermatitis. As these new technologies spread, the challenge will be to develop new methodologies to analyse and quantify the long time frames and complex nutrition health relationships associated with these functional foods. Because new functional food products are being developed continuously, it is important to ensure that economic analyses of the impacts of these interventions are carried out using appropriate methodologies.

DISCUSSION

Micronutrient interventions provide a useful illustration of how a nutritional change can result in health and economic outcomes with societal benefits. The efficacy and effectiveness of increased micronutrient consumption in alleviating micronutrient deficiencies is well established, while the economic benefits of improved micronutrient intake have been studied extensively in high, low and middle income countries. As a public health tool, micronutrient fortifications are often cited as one of the most cost-effective means of quickly improving a
targeted population’s QOL. While much of the research has focused on low and middle
income countries, the tools, methods, and lessons are broadly applicable. The possibility of
analysing the cost-effectiveness potential of micronutrient interventions should be fully
explored.

The relationship between diet and economic activity is complicated and evidence of
causality runs in both directions. When people are adequately nourished they are in better
health and more productive, and as people become wealthier they can afford to eat better and
their health improves. The relationship between improved nutrition and a country’s national
income has been studied in some low and middle income countries. While the basic
malnutrition is an important public health concern in the low and middle income world, to
date much of the economic research related to malnutrition has focused on micronutrient
deficiencies, sometimes referred to as the hidden hunger. Humans require small doses of a
number of different micronutrients in order to maintain normal bodily function. Though it is
possible to obtain an adequate dose from a healthy diet, in some situations, especially in low
and middle income countries, proper micronutrient nutrition is not always possible. As a
result, micronutrient deficiencies affect a significant portion of the population, with associated
adverse health effects ranging from blindness to severe birth defects. The costs of treating
these deficiencies as well as the productivity lost due to micronutrient deficiency related
morbidity and mortality have been found in various studies to be economically significant,
and interventions aimed at correcting micronutrient deficiencies have generally proved to be
cost effective. Micronutrient interventions provide a compelling example of an area in which
nutrition improvements benefit society from an economic perspective.

In developed countries, a change in unbalanced or detrimental food habits can result in
substantial health care cost savings. Numerous factors not related to nutrition, including
 genetic and lifestyle issues influence obese subjects’ ability to lose excess weight and
overweight and obesity can only partially be alleviated by adapted nutrition. The potential
benefits of healthier food habits and dietary improvements might have a higher impact in
preventing weight gain and maintenance of a correct body mass index. In general, findings of
this literature review indicate that dietary improvements can result in substantial health care
cost savings. This should be reflected in nutrition recommendations and nutrition counselling
as an added value to health benefits on both individual and target population levels.

The functional food market is growing rapidly. The potential for significant savings
across a wide range of diseases illustrate the largely untapped potential of functional foods to
reduce the incidence of nutrition-related chronic diseases and healthcare costs. Coronary heart
disease is a leading cause of death and a significant health concern in the developed world. As
such, it is not surprising that the majority of the functional food studies detected in this search
were related to functional foods designed to reduce the risk of CHD. From an economic
analysis standpoint, the tools and biomarkers are very similar to methods used in pharmaco-
economic evaluations of statin-type pharmaceuticals. Although this makes an economic
analysis modelling of CHD reducing functional foods relatively easy for economic
researchers, a substantial number of differences exist between developing economic
evaluation models of pharmaceuticals versus functional foods. These differences are related
mainly to the need for different approaches to measure effectiveness. While it is clear that in
the case of drugs RCTs are the standard, in the case of nutrition, population-based, properly
conducted observational studies should be the focus. In fact, effectiveness of the interventions
on real life basis is extremely important because many context dependent factors could
influence the final outcomes of these interventions. Further investigation of the costs of such
approaches is needed, but this will be challenging because of the confounding factors and long
timelines associated with analyzing a number of nutrition-related diseases. This makes a
complete analysis complex. Though small in number, studies available to date suggest that
functional foods are cost-effective and can be powerful tools to reduce illness and the
associated costs.

A limitation to this work is that the literature search and interpretation focused
primarily on the economic side of the “value for money” equation rather than on the health-
related quality of life (HRQOL) value outcome side. A critical review of the effectiveness
outcomes (including HRQOL) can be an important consideration but was beyond the scope of
the present paper. It should also be noted that the term “cost-effective” has been used in a
number of studies cited in this review as a proxy for cost saving. In reality, cost effectiveness
is not solely about cost “savings”, but can in fact involve increasing expenditures. This is the
case when the added value (e.g. improved QOL) of a nutrition intervention can be
demonstrated to offset the additional costs.

CONCLUSION

The range of studies presented demonstrate that from the most basic level of providing
adequate nutrition, to simply improving normal diets by the addition of healthy food or the
removal of unhealthy foods, or through the introduction of functional foods which are
designed to provide a health benefit beyond normal levels, nutrition can be a powerful force in
improving both the health and economic status of society. Much of the work to date has been
ad hoc with economic analyses based largely on the particular subject area and without an
overarching, well-defined framework. Future research would benefit from the development of
such a model since it would allow for a uniform and complete measurement of the economic
costs and benefits borne by all stakeholders. With increasing pressure on healthcare budgets
across the world, the potential to cost-effectively “demedicalize” health care costs with
nutrition should be fully examined as opportunities present themselves. The fact that many of
the interventions described in this review, which have proved to be cost effective, have not yet
been implemented implies that policymakers and the public need better information on the
economic potential of nutrition-related health effects. In summary, further development of the
methods for economic evaluations of nutrition interventions and promoting their use to inform
public policy decision makers should be considered priorities in setting future research
direction.

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Declaration of Interest: none
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Table 1 Databases consulted, systematic literature review

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<tr>
<th>Database Name</th>
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<th>Records Content (see notes)</th>
<th>Key Words</th>
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<td>PAIS</td>
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a denotes abstracts, b denotes books, c denotes chapters, j denotes journal articles, l denotes bibliography,
o denotes software, r denotes reviews, s denotes study, t denotes theses/dissertations, v denotes collective
volumes, w denotes working papers * denotes discontinued

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<tr>
<th>Reference</th>
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<td>Loevinsohn et al. (1997)</td>
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<td>Cost effectiveness of reducing child mortality</td>
<td>First year avg. cost: universal approach $67.21/death averted; broad targeting $144.12/death averted; narrow targeting $257.20/death averted</td>
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<td>Horton (2008)</td>
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<td>Economic calculations</td>
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<td>Economic losses</td>
<td>Cost effectiveness of nutrition interventions found to be very high</td>
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<td>Horton et al. (2003)</td>
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<td>Baltussen et al. (2004)</td>
<td>Women 30-44 and perinatal infants in four regions (South America, Africa, Europe, Southeast Asia)</td>
<td>Population model</td>
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<td>Ma et al. (2008)</td>
<td>General population</td>
<td>Cost effectiveness analysis</td>
<td>Iron and zinc fortification vs. no fortification; dietary diversification</td>
<td>Iron and zinc deficiency</td>
<td>Biofortification showed the lowest costs per capita (I$0.01) among interventions on iron and zinc deficiency; dietary diversification through</td>
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<td>Study Reference</td>
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<td>Health Outcomes</td>
<td>Cost Effectiveness</td>
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<td>Rouse (2003)¹⁹</td>
<td>Antenatal population in Zaire, New Guinea, Nepal</td>
<td>RCTs in Zaire and New Guinea; double-blind randomized cluster in Nepal</td>
<td>Iodine supplementation vs. no supplementation (Zaire, New Guinea); vitamin A/β-carotene supplementation vs. no supplementation (Nepal)</td>
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<td>Romano et al. (1995)²⁰</td>
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<td>Secondary data from RCTs and other sources</td>
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<td>Llanos et al. (2007)²¹</td>
<td>General population in Chile</td>
<td>Ex-post economic analysis</td>
<td>Folic acid fortification vs. no fortification</td>
<td>Neural tube defects; infant mortality</td>
<td>Intervention costs per neural tube defect case and infant death averted were IS$1,200 and IS$11,000 respectively; cost per DALY averted was IS$89; net cost savings of fortification of IS$2.3 million</td>
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<tr>
<td>Bentley et al (2008)²²</td>
<td>US population subgroups divided by age, gender,</td>
<td>Cost effectiveness analysis</td>
<td>Folic acid fortification of enriched grain products vs. no fortification</td>
<td>Neural tube defects, myocardial infarctions, colon cancers, B12 deficiency maskings</td>
<td>266,649 QALYs gained with US $3.6 billion saved over the long run by increasing fortification levels</td>
</tr>
</tbody>
</table>

- RCTs: Randomized Controlled Trials
- B/C: Benefit/Cost Ratio
- DALY: Disability Adjusted Life Year
- IS: International Dollar
- QALY: Quality Adjusted Life Year
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<tr>
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<td>Jentink et al. (2008)</td>
<td>Women of child bearing years in Netherlands</td>
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<td>Folic acid fortification vs. no fortification</td>
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<td>Bulk food fortification with folic acid cost effective if enrichment costs remain below € 5.5 million</td>
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<tr>
<td>Fiedler et al. (2009)</td>
<td>General population in 48 countries</td>
<td>Cost effectiveness analysis of 122 interventions</td>
<td>Biofortification with multiple micronutrients vs. no biofortification</td>
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<td>Zimmerman et al. (2004)</td>
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<td>Scenario approach</td>
<td>Vitamin A biofortification with GM rice vs. no fortification</td>
<td>Vitamin A deficiency</td>
<td>Annual health improvements found to be worth between US $16 million and $88 million; rates of return on R&amp;D range between 66% and 133%</td>
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<tr>
<td>Bouis (2002)</td>
<td>General population in south Asia</td>
<td>Economic simulation model</td>
<td>Effects of investments in plant breeding vs. alternate investments on iron deficiency</td>
<td>Benefit to cost ratio; anemia cases prevented; annual cost</td>
<td>Ratio of 19 for returns to better iron nutrition in humans (internal rate of return 29%); ratio of 79 if benefits to increased agricultural productivity are included (internal rate of return 44%); 44 million cases of anemia prevented over 25 years if improved varieties planted on 10% of rice &amp; wheat areas in Bangladesh &amp; India; total cost of $1/anemia case prevented</td>
</tr>
<tr>
<td>Meenakshi et al. (2010)</td>
<td>General population in several countries</td>
<td>Cost effectiveness analysis</td>
<td>Biofortification of several crops vs. fortification and supplementation</td>
<td>Multiple micronutrient deficiencies</td>
<td>Most costs per DALY saved through biofortification are highly cost effective with benefit:cost ratios over 1.0 in</td>
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</tbody>
</table>
Stein et al. (2006)\textsuperscript{30} & General population in India & Economic simulation and cost effectiveness analysis & Vitamin A biofortification of GM rice vs. no fortification & Vitamin A deficiency & Cost per DALY saved by use of golden rice ranged from US $3.06 (high impact scenario) to $19.40 (low impact scenario) \\
Stein et al. (2007)\textsuperscript{31} & General population in India & Dose response function & Zinc biofortification vs. no biofortification & Zinc deficiency & Zinc biofortification of rice and wheat could reduce burden of zinc deficiency by 20\% to 51\% and save 0.6 to 1.4 million DALYs each year; cost to save one DALY found to be US $0.73 to $7.31 \\
Stein et al. (2008)\textsuperscript{32} & General population in India & Cost benefit analysis & Iron biofortification of rice and wheat vs. no biofortification & Iron deficiency & Iron biofortification of rice and wheat can reduce lost DALYs by between 19\% with a cost per DALY saved of US $5.39 (pessimistic scenario) and 58\% with a cost per DALY saved of US$0.46 \\
Dalziel et al. (2009)\textsuperscript{33} & Women capable of or planning a pregnancy in Australia and New Zealand & Secondary data from published RCTs & Set of intervention options promoting folic acid/folate consumption & Neural tube defects & Population-wide campaigns promoting use of supplements and mandatory supplement use most effective at reducing neural tube defects; population wide and targeted approaches were cost effective, as was extending voluntary fortification, but
<table>
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<tr>
<td>Fiedler et al. (2010)</td>
<td>General population in Uganda</td>
<td>Cost effectiveness analysis</td>
<td>Vitamin A fortification of food oil and sugar vs. no fortification</td>
<td>Vitamin A deficiency</td>
<td>Cost per DALY averted is US $82 for sugar fortification and US $18 for oil; vitamin A fortification of vegetable oil is thus 4.6 times more cost effective than of sugar</td>
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<tr>
<td>Manyong et al. (2004)</td>
<td>Children and pregnant/lactating women in Nigeria</td>
<td>Ex-ante evaluation based on secondary data</td>
<td>Impact of vitamin A fortified cassava on vitamin A deficiency vs. no fortification</td>
<td>Vitamin A deficiency</td>
<td>Internal rate of return from biofortification program would range between 92.4% (pessimistic) and 165.3% (optimistic), representing gains of between $10 million and $63 million annually</td>
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<td>Chow et al. (2010)</td>
<td>General population in India</td>
<td>Cost effectiveness analysis</td>
<td>Biofortification of GM mustard vs. high-dose vitamin A supplementation vs. industrial fortification of mustard oil</td>
<td>Vitamin A deficiency</td>
<td>Expanding vitamin A supplementation was least costly ($23-$50 per DALY averted and $1,000 to $6,000 per death averted); GM fortification would avert 5-6 million more DALYs and 8,000-46,000 more deaths but was 5 times more costly; industrial fortification was dominated by both GM fortification and supplementation</td>
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<tr>
<td>Sharieff et al. (2008)</td>
<td>Children in Karachi</td>
<td>Cost benefit analysis</td>
<td>Iron biofortification vs. no biofortification</td>
<td>Reduction in diarrhea and improvement in</td>
<td>Present value of incremental benefit calculated to be US</td>
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mandatory fortification was not cost effective; promoting a folate-rich diet was least cost effective
<p>| Pakistan |  | hemoglobin concentrations | $106, indicating home fortification may improve clinical outcomes at a reasonable cost |</p>
<table>
<thead>
<tr>
<th>Reference</th>
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<tr>
<td>Dalziel et al. (2007)⁷</td>
<td>General population in various countries</td>
<td>Cost effectiveness analysis based on trial results; modeled cost utility analysis</td>
<td>10 nutrition interventions</td>
<td>Various depending on study</td>
<td>Cost effectiveness analysis yielded differential costs between AU $0.24/person (Multi Media 2 fruit 5 veg Campaign) and $1,203/person (nurse counseling in GP); cost utility was between AU $46 (Multi Media 2 fruit 5 veg Campaign) and $19,800 (work force group Gutbusters Workplace)</td>
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<td>Frazao (1999)⁴⁰</td>
<td>General population in US</td>
<td>Cost of illness approach</td>
<td>Multiple dietary improvement vs. no dietary change</td>
<td>Reductions in CHD, cancer, stroke, diabetes, hypertension, obesity, osteoporosis</td>
<td>Estimated that healthier diets might prevent US $71 billion per year in medical costs, lost productivity and premature deaths</td>
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<tr>
<td>Oster et al. (1996)⁴¹</td>
<td>Persons 35-69 years in US with cholesterol levels 5.17 mmol/L or higher who do not have CHD</td>
<td>Secondary data from Framingham study, NHANES study and population data</td>
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<td>1% to 3% reduction in saturated fat intake would reduce incidence of CHD by 32,000 events and result in savings of US $1.4 billion to $12.7 billion over 10 years</td>
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<tr>
<td>Bibbins-Domingo et al. (2010)⁴²</td>
<td>US general population</td>
<td>CHD policy model based simulation</td>
<td>Reduction of 3 grams/day in dietary salt compared to other interventions</td>
<td>Reduction in CHD, myocardial infarctions</td>
<td>Reduction in salt intake of 3 g/day would save between 194,000 and 392,000 QALYs annually and between US</td>
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</table>

*Table 3 Economic studies of dietary improvements*
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<td>Dietary reduction of calories, salt, unsaturated fat vs. no dietary change</td>
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<tr>
<td>Dall et al. (2009b)</td>
<td>US general population</td>
<td>Economic simulation model based on secondary data</td>
<td>Dietary reduction in calories and salt vs. no dietary change</td>
<td>Permanent reductions in daily intake of 100 kilocalories would increase national productivity by US $45.7 billion annually; long-term sodium reductions of 400 mg/day would increase productivity by $2.5 billion annually</td>
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<tr>
<td>Asaria et al. (2007)</td>
<td>General population in 23 countries</td>
<td>Based on longitudinal study</td>
<td>15% reduction in salt intake vs. normal salt consumption; implementation of four key elements of WHO Framework Convention on Tobacco Control</td>
<td>Reduction in cardiovascular disease and cancer 13.8 million deaths could be averted over the 2006-2015 period; cost would be less than US $0.40/person/year in low and lower middle income countries and between $0.50 and $1.00 in upper middle income countries</td>
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<td>Smith-Spangler et</td>
<td>US adults aged 40-85</td>
<td>Markov model with 4 health</td>
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<tr>
<td>al. (2010)</td>
<td>46 years states</td>
<td>Industry collaboration to reduce sodium in processed foods vs. a sodium tax</td>
<td>Infarctions averted, strokes averted</td>
<td>9.5% averts 513,885 strokes and 480,358 MIs, increases QALYs by 2.1 million, and saves US $32.1 billion in medical costs; sodium tax reducing sodium intake by 6% increases QALYs by 1.3 million and results in $22.4 billion in cost savings</td>
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<td>McCarron et al. (2004)</td>
<td>US adult population RCTs and prospective longitudinal studies</td>
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<td>Avenell et al. (2004)</td>
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<td>Dallongeville et al. (2011)</td>
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<td>Costs per life-year saved are smallest for the information campaign, then value-added tax reduction, then food stamp policy</td>
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<td>Nnoaham et al. (2009)</td>
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<td>Targeted food taxes and/or subsidies vs. no taxes and/or subsidies</td>
<td>Reductions in mortality from cardio vascular disease and cancer</td>
<td>Each of the four policy instruments examined would be economically regressive; use of tax proceeds to subsidize consumption of fruits and vegetables could lead to public health gains</td>
</tr>
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<td>Marshall (2000)</td>
<td>UK general population Comparison of effects of fiscal</td>
<td>Extension of value-added tax to increased</td>
<td>Reduction in ischaemic heart</td>
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<tr>
<td>Study</td>
<td>Population</td>
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<tr>
<td>Mytton et al. (2007)²⁴</td>
<td>UK general population</td>
<td>Economic model based on consumption data and elasticity values</td>
<td>Taxing principal sources of dietary fat vs. taxing unhealthy foods based on SSCg3d score vs. taxing foods to achieve best health outcome</td>
<td>Reduction in mortality from cardiovascular disease</td>
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<td>Fat taxes have the potential to result in a modest reduction in mortality; however poorly designed taxes have the potential to adversely affect consumption of healthy foods</td>
</tr>
<tr>
<td>Cash et al. (2005)²⁵</td>
<td>US general population</td>
<td>Empirical simulations using Continuing Study of Food Intake by Individuals data</td>
<td>Subsidies for consumption of fruits and vegetables vs. no subsidies</td>
<td>Reduction in incidence of CHD and ischemic stroke</td>
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<td>Present value of cost per life saved due to thin subsidies US $1.8 million for vegetables alone; $2.19 million for fruit alone; $1.29 million for fruits and vegetables; results vary by low, medium and high income households</td>
</tr>
<tr>
<td>Varyam et al. (2006)²⁶</td>
<td>Non-Hispanic Caucasian US adults</td>
<td>Difference in differences method based on survey results</td>
<td>Before and after Nutrition Labeling and Information Act (NLEA)</td>
<td>Body weight and probability of obesity</td>
</tr>
<tr>
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<td>Total monetary benefit of decrease in body weight between US $63 billion and $166 billion, well exceeding program costs</td>
</tr>
<tr>
<td>Magnus et al. (2009)²⁷</td>
<td>Australian children 5-14 years</td>
<td>Extrapolations based on RCTs, cross-sectional and longitudinal studies</td>
<td>Banning ads for energy-dense, nutrient-poor food and beverages during peak children’s TV viewing times</td>
<td>Changes in BMI; DALYs saved</td>
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<td>Intervention yielded a gross incremental cost effectiveness ratio of AU $3.70; 37,000 total DALYs were saved; present value of future health care costs saved was $300 million</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Population</td>
<td>Analysis Type</td>
<td>Outcome</td>
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<td>Gray et al. (2006)</td>
<td>Canada</td>
<td>Canada general population</td>
<td>Cost benefit analysis based on secondary data</td>
<td>Trans fat ban vs. voluntary labeling system vs. mandatory labeling system</td>
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<tr>
<td>Sacks et al. (2010)</td>
<td>Australia</td>
<td>Adult population of Australia</td>
<td>Cost effectiveness analysis</td>
<td>Traffic light nutrition labeling vs. junk food tax</td>
</tr>
<tr>
<td>Rajgopal et al. (2002)</td>
<td>US state of Virginia</td>
<td>3,100 limited income adults having previously participated in the Expanded Food and Nutrition Education Program (EFNEP)</td>
<td>Cost benefit analysis</td>
<td>Prior participation in EFNEP vs. no participation</td>
</tr>
<tr>
<td>Schuster et al. (2003)</td>
<td>US state of Iowa</td>
<td>368 limited income adults having previously</td>
<td>Cost benefit analysis</td>
<td>Prior participation in EFNEP vs. no participation</td>
</tr>
<tr>
<td>Study Authors and Year</td>
<td>Study Description</td>
<td>Methods</td>
<td>Prevention Goals</td>
<td>Cost Benefit Analysis</td>
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<tr>
<td>Wessman et al. (2001)⁶²</td>
<td>Limited income adults in US state of Iowa having previously participated in the Expanded Food and Nutrition Education Program (EFNEP)</td>
<td>Cost benefit analysis</td>
<td>Prior participation in EFNEP vs. no participation</td>
<td>Prevention of three types of diseases: Type A (life threatening), Type B (non life threatening), Type C (conditions requiring one-time treatment)</td>
</tr>
<tr>
<td>Dollahite et al. (2008)⁶³</td>
<td>5,730 low income New York state residents</td>
<td>Pretest, posttest design with epidemiological modeling approach</td>
<td>Series of 6 or more food/nutrition lessons</td>
<td>Cost, health benefits in QALYs, monetized benefits</td>
</tr>
<tr>
<td>Gans et al. (2006)⁶⁵</td>
<td>10,144 New England participants including 1,425 Hispanics</td>
<td>Randomized trial based cost effectiveness study</td>
<td>Six minimal contact nutrition interventions</td>
<td>Total blood cholesterol levels using fingerstick methods</td>
</tr>
<tr>
<td>Dalziel et al. (2006)⁶⁶</td>
<td>Lyon Diet Heart Study</td>
<td>Cost utility analysis</td>
<td>Mediterranean diet vs. prudent Western diet</td>
<td>Morbidity and mortality from CHD</td>
</tr>
<tr>
<td>Study Reference</td>
<td>Number of Participants</td>
<td>Study Design</td>
<td>Intervention/Outcome</td>
<td>Cost Estimation/Effectiveness Ratio</td>
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<td>Panagiotakos et al. (2007) (^67)</td>
<td>3,042 adults in Greece with no clinical evidence of CVD</td>
<td>Cross sectional study with a questionnaire</td>
<td>Adherence to Mediterranean diet vs. no adherence</td>
<td>CHD</td>
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<tr>
<td>Daviglus et al. (2010) (^68)</td>
<td>Eligible surviving participants (&gt; 65 yrs) from Chicago Western Electric Study</td>
<td>Longitudinal based</td>
<td>3 strata of fruit and vegetable intake: 14 cups/month (low); 14-42 cups/month (medium); &gt; 42 cups/month (high)</td>
<td>Cardiovascular disease and cancer</td>
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<tr>
<td>Gundgaard et al. (2003) (^69)</td>
<td>20% sample of Danish population followed 1993 to 1997</td>
<td>Based on a longitudinal study</td>
<td>Increased intake of fruits and vegetables to meet dietary recommendations vs. baseline intake</td>
<td>Morbidity and mortality from cancers</td>
</tr>
<tr>
<td>Walker et al. (2009) (^70)</td>
<td>Older population in Santiago, Chile</td>
<td>Economic evaluation to accompany CENEX study</td>
<td>Programme for complementary food in older people</td>
<td>Pneumonia incidence, walking capacity, and body mass index</td>
</tr>
<tr>
<td>Tomson et al. (1995)</td>
<td>Subjects with total cholesterol between 7.0 and 7.8 mmol/L without ischaemic heart disease or diabetes mellitus</td>
<td>RCT</td>
<td>Medium-intensity strategy following Swedish guidelines for non-pharmacological treatment of hypercholesterolaemia vs. low-intensity strategy</td>
<td>Serum cholesterol and costs of intervention</td>
</tr>
<tr>
<td>Reference</td>
<td>Population</td>
<td>Study Design</td>
<td>Intervention/comparison</td>
<td>Outcome(s) measured</td>
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<tr>
<td>Tice et al. (2001)</td>
<td>US general population targeted at those with hyperhomocystenemia</td>
<td>Cost effectiveness analysis using Coronary Heart Disease Policy Model</td>
<td>Hypothetical diet fortified with enriched grains to increase folic acid by 100 microg/day vs. vitamin therapy consisting of 1 mg folic acid and 0.5 mg cyanocobalamin/day vs. no fortification</td>
<td>Incidence of myocardial infarction and death from CHD; QALYs saved; medical costs</td>
</tr>
<tr>
<td>Gerber et al. (2006)</td>
<td>German general population</td>
<td>Cost benefit analysis with Markov model</td>
<td>Consumption of plant sterol enriched margarine vs. no consumption</td>
<td>CHD mortality and morbidity</td>
</tr>
<tr>
<td>Martikainen et al. (2007)</td>
<td>Finnish men and women ages 30, 40, 50, 60</td>
<td>Cost effectiveness analysis using Bayesian modeling</td>
<td>Consumption of plant stanol esters in spread vs. no consumption</td>
<td>CHD prevention</td>
</tr>
<tr>
<td>Gyles et al. (2010)</td>
<td>Canadian general population</td>
<td>Modified cost of illness approach</td>
<td>Increased consumption of foods enriched with plant sterols vs. no</td>
<td>CHD reduction</td>
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<tr>
<td>Study</td>
<td>Population</td>
<td>Methodology</td>
<td>Intervention</td>
<td>Outcome</td>
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<tr>
<td>Malla et al. (2007)</td>
<td>Canadian general population</td>
<td>Cost of illness approach</td>
<td>Consumption of trans fat free canola oil vs. no consumption</td>
<td>CHD reduction</td>
</tr>
<tr>
<td>Schmier et al. (2006)</td>
<td>US male population having suffered myocardial infarction</td>
<td>Decision analytic model</td>
<td>Omega-3 supplementation vs. no supplementation</td>
<td>Deaths delayed, cost per death delayed, fatal MIs avoided, cost per fatal MI avoided</td>
</tr>
<tr>
<td>Coyte (2005)</td>
<td>Canadian general population</td>
<td>Economic burden of illness approach</td>
<td>Increased consumption of flax products vs. no increase in consumption</td>
<td>CVD, type 2 diabetes</td>
</tr>
</tbody>
</table>
Figure 1 Search strategy flow chart