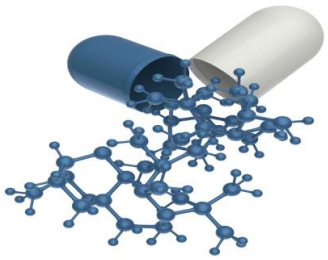
Targeted Use of Complementary Medicines: *Potential Health Outcomes & Cost Savings in Australia*



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A Frost & Sullivan Economic Report

Christopher Shanahan, M.S.
Robert de Lorimier, Ph.D.

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EXECUTIVE SUMMARY

Project Objective

The escalating costs associated with the increasing burden of disease in Australia are a major challenge for government, private health insurers and individuals. There is growing pressure to find solutions that will improve health outcomes and thus reduce health care expenditures. One available option is to motivate at risk individuals to adopt a prevention regimen that aims to reduce the risk of the occurrence of costly adverse events associated with major chronic disease in terms of hospital separations (the process by which a hospital records the end of a set of treatments associated with a specific medical event) and lost wage income due to illness. Complementary medicines (CM) use in well-defined high-risk populations is one type of regimen that could help decrease the occurrence of disease-attributed medical events and the economic consequences that could occur.

The objective of this report is to determine the potential net economic savings that could be realised given the usage of CM that are scientifically shown to reduce the occurrence of disease-related events among targeted populations. Specifically, this report will attempt to show that the use of specific CM can result in health care cost savings by preventing costly disease-related events.

A review of the scientific literature that covers six CM regimens across four disease conditions was conducted. From this review, an overall change in the relative risk of a given disease-related event resulting from the use of each of the CM regimens was derived. These relative risk reduction statistics were then used as an input into a cost-benefit scenario analysis to determine the potential change in hospital utilisation costs and wage income gains that could be realized if people in a specified high-risk population were to use each of the CM regimens that have scientifically substantiated health benefits. This report includes the following disease conditions, target high-risk populations, and associated CM regimens:

- Women aged 50 and over with **osteoporosis or osteopenia** and the potential net health care cost savings and productivity gains when using the combination of calcium and vitamin D or when using a magnesium regimen;
- All Australians aged 55 or over with **cardiovascular disease (CVD)** and the potential net health care cost savings and productivity gains when using omega-3 fatty acids or a folic acid, B6 and B12 regimen;
- All Australians aged 55 or over with **age-related macular degeneration (AMD)** and the potential net health care cost savings and productivity gains when using lutein and zeaxanthin;
- All Australians aged 20 or over with **moderate major depression** and productivity gains from the use of St. John's wort.

The objective of this report is to determine the potential net economic savings that could be realised given the usage of CM that are scientifically shown to reduce the occurrence of disease-related events among a targeted population.

Potential net benefits of $1.8 billion and $249 million can be realised from the use of calcium and vitamin D or magnesium, respectively.

Findings Summary

Osteoporosis:

In the case of osteoporosis-attributed bones fractures, the use of a calcium and vitamin D regimen and a magnesium regimen were explored to determine potential health care cost savings and productivity gains if all women aged 50 and over with osteopenia or osteoporosis used these CMs at preventive intake levels. Key findings for each case study include:

- Calcium and vitamin D
  - Relative risk reduction: 19.7%
  - Average annual medical events avoided (2015-2020): 37,715 avoidable osteoporosis-attributed bone fractures
  - Average annual avoided hospital separation expenditure (2015-2020): $922 million
  - Average annual productivity gains (2015-2020): $900 million
  - Average annual net economic benefit, 2015-2020: $1.8 billion
  - Average annual benefit/cost ratio, 2015-2020: $22.34 per $1 spent on CM regimen

- Magnesium
  - Relative risk reduction: 5.2%
  - Average annual medical events avoided, 2015-2020: 7,815 avoidable osteoporosis-attributed bone fractures
  - Average annual avoided hospital separation expenditure, 2015-2020: $212 million
  - Average annual productivity gains, 2015-2020: $187 million
  - Average annual net economic benefit, 2015-2020: $249 million
  - Average annual benefit/cost ratio, 2015-2020: $2.50 per $1 spent on CM regimen

Cardiovascular Disease (CVD):

This report also explores the burden of cardiovascular disease (CVD) on Australian society and the potential health and economic benefits that can be realised if an omega-3 fatty acid regimen or a folic acid, B6 and B12 regimen was utilised by all Australians aged 55 and over diagnosed with CVD. Key findings for each case study include:

- Omega-3 fatty acids
    - Relative risk reduction: 4.9% (hospital separations) and 14.1% (CVD-attributed deaths)
    - Average annual medical events avoided, 2015-2020: 6,984 avoided CVD-attributed hospital separations and 2,473 CVD-attributed deaths
    - Average annual avoided hospital separation expenditure, 2015-2020: $194 million
    - Average annual productivity gains, 2015-2020: $405 million
    - Average annual net economic benefit, 2015-2020: $530 million
    - Average annual benefit/cost ratio, 2015-2020: $8.49 per $1 spent on CM regimen

- Folic Acid, B6 and B12
    - Relative risk reduction: 3.3%
    - Average annual medical events avoided, 2015-2020: 4,905 avoided CVD-attributed hospital separations
    - Average annual avoided hospital separation expenditure, 2015-2020: $150 million
    - Average annual productivity gains, 2015-2020: $68 million
    - Average annual net economic benefit, 2015-2020: $176 million
    - Average annual benefit/cost ratio, 2015-2020: $4.57 per $1 spent on CM regimen

Among all Australians aged 55 and over with CVD, $530 million and $176 million in potential net benefits can be realised from the use of omega-3 fatty acids or a folic acid, B6 and B12 regimen, respectively.

Avoiding AMD hospital separations and decreasing the severity of major depression can lead to positive health care savings and productivity gains.

Age Related Macular Degeneration (AMD):

Next, a review of the lutein and zeaxanthin scientific literature was conducted with the aim of qualifying and quantifying the expected change in the risk of an age related macular degeneration (AMD) hospital separation event given the use of lutein and zeaxanthin at preventive intake levels. Key findings include:

- Lutein and Zeaxanthin
    - Relative risk reduction: 22.4%
    - Average annual medical events avoided, 2015-2020: 1,095 avoidable age-related macular degeneration hospital separations
    - Average annual avoided hospital separation expenditure, 2015-2020: $27 million
    - Average annual productivity gains, 2015-2020: $27 million
    - Average annual net economic benefit, 2015-2020: $36 million
    - Average annual benefit/cost ratio, 2015-2020: $3.02 per $1 spent on CM regimen

Depression:

The last case study explored is the use of St. John's wort and the potential gains in quality of life among those Australians aged 20 and over suffering from moderate major depression. Specifically, this case study examines the current state of the scientific literature demonstrating that the use of St. John's wort can potentially yield a significant enhancement in the quality of life by means of lowering the severity of the disease symptoms from moderate major depression to mild major depression and, consequently, enhances their wage earnings potential. Key findings for each case study include:

- St. John's wort:
    - Reduction in chance of not experiencing a successful diagnosis transition: 24.0%
    - Average annual medical successful diagnosis transitions from moderate major depression to mild major depression, 2015-2020: 40,855 successful transitions
    - Average annual productivity gains, 2015-2020: $340 million
    - Average annual net economic benefit, 2015-2020: $300 million
    - Average annual benefit/cost ratio, 2015-2020: $8.05 per $1 spent on CM regimen

In summary, this report finds that significant health care cost savings and productivity gains could be realised in Australia from the use of certain CMs that have a substantial impact on the risk of costly disease-attributed events in high-risk populations. Given these economic gains and the potential positive health outcomes these CMs should be considered as a useful tool for reducing the burden of disease in Australia.

This report demonstrates that the use of specific complementary medicines among specified high risk populations can lead to positive health care cost savings.

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CHAPTER 1 INTRODUCTION

A less-than-healthy society leads to an increase in medical service expenditure and a loss in labour productivity. This means less tax revenue for Commonwealth and State and Territory governments and increased health care costs; in other words, a less-than-healthy economy.

Problem Statement

The burden of disease in Australia, and the economic costs associated with it, is an increasingly top-of-mind issue among policymakers. In 2013, over $140 billion was spent on health care services, which is nearly 9.1% of Australia's total gross domestic product (Australian Bureau of Statistics, 2014). A substantial portion of this cost is related to events that require costly inpatient procedures and emergency room visits, pharmaceuticals, home/nursing care services, and outpatient visits. Forty-two per cent of the total national health care expenditure is paid by the Commonwealth government, 27% is paid by the State and Territory governments, 22% by private insurance companies and other sources of private funding, and 17% is paid out-of-pocket by the individual (AIHW Health Expenditure Database, 2014). An additional economic burden of disease occurs in terms of lost productivity. Coronary heart disease and stroke were among the principal contributors to premature death, and major depression, bone disorders and age-related eye disease were among the top causes of disability (Department of Health, Queensland Government, 2013).

Due to the complexity of this social issue, policymakers are under escalating pressure to find solutions. One option of interest is prevention, which is a set of interventions or intervening behaviour modifications that inhibit or delay the manifestation of the chronic diseases and the attributed medical service utilisation events that drive up these economic costs. There are two principal types of prevention. Primary prevention is an intervention or intervening behaviour modification that directly decreases the risk of developing the disease in the first place and includes interventions such as immunisations or intervening behaviour modifications that reduce the exposure to harmful environmental factors, such as being around second-hand smoke (Woolf et al., 2009). Primary prevention is the best way to avoid long-term health care costs. Secondary prevention is an intervention or intervening behaviour modification that reduces the severity of diseases once the individual has been diagnosed with the disease (Woolf et al., 2009). Secondary prevention offers an opportunity for addressing short term health care costs because treatment services related to chronic disease complications are a major contributor to the health care cost system.

Understanding the possible economic benefits that can be achieved through the use of complementary medicines requires an understanding of the body of science that demonstrates the complementary medicines' efficacy.

The social benefits of prevention seem instinctual, but the economic benefits of prevention are less certain. Proponents state that prevention, especially the prevention of costly disease-attributed medical events and related services can help control increasing health care expenditures. However, some observers question whether it is cost effective to invest in prevention (Cohen, Neumann, & Weinstein, 2008; Russell, 2007). Clearly, a decline in the health of a society leads to an increase in medical service expenditures and a loss in labour productivity. This means less tax revenue for the Commonwealth, State, and Territory governments and increased health care costs; in other words, a less-than-healthy economy. Thus, if there are preventive regimens that have a body of scientific evidence showing that their use can lead to a decreased chance of costly, adverse events, then these should be considered as viable tools for moving society toward more optimal physical and economic health. However, the cost of a given prevention regimen underlines the necessity to look for smarter ways to control the associated costs by properly identifying high-risk populations where the greatest health benefits can be realised, such as using technologies that identify high-risk populations, adopting a health care model that incentivises stakeholders to address the antecedents of disease, and increasing prevention education.

The adoption of a low-cost preventive regimen, such as the daily use of CM, among a certain, high-risk population, is one option that could help decrease the occurrence of disease-attributed medical events and the economic consequences that could occur. CM is a broad term used to describe a wide range of health care medicines, therapies and other products that are not generally considered within the domain of conventional medicine (per NHMRC). In the context of the Australian regulatory environment and of this report, complementary medicines include vitamin, mineral and herbal products which make therapeutic claims. CMs come in many forms, including tablets, capsules, liquids, powders and more. A significant amount of scientific research has been conducted looking at the direct health benefits of using CM and numerous studies demonstrate that many of these medicines have a positive effect on reducing the risk of a secondary disease event.

This report explores the possible economic benefits that could be derived from using various CM regimens through the avoided hospital separation expenditures associated with disease events, and further calculates the additional indirect benefits through increased quality and quantity of remaining life years. In other words, this report assesses the potential net economic benefits that could be gained given the use of CM with scientifically-substantiated evidence by way of reducing the event occurrence risk of disease-attributed events among high-risk populations. Specifically, this report outlines a systematic approach to understanding and evaluating the scientific literature for each of the CM regimens explored in the study, and shows how to translate the health benefits derived from the use of CM into economic net benefits in terms of avoided health care costs and/or gains in productivity.

First, this report addresses the burden of osteoporosis-attributed bone fractures and the consequential costs of medical services. It examines the possible reductions in health care costs and increases in wage income savings when the target population of women aged 50 and over with diagnosed osteopenia or osteoporosis fully-utilise calcium and vitamin D or magnesium regimens. Then, reduction of cardiovascular disease (CVD) costs and productivity savings are explored when adults aged 55 and over with diagnosed CVD use omega-3 fatty acids or a folic acid, B6 and B12 regimen. The costs of age-related macular degeneration (AMD) and the possible reduction in health care costs and productivity savings when adults aged 55 and over diagnosed with AMD use lutein and zeaxanthin is then reviewed. Finally, changes in the severity of major depression and the reduction in productivity losses among adults aged 20 and over with moderate major depression when using St. John's wort is explored in order to determine if there are positive net benefits yet to be realised among the Australian populace.

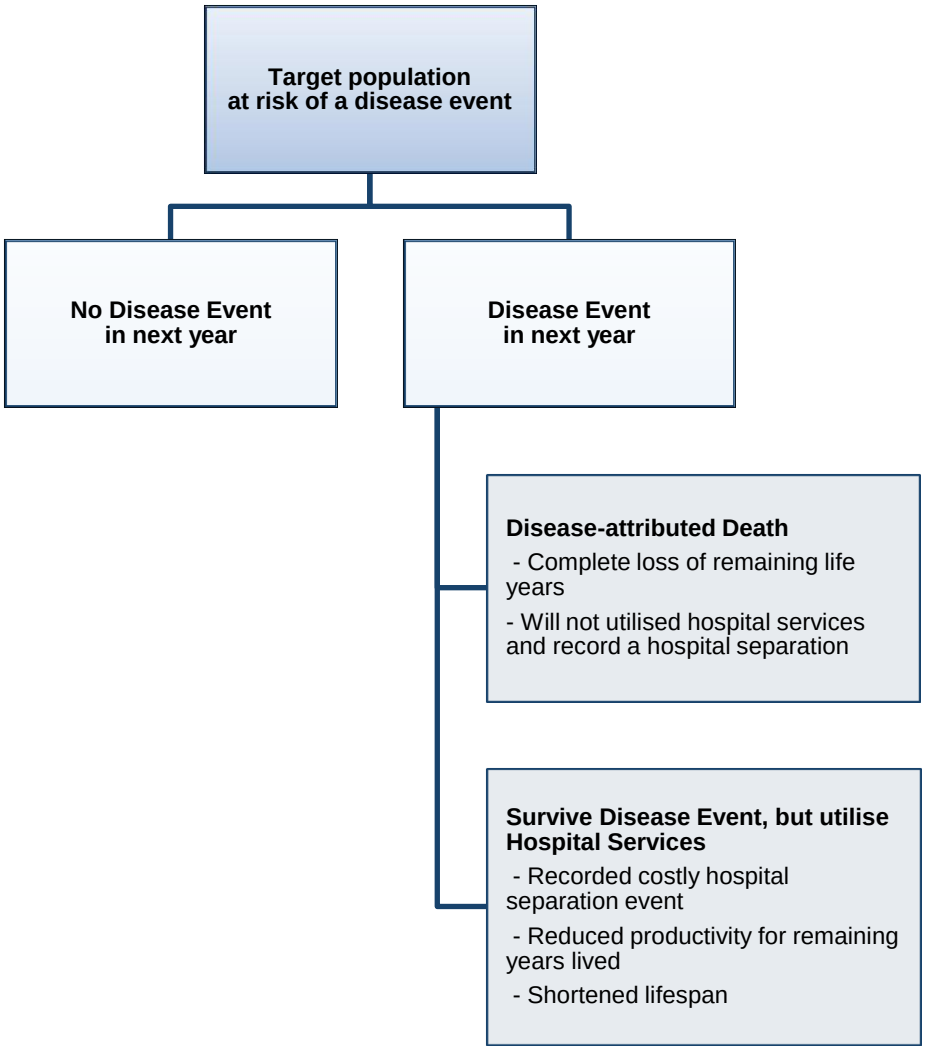
This report demonstrates that the use of specific complementary medicines among those consumers that are at a high risk of experiencing a costly disease-related event can lead to positive health care cost savings.

This analysis is based on comparing two health state scenarios in order to identify the potential savings or loss that can be realised if one scenario of events occurred versus another.

Research Methodology—From Health Benefits to Wealth Benefits

The cost-benefit analysis (CBA) tool presented in this report is based on assessing various cost scenarios to identify the potential savings or losses that can be realised if one scenario of events occurred versus another. Figure 1 illustrates the two basic types of possible disease event outcomes that an individual in an observed target population could face per year—morbidity or mortality. The first possible outcome of a specified disease is that the individual will not experience any type of disease event and does not have to utilise any hospital service, nor will they die. They live another year without experiencing a disease-related event. Another possible outcome is that an individual will suddenly die from the condition. The sufferers of a sudden disease-attributed death would not utilise hospital services. Another possible outcome is that the given individual will experience increased morbidity requiring increased spending on hospital services and medications, but will not die from the disease event in the observed point in time.

Figure 1—Disease Event Outcome Possibilities

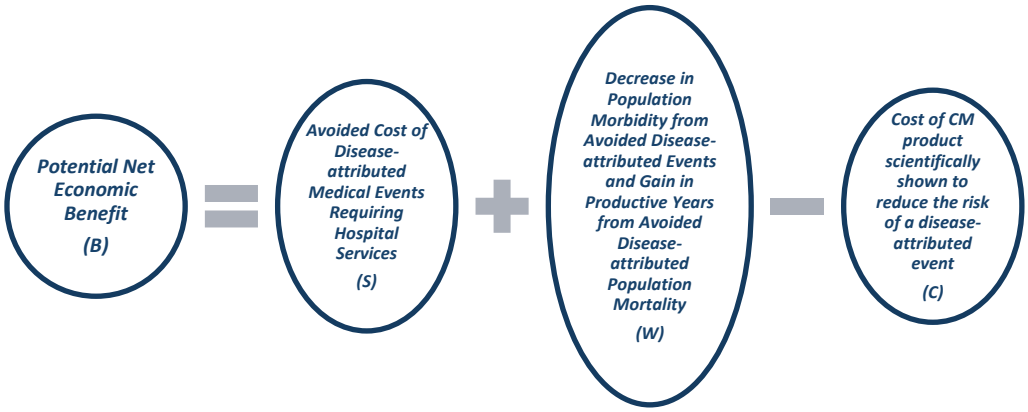


A medical event is equivalent to a hospital separation event as reported by the Australian Institute of Health and Welfare (AIHW), or Osteoporosis Australia in the case of osteoporosis-attributed bone fractures, which both report medical care services and associated expenditures by disease (Australian Hospital Data 2011–12, AIHW; Burden of Disease Analysis 2012–2022, Osteoporosis Australia). Specifically, a hospital separation is the process by which a hospital records the cessation of a set of treatments associated with a specific medical event (Australian Hospital Data 2011–12, AIHW). In other words, a medical event is defined as a case of a person experiencing an event that requires professional medical attention and, consequently, hospital or medical services such as outpatient or office-based provider visits, hospital inpatient stays, emergency department visits, prescribed medications, and home nursing.

Hospital separations are a good proxy for a disease event outcome because they are directly tied to the cost of treatment.

The cost-benefit model shown in Figure 2 flows from the disease event outcomes tree displayed in Figure 1. The benefits and costs considered in this model are avoided population medical expenditures related to hospital service utilisation (S), enhanced population quality of life and reduced population mortality from avoided disease-attributed medical events and deaths (W), and the annual population cost of a given CM utilised at disease-attributed event-preventive intake levels (C). The calculation of these potential population savings and costs provide an economic indication of the net monetary benefits that the use of a given CM can yield for society.

Figure 2—Generalised Cost Benefit Model and Associated Cost Benefit Variables



The cost-savings calculation compares the following two scenarios among a specified target population which is expected to receive the most benefits from using the CM:

A) Continued use of a given CM at current usage levels and

B) 100% utilisation of a given CM in the target population.

Relative risk reduction is a measure of the expected efficacy of the regimen under study. This measure can be used to determine the number of people who would need to take a given CM regimen to prevent one disease event.

Specifically, this model calculates the difference in benefits and cost between the two scenarios by identifying the change in each of cost/benefit variables and determining if the case of 100% utilisation generates net savings and gains compared to the current scenario in a given year. If this is the case for a pre-defined target population, then the implied recommendation is that a given CM user who is at a high risk of experiencing a disease event ought to include the benefit-conferring CM into their disease-event prevention regimen. With respect to how to best define a high-risk target population, there are multiple approaches that can be utilised such as looking at hospital separation statistics and identifying the population cohort as defined by basic demographic dimensions, such as gender, age or ethnicity, and including only those cohorts that are at the highest risk of experiencing a given disease-attributed event relative to the population at large.

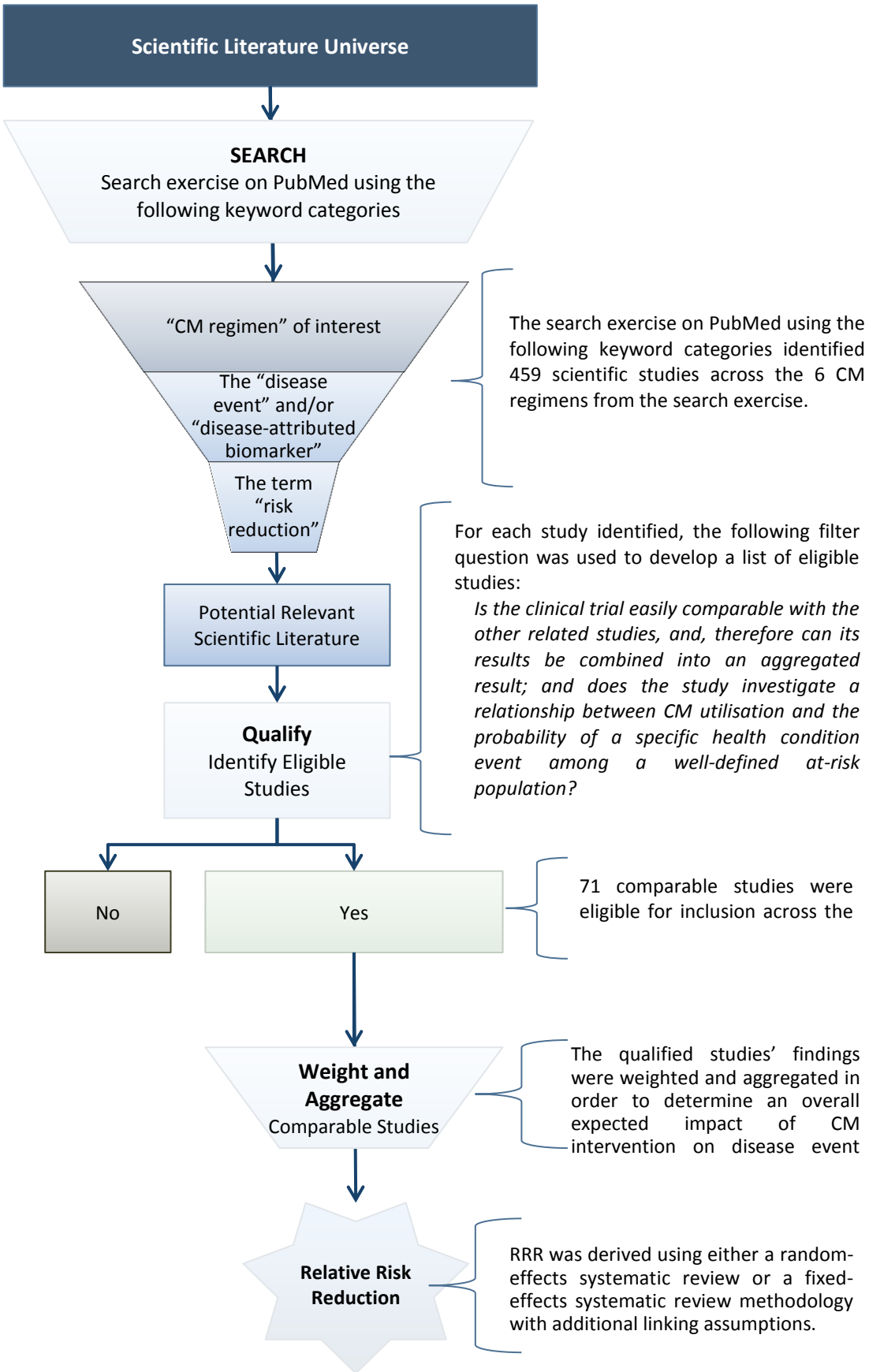
Due to data availability limitations, the current model does not follow individual people over time. In other words, this economic model treats all of the people in the target population as a homogeneous set of people that share as many characteristics as possible, including risk of a disease-attributed event. Also, the current model looks at each year as a separate independent scenario analysis and thus only average costs and benefits are calculated on an annual basis, which is then adjusted by the time period and cost/price inflation. The ideal situation would be to track an individual's risk by looking at their individual risk factors, such as their age, gender, specific biomarkers, etc., and then sum up each individual's potential costs and benefits to arrive at the total target population figures. Future work will look to close this gap, but there is enough information provided for a decision maker to determine the relative cost effectiveness of a given CM.

It should also be noted that not all costs and benefits from using or not using a given CM is incorporated into this equation. This equation is a generalised model that determines the net economic effect of using a given CM on the odds of a predefined set of event outcomes. Because of the additive nature of the model, one can easily add-in additional expected health benefits that are related or not related to the disease condition of interest. However, for the purposes of this study, each case study's cost and benefits mix is conservatively defined to be in line with the hypothesised relationship between CM use and a specified disease-attributed event for a given year. Finally, this model looks at annualised savings and gains that can be derived in a specific time period if use of a given CM occurred, but does not include future residual health care cost savings. It does capture future productivity gains through the variable L_{Pop}. Future research can easily incorporate residual health care cost savings. This also implies that the potential net financial benefits from using a given CM reviewed in this study is expected to be a conservative estimate.

In order to determine the number of avoidable adverse events between the two states, the relative risk of these events occurring between the two states is required. Relative risk reduction (RRR) is a measure of the expected efficacy of the regimen under study (Barratt et al. 2004). This measure can, in turn, be used to determine the number of people who would need to take a given CM regimen to prevent one disease event and/or death. This metric is derivable from the CM's associated scientific literature, especially randomised controlled trials (RCTs) which aim to determine an overall treatment's effect on the outcome of a given event when a treatment regimen is applied to the treatment group versus a control group. From these types of analyses, risk—and subsequently risk reduction of an event occurring—can be calculated and applied into a game theory-based cost-benefit model that helps key decision makers (including patients, health care professionals, governments, insurance companies, and employers) to determine whether a treatment is cost-effective and worth pursuing.

In order to infer the expected benefits from using a given CM related to the risk of a specific disease event occurring, and converting these findings into monetary units, a systematic review of a given CM regimen's scientific literature is typically undertaken in order to determine what the expected risk reduction will be. The output of a given CM's systematic review is then used to calculate the relative risk of disease event occurrence between the control group and the treatment group. Specifically, the goal is to collect a set of studies that test the same hypothesised relationship between the use of a given CM and the change in risk of experiencing a pre-defined medical event requiring costly treatment services. This approach allows for a systematic and objective approach to weigh each of the qualified reported effects and combine them to estimate a reasonable risk reduction factor that can be used to determine the number of avoided events and expenditures, if a given patient were to use a CM at a given intake level.

Figure 3—Literature Review Process



Specifically, the literature review process that this manuscript uses can be summarised into the following three steps:

1) **Search—find all scientific literature related to both the given chronic disease and the CM**

The first step was to conduct a scientific literature search exercise and build a database of studies that investigate the use of a given CM regimen of interest for the specific health condition of interest, as indicated by the study's match to keywords. For the analysis, the US National Library of Medicine's PubMed database was used to identify the relevant universe of studies using a set of keyword combinations. Keyword categories included:

- The CM regimen
- The disease event and/or biomarker of interest
- The term "risk reduction."

In total, 459 scientific studies were identified during the search exercise across the six CM regimens explored in this analysis and included a wide mix of study types including case studies, observational epidemiologic studies, and clinical trials adhering to best practice scientific methodologies.[1] All studies were retrieved and reviewed over the course of more than a year of research, from 1 February, 2013 to 30 June, 2014.

2) **Qualify—identify an eligible set of studies that investigate a causal relationship between CM utilisation and the disease event risk of interest**

Using systematic review best practices and defensible assumptions, the eligibility of a study's inclusion was dependent on the following criteria:

- Is the clinical trial easily comparable with the other related studies, and, therefore, can its results be combined into an aggregated result; and does the study investigate a relationship between CM utilisation and the probability of a specific health condition event among a well-defined at-risk population?

In total, 459 scientific studies were identified during the search exercise across the 6 CM regimens explored in this analysis and 71 studies were used in the risk reduction assessment.

1 In the case of St. John's wort, the meta-analysis results of Linde, Berner, and Kriston (2009) were used in this analysis. Following a similar search-qualify-aggregate systematic review approach followed by the authors of this analysis, 79 studies were identified during the search exercise and 18 studies were identified as eligible for inclusion in the weighting and aggregation step.

Randomised controlled trials (RCT) were preferred because they are designed to directly test for a cause-and-effect relationship between treatment and outcome, and their outcomes are the easiest to compare across studies. A study was not selected for inclusion in the analysis on the basis of the magnitude, direction, or statistical significance of the reported findings, nor was dose size considered as an eliminating factor in order to maximize a study's odds of being included in the qualified set. In total, 71 studies were eligible for inclusion in the next weighting and aggregation step of the systematic review across the six CM reviewed in this report.

3) **Weight and Aggregate—weighting and aggregating the studies' findings in order to determine an overall expected impact of CM intervention on disease event occurrence**

Each study's findings in the eligible set are weighted by the inter- and intra-study variance introduced by a given study's characteristics. Then, all of the studies in the set are aggregated in order to derive an overall expected risk reduction metric. There are multiple means to aggregation, but the most common and preferred aggregation process is a random-effects literature review model, which allows one to properly assess the results of a set of studies that address the same research question although each study varies in terms of sample size, regimen dose size, study protocol, research team, and a host of other study qualities (DerSimonian & Laird, 1986; DerSimonian & Kacker, 2007). In other words, the random-effects model helps to control for the differences in the quality of a given scientific study by weighting those studies that have smaller sample sizes and different research parameters.

For the purposes of this manuscript, a random-effects literature review method was utilised in the cases of calcium and vitamin D, omega-3, and vitamin B. In the case of St. John's wort, the meta-analyses conducted by the authors Linde, Berner, and Kriston (2009) was cited. In the case of magnesium and lutein and zeaxanthin, the breadth and depth of the available set of eligible studies was limiting, either due to the quantity of studies in general, or because the overall literature explores disease event risk-indicating biomarkers. In these cases, a fixed-model literature review approach was used, which is similar to the random-effects model except that inter-study variance is not controlled. The fixed-effects model simply uses the relative sample size of each study to derive the study weights. Furthermore, an additional assumption was required in these case studies to link the expected impact of using a given CM on disease event risk when the expected relationship between CM utilisation and a certain disease event risk-indicating biomarker is only known. In these cases, the simplest propositional logic was developed and used to connect these relationships. Further details on the specific logic used to deduce relative risk metrics are provided in each CM's respective chapter. A summary of literature reviews are shown in Table 1.1.

It is important to note that there is variance in the amount and type of scientific literature that shows evidence of the health benefits that can be derived from the use of CM. Each CM's known, expected health benefits exist at varying levels of understanding, agreement, and acceptance among the scientific community. For example, the health benefits of using calcium and vitamin D are well-understood and generally recognised as an effective tool in lowering the odds of an osteoporosis-attributed bone fracture. However, for other CM explored in this report, the mechanisms of action are still not fully understood or even fully recognised by the scientific community, such is the case of omega-3, despite decades of randomised control trials testing various direct relationships between CM use and a given disease-attributed event.

Thus, each CM case study reviewed in this report was analysed independently from one another, and cross-comparisons should be avoided. This is because the scientific literature does not support this approach; event risk for each CM was examined in a controlled setting, independent of the use of other CM. Also, benefits of different CMs (such as omega-3 fatty acids and folic acid, B6 and B12) in reducing the risk of a single disease (such as CVD) cannot be considered to be additive because each CM has different mechanisms of action and the scientific community does not fully understand whether using multiple CMs will result in an accumulative, synergistic, or antagonistic effect.

Table 1.1—Summary of Findings: Description of Literature Reviews

Complementary Medicine	Event Type	Target Population	# of People in Target Population in Australia, 2015	Number of Studies from Search	Number of Eligible Studies	Sample Size of Eligible Studies, people
Calcium and vitamin D	Osteoporosis-attributed bone fractures	Women aged 50 and over with Osteopenia and Osteoporosis	1.9 million	49	7	50,828
Magnesium	Osteoporosis-attributed bone fractures	Women aged 50 and over with Osteopenia and Osteoporosis	1.9 million	12	2	1,096
Omega-3	CVD-attributed hospital separations	All adults aged 55 and over with diagnosed CVD	866,000	95	18	63,958
Omega-3	CVD-attributed Deaths	All adults aged 55 and over with diagnosed CVD	866,000	95	14	59,242
Folic Acid, B6 and B12	CVD-attributed hospital separations	All adults aged 55 and over with diagnosed CVD	866,000	104	7	27,742
Lutein and Zeaxanthin	AMD-attributed hospital separations	All adults aged 55 and over with diagnosed AMD	168,000	25	5	9,706
St. John's wort	Successful transitions from moderate to mild major depression	All adults aged 20 and over with diagnosed moderate major depression	235,000	79	18	3,064

Table 1.2—Summary of Findings: Description of Literature Reviews (continued)

Complementary Medicine	Study Event Rates	RRR[2] (Confidence Interval (CI) 95%: Lower - Upper)	Expected Number of Avoided Events, 2015
Calcium and vitamin D	10%	19.7% (CI 95%: 18.3% to 21.1%)	36,783
Magnesium	8%	5.2% (CI 95%: 1.8% to 7.1%)	7,622
Omega-3 and CVD-attributed Hospital Separations	16%	4.9% (CI 95%: 3.3% to 6.4%)	6,811
Omega-3 and CVD-attributed Deaths	4%	14.1% (CI 95%: 12.6% to 15.6%)	2,418
Folic Acid, B6 and B12	16%	3.3% (CI 95%: 1.6% to 5.1%)	4,784
Lutein and Zeaxanthin	3%	22.4% (CI 95%: 0.6% to 49.6%)	1,068
St. John's wort	65%[3]	24.0% (CI 95%: 14.8% to 33.1%)	39,845

2 Relative risk reduction (RRR) of an event occurring between the experimental group versus the control group. See each chapter's explanation of the derivation of RRR for more details.
3 Per cent of the population that did not experience a successful diagnosis transition from moderate major depression to mild major depression. In other words, the relative probability increase of a successful diagnosis transition from moderate to mild major depression.

Economic Findings Summary

Significant health care cost savings and productivity gains can be realised by key stakeholders in society from the use of CMs that have a demonstrable and substantial effect on the risk of costly disease-attributed events when high-risk populations are targeted. The case studies explored in this manuscript show that there is significant health care cost savings potential and productivity gains to be earned by the health care system which can be realised through a concerted effort in identifying high-risk populations and motivating them to use CM with substantiated efficacy. Understanding the link between the health potential from full utilisation of a given CM regimen with scientifically-substantiated efficacy and health potential, will help key stakeholders in the short and long terms. Patients, general practitioners, employers, and public and private insurance companies will be equipped to make better decisions and recommendations on the best course of action to help minimise current and future societal costs while maximising benefits.

Table 1.3—Summary of Findings: Economic Benefits from Using Complementary Medicines, $ Million, 2015[4]

Complementary Medicine	Avoided Hospital Separations Costs (S)	Total Productivity Gains (W)	Total Cost of CM (C)	Net Economic Benefit (B)	Share of Net Benefits (% of B)			
					Common-wealth Gov't	State and Territory Gov't	Private Insurance[5]	Individ-uals
Calcium and vitamin D	$866.7	$834.7	($80.2)	$1,621.3	27.9%	14.5%	6.4%	51.2%
Magnesium	$199.6	$173.0	($150.0)	$222.5	35.8%	15.0%	6.9%	42.3%
Omega-3	$182.7	$376.4	($69.4)	$489.7	26.0%	10.4%	4.1%	59.5%
Folic Acid, B6 and B12	$140.7	--	($41.7)	$99.0	39.2%	18.2%	8.7%	33.9%
Lutein and Zeaxanthin	$24.5	$24.0	($18.4)	$30.1	36.4%	14.1%	6.3%	43.2%
St. John's wort	--	$295.8	($40.1)	$255.7	20.7%	3.3%	0.0%	76.0%

4 All monetary figures presented in this reported are in Australian dollars

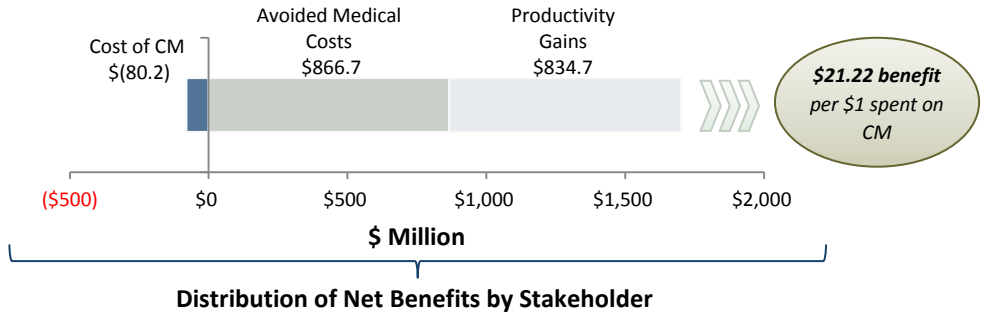
5 Includes other private sources of payments

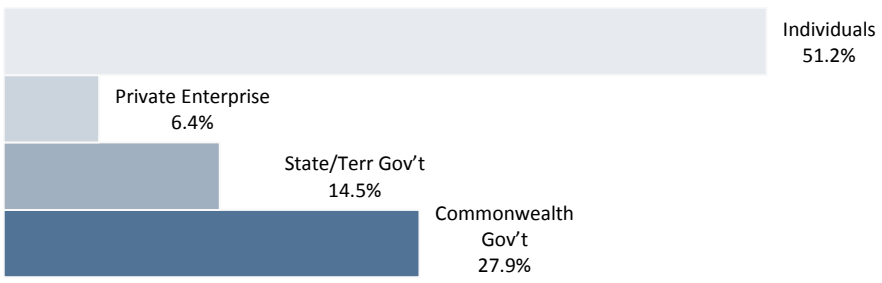
Calcium and Vitamin D

- **Target Population:** In 2015, there will be **1.9 million women** aged 50 and over with osteopenia or osteoporosis who are at risk of experiencing a costly disease-attributed bone fracture.
- **Adverse Outcome Risk: 10%** of the target population will experience an osteoporosis-attributed bone fracture based on the review of the calcium and vitamin D scientific literature.
- **Science-based Impact of Calcium and Vitamin D Use:** The relative risk of an individual in the target population experiencing a disease-attributed adverse outcome is reduced by **19.7%** given the use of calcium and vitamin D at preventive intake levels. This translates into a potential of **36,783** avoidable disease-attributed events in 2015 given 100% utilisation of the CM.
- Economic Implications:
  - Avoidable Hospital Separations Costs (S): **$866.7 million**
  - Total Productivity Gains (W): **$834.7 million**
  - Total Cost of Calcium and Vitamin D (C): **$80.2 million**
  - Net Economic Benefit (B): **$1,621.3 million**
- Distribution Share of Net Benefits:
  - Commonwealth Government: **27.9%**
  - State and Territory Governments: **14.5%**
  - Private Insurance and Enterprises: **6.4%**
  - Individuals: **51.2%**

Given the utilisation of calcium and vitamin D complementary medicines at preventive daily intake levels by all Australian women age 50 and older diagnosed with osteoporosis, $1.6 billion in avoidable hospital utilisation costs and productivity gains are potentially realisable in 2015.

Figure 4—Calcium and Vitamin D Summary Economic Results, AU$ million, 2015



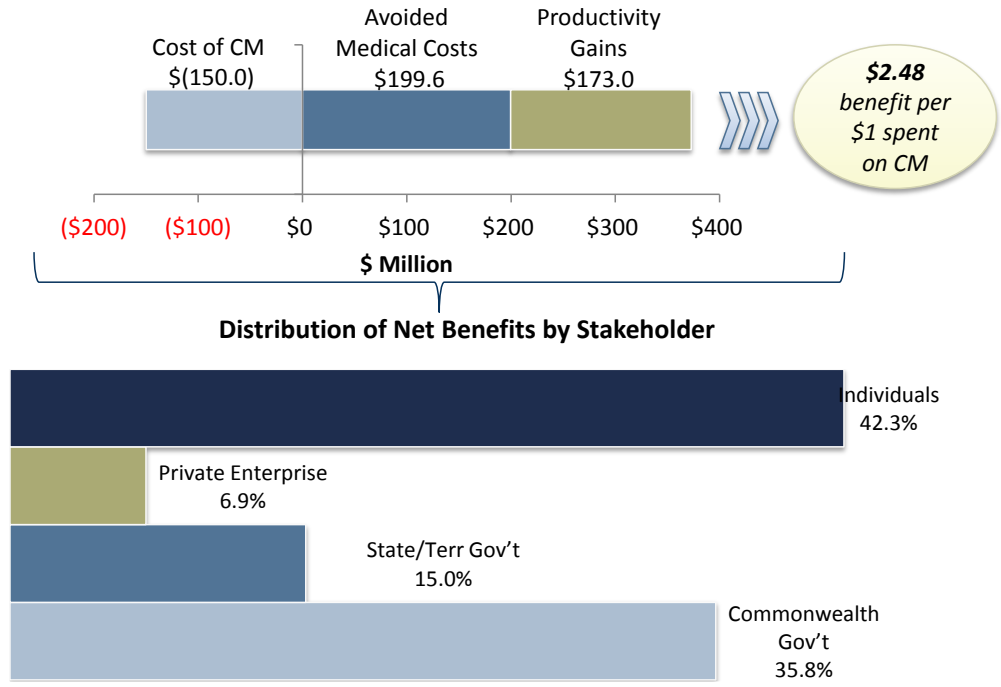


Magnesium complementary medicine intake could result in almost $223 million in avoidable hospital utilisation costs if all Australian women aged 50 and older diagnosed with osteopenia or osteoporosis were to use magnesium CMs at preventive intake levels in 2015.

Magnesium

- **Target Population:** In 2015, there will be **1.9 million women** aged 50 and older with osteopenia or osteoporosis at risk of experiencing a costly disease-attributed bone fracture.
- **Adverse Outcome Risk: 8%** of the target population will experience an osteoporosis-attributed bone fracture based on the review of the magnesium scientific literature.
- **Science-based Impact of Magnesium Use:** The relative risk of an individual in the target population experiencing a disease-attributed adverse outcome is reduced by **5.2%** given the use of magnesium at preventive intake levels. This translates into a potential **7,622** avoidable disease-attributed events in 2015 given 100% utilisation of the CM.
- Economic Implications:
  - Avoidable Hospital Separations Costs (S): **$199.6 million**
  - Total Productivity Gains (W): **$173.0 million**
  - Total Cost of Magnesium (C): **$150.0 million**
  - Net Economic Benefit (B): **$222.5 million**
- Distribution Share of Net Benefits:
  - Commonwealth Government: **35.8%**
  - State and Territory Government: **15.0%**
  - Private Insurance and Enterprises: **6.9%**
  - Individuals: **42.3%**

Figure 5—Magnesium Summary Economic Results, AU$ million, 2015

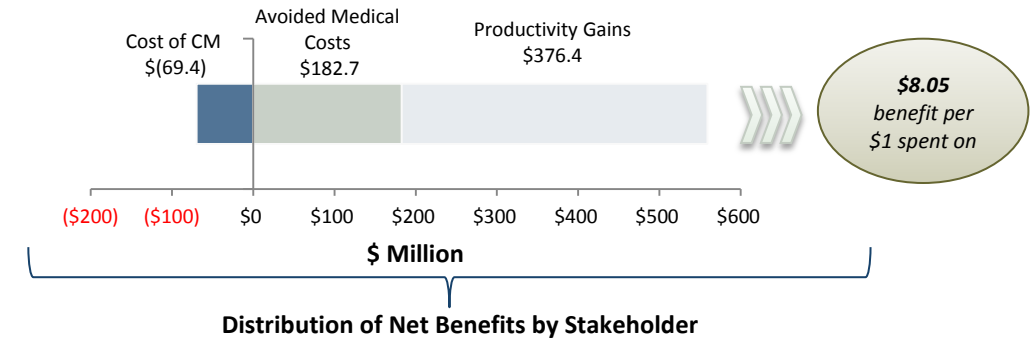


Omega-3

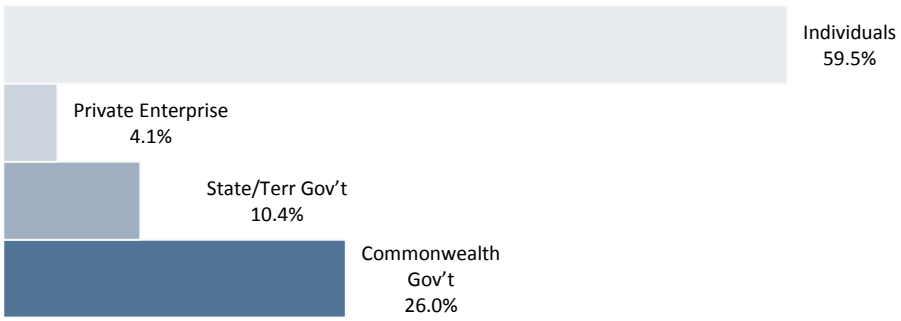
- **Target Population:** In 2015, there will be **866,000** people aged 55 and over with diagnosed CVD at risk of experiencing a costly CVD-attributed hospital separation.
- **Adverse Outcome Risk: 16%** of the target population will experience a CVD-attributed hospital separation and **4%** will experience a CVD-attributed death based on the review of the omega-3 scientific literature.
- **Science-based Impact of Omega-3 Use:** The relative risk of an individual in the target population experiencing a CVD-attributed adverse outcome is reduced by **4.9%** given the use of omega-3 at preventive intake levels. The relative risk reduction of a CVD-attributed death is **14.1%**. This translates into a potential of **6,811** avoidable disease-attributed events and 2,418 avoided deaths in 2015 given 100% utilisation of omega-3 complementary medicines.
- Economic Implications:
    - Avoidable Hospital Separations Costs (S): **$182.7 million**
    - Total Productivity Gains (W): **$376.4 million**
    - Total Cost of Omega-3 (C): **$69.4 million**
    - Net Economic Benefit (B): **$489.7 million**
- Distribution Share of Net Benefits:
    - Commonwealth Government: **26.0%**
    - State and Territory Governments: **10.4%**
    - Private Insurance and Enterprises: **4.1%**
    - Individuals: **59.5%**

The potential avoided hospital utilisation costs and productivity gains related to CVD through full utilisation of omega-3 complementary medicines at preventive intake levels among the target population can be as much as $489.7 million in 2015.

Figure 6—Omega-3 Summary Economic Results, AU$ million, 2015



Distribution of Net Benefits by Stakeholder

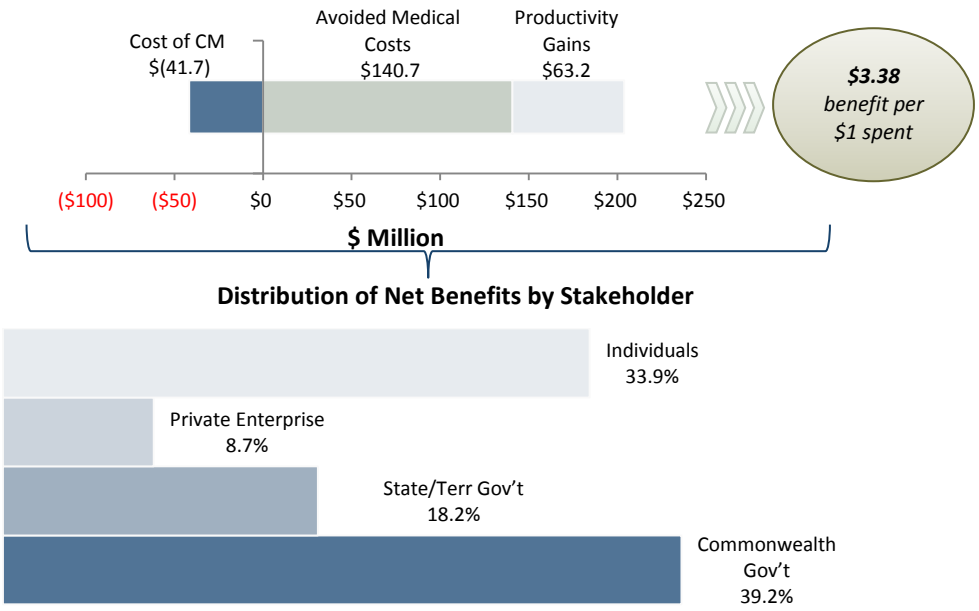


The full utilisation of B Vitamins folic acid, B6 and B12 among the target population at preventive intake levels can yield a net $99 million in 2015.

Folic Acid, B6 and B12

- **Target Population:** In 2015, there will be **866,000** people aged 55 and over with diagnosed CVD at risk of experiencing a costly CVD-attributed hospital separation.
- **Adverse Outcome Risk: 16%** of the target population will experience a CVD-attributed hospital separation based on the review of the folic acid, B6, and B12 scientific literature.
- **Science-based Impact of Folic Acid, B6 and B12 Use:** The relative risk of an individual in the target population experiencing a disease-attributed adverse outcome is reduced by **3.3%** given the use of the folic acid, B6 and B12 at preventive intake levels. This translates into a potential of **4,784** avoidable disease-attributed events in 2015 given the 100% utilisation of the folic acid, B6 and B12 complementary medicines.
- Economic Implications:
  - Avoidable Hospital Separations Costs (S): **$140.7 million**
  - Total Productivity Gains (W): **$63.2 million**
  - Total Cost of Folic Acid, B6 and B12 (C): **$41.7 million**
  - Net Economic Benefit (B): **$99.0 million**
- Distribution Share of Net Benefits:
  - Commonwealth Government: **39.2%**
  - State and Territory Governments: **18.2%**
  - Private Insurance and Enterprises: **8.7%**
  - Individuals: **33.9%**

Figure 7—Folic Acid, B6 and B12 Summary Economic Results, AU$ million, 2015

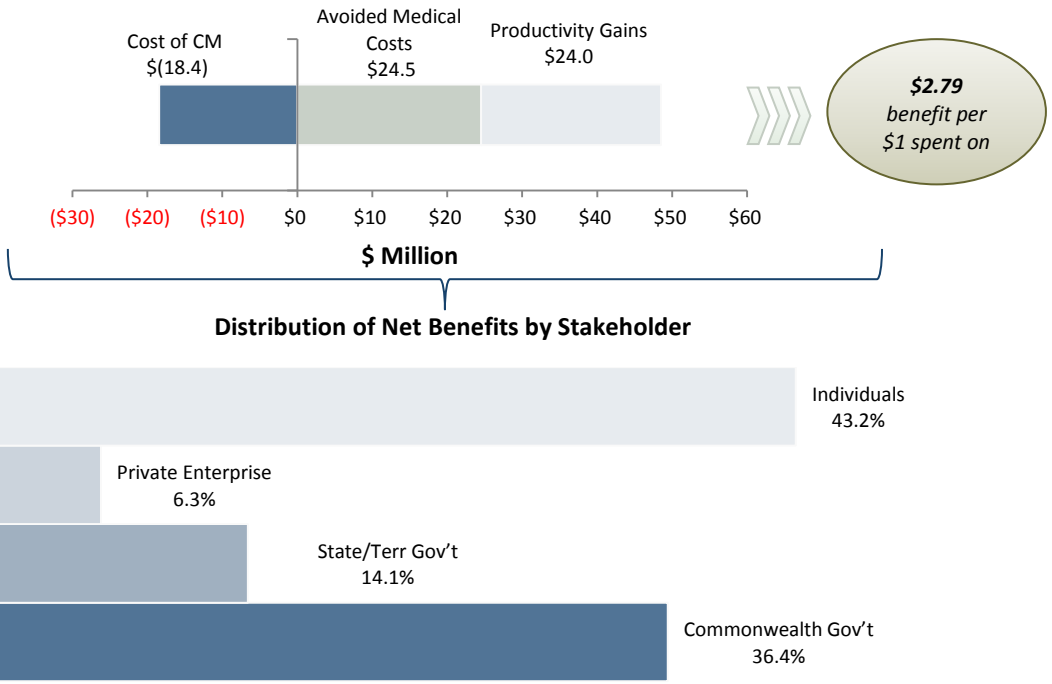


Lutein and Zeaxanthin

- **Target Population:** In 2015, there will be **168,000** people aged 55 and over diagnosed with age-related macular degeneration (AMD) at risk of experiencing a costly AMD-attributed hospital separation.
- **Adverse Outcome Risk: 3%** of the target population will experience an AMD-attributed hospital separation based on the review of the lutein and zeaxanthin scientific literature.
- **Science-based Impact of Lutein and Zeaxanthin Use:** The relative risk of an individual in the target population experiencing an AMD-attributed adverse outcome is reduced by **22.4%** given the use of lutein and zeaxanthin at preventive intake levels. This translates into a potential of **1,068** avoidable disease-attributed events in 2015 given the 100% utilisation of lutein and zeaxanthin complementary medicines.
- Economic Implications:
  - Avoidable Hospital Separations Costs (S): **$24.5 million**
  - Total Productivity Gains (W): **$24.0 million**
  - Total Cost of Lutein and Zeaxanthin (C): **$18.4 million**
  - Net Economic Benefit (B): **$30.1 million**
- Distribution Share of Net Benefits:
  - Commonwealth Government: **36.4%**
  - State and Territory Governments: **14.1%**
  - Private Insurance and Enterprises: **6.3%**
  - Individuals: **43.2%**

Based on the deduced eye health benefit from using lutein and zeaxanthin CMs, this study found that the net economic benefit potential of lutein and zeaxanthin use in terms of avoided hospital separations can amount to $30.1 million in 2015.

Figure 9— Lutein and Zeaxanthin Summary Economic Results, AU$ million, 2015

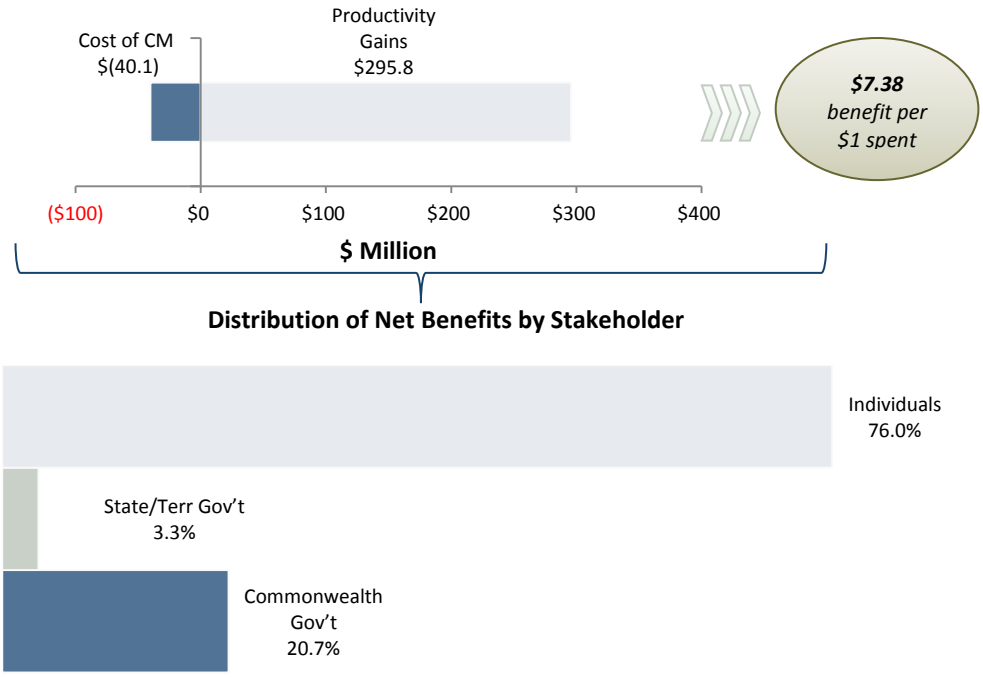


St. John's wort has been scientifically shown to have a significant impact on lowering the severity of major depression, and consequently, net productivity gains can yield a net benefit of $255.7 million in 2015.

St. John's wort

- **Target Population:** In 2015, there will be **235,000** people aged 20 and over diagnosed with moderate major depression.
- **Adverse Outcome Risk: 35%** of the target population experienced a successful diagnosis transition from moderate major depression to mild major depression, meaning that the remaining 65% did not see an improvement.
- **Science-based Impact of St. John's wort Use:** The chance of an individual in the target population not experiencing a successful diagnosis transition is reduced by **24.0%** given the use of St. John's wort at preventive intake levels. This translates to a potential of **39,845** additional successful diagnosis transitions in 2015 given the use of St. John's wort complementary medicines among the entire target population
- Economic Implications:
  - Total Productivity Gains (W): **$295.8 million**
  - Total Cost of St. John's wort (C): **$40.1 million**
  - Net Economic Benefit (B): **$255.7 million**
- Distribution Share of Net Benefits
  - Commonwealth Government: **20.7%**
  - State and Territory Governments: **3.3%**
  - Individuals: **76.0%**

Figure 10— St. John's wort Summary Economic Results, AU$ million, 2015



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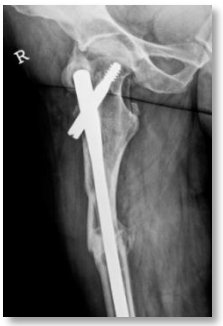

CHAPTER 2 THE ECONOMIC BENEFITS FROM AVOIDED OSTEOPOROSIS-ATTRIBUTED FRACTURES FROM CALCIUM AND VITAMIN D AND MAGNESIUM UTILISATION

More than 1.8 million Australians (3.1%) are believed to have lived with osteopenia or osteoporosis in 2013.

Problem Statement

Osteoporosis is a disease in which the density and quality of bone are reduced, leading to weakness of the skeleton (Watts, Abimanyi-Ochom, and Sanders, 2013). The condition increases the risk of fracture, particularly at the hip, spine, and wrist. More than 1.8 million Australians are believed to live with osteopenia or osteoporosis (Australian Bureau of Statistics, 2011–12). However, it can be safely assumed that data about diagnosed cases underestimates the actual prevalence of this condition because osteoporosis has no symptoms and is often undiagnosed until a fracture occurs. A recent study by Osteoporosis Australia estimates that the actual prevalence, just among the population aged 50 and over, is more than 1 million (Watts, Abimanyi-Ochom, and Sanders, 2013). Furthermore, women account for approximately 80% of the prevalence of this condition in this particular population (Watts, Abimanyi-Ochom, and Sanders, 2013).

The study also estimated that there were 140,822 fractures in 2012 that could be attributed to either osteoporosis or osteopenia. Furthermore, there will be a 30% increase in the annual number of fractures resulting from these conditions by 2022, resulting in over 183,000 fractures per annum (Watts, Abimanyi-Ochom, and Sanders, 2013).

While osteoporosis usually does not directly cause deaths, osteoporotic fractures can lead to premature deaths, especially among the elderly. The burden of disease study by Osteoporosis Australia estimates that there were roughly 3,480 deaths resulting from fractures attributed to osteoporosis or osteopenia in 2012, of which the vast majority occurred in those aged 70 years and older. The majority of these deaths were associated with a fracture of the hip (49%), while a further 16% were associated with a vertebral fracture (Watts, Abimanyi-Ochom, and Sanders, 2013).

Australians over the age of 50 with either osteoporosis or osteopenia are estimated to have cost society over $2.87 billion in 2013 (Watts, Abimanyi-Ochom, and Sanders, 2013; author calculations). Based on the above-mentioned growth rate of fractures, in 2015, the total costs are predicted to be over $3.19 billion. These costs include ambulance services, hospitalisations, emergency department and outpatient services, rehabilitation, aged care, and community services.

Australian women over the age of 50 with either osteoporosis or osteopenia cost society over $2.87 billion in 2013.

Table 2.1—Burden of Osteoporosis: All Women 50 and Over, 2013 - 2020

Metric	Measure	2013	2015	2015 to 2020
Target population with osteoporosis and osteopenia, people[6]	--	1,814,772	1,856,170	--
Total osteoporosis-attributed bone fracture hospital separations[7]	--	101,037	104,634	643,486
Risk of bone fracture hospital separation events[8]	5.6%	--	--	--
Discount on residual person years due to occurrence of osteoporosis-attributed hospital separation (D)[9]	0.31	--	--	--
Average remaining life expectancy per member of the target population, years (L)[10]	7	--	--	--
Mean claimed expenditures per person[11]	--	$28,411	$31,018	--

The following chapter makes the case that there are potentially significant health care cost savings and productivity gains that can be realised through the use of calcium and vitamin D, or magnesium. Specifically, the following case studies show a process whereby a decision maker first examines the body of scientific literature that tests the link between the use of a specified CM and the risk of an osteoporosis-attributed bone fracture in order to determine an overarching expected level of risk reduction. These aggregated risk reduction factors are then fed into a game theory-based cost-benefit scenario analysis model with the intent to determine the potential health care cost savings and productivity gains realised if the entire population of Australian women aged 50 and older were to adopt either a calcium and vitamin D, or magnesium regimen. Substantially positive net benefits will provide support for the decision maker in arriving at an optimal health, and wealth, choice.

6 Includes only women aged 50 and over. Source: Watts, Abimanyi-Ochom, and Sanders, 2013; author calculations

7 Source: Watts, Abimanyi-Ochom, and Sanders, 2013; author calculations

8 Bone fracture event risk among target population

9 Source: Australian Institute of Health and Welfare 2011–12; Feldman and Johansson, 2013; author calculations

10 Source: Australian Institute of Health and Welfare 2011–12; Feldman and Johansson, 2013; author calculations

11 Total claimed expenditures on osteoporosis-attributed hospital separations divided by total osteoporosis-attributed bone fracture hospital separations

Calcium and Vitamin D

Product Description

Calcium is an essential mineral that is stored in the bones of the human body. It is not only required for the normal development and maintenance of the skeleton, but also to ensure the optimal operation of neuromuscular and cardiac functions (Memorial Sloan-Kettering Cancer Centre, 2014). While the required intake of calcium is typically met through the consumption of calcium-rich foods such as dairy products, nuts, and fish, the absorption and metabolism of this mineral is dependent on vitamin D (Memorial Sloan-Kettering Cancer Centre, 2014).

There are two main types of vitamin D. The first, named D3 or cholecalciferol, is produced naturally by the body through a reaction to sunlight on the skin and is the more potent of the two. The other, which is known as D2 or ergocalciferol, is found in a limited range of foods. The primary function of vitamin D in the human body is to improve the efficiency of the small intestine in absorbing serum calcium and phosphorus from a regular diet, in order to regulate the concentration of these minerals in the body to within acceptable limits (Memorial Sloan-Kettering Cancer Centre, 2014). Sufficient vitamin D intake is particularly important in low-light conditions, as the body's ability to synthesise the compound is dependent on exposure to sunlight.

Older adults (>51 years of age) are recommended to have at least 10 to 15 micrograms of vitamin D per day in their diet. They are also advised to consume at least 1,300 milligrams of calcium in their daily diet (Nutrient Reference Value – Australia and New Zealand).

Table 2.2—Calcium and Vitamin D: Product Description, 2013 and 2015

Metric	Measure
Expected median daily cost of CM per capita, 2013[12]	$0.15 per day
Expected annual median cost of CM per capita, 2015[13]	$55.19 per year
Current CM usage rates among target population[14]	19%
Cost of CM utilisation of the target population, 2015	$80.2 million

12 These estimates were based the average retail price, per dose, of a selection of top-selling calcium and vitamin D products for sale in Australia through Internet sales channels.
13 This measure is calculated as the product of the expected median daily cost of calcium and vitamin D per capita, at preventive intake levels, and for 365.25 days per year.
14 Source: Osteoporosis Australia, 2013; Brownie, 2005; author calculations

The relative risk reduction of an osteoporosis-attributed fracture event given the use of calcium and vitamin D at preventive daily intake levels is a 19.7% reduction in risk.

Approximately 19% of women aged 50 and older are regular users of calcium and vitamin D CM (Osteoporosis Australia, 2013; Brownie, 2005). This suggests that 81% of the target population are not realising the benefits of regular usage and, thus, are not avoiding the associated expenditures. However, it is expected that women who have been diagnosed with osteopenia or osteoporosis have higher calcium and vitamin D utilisation rates, likely as high as one-third of the target, addressable population. Furthermore, a review of the retail calcium plus vitamin D products on the market revealed that the cost of a daily dose of calcium and vitamin D ranges from $0.08 to $1.35. The median cost of calcium and vitamin D was $0.15 per day in 2013. Using this figure, the expected cost of consumption for each woman aged 50 and older diagnosed with osteopenia or osteoporosis would be $55.75 per person in 2015.

Clinical Research Review

There has been a significant amount of research exploring the benefits of calcium and vitamin D utilisation among the elderly, with the goal of minimising osteoporosis and its complications. In order to quantify the possible health effects of calcium and vitamin D utilisation, Shanahan and de Lorimier (2013) conducted a rigorous search of the scientific literature that focused on published studies quantifying the effect of utilisation on fracture risk. Studies that tested for a direct causal relationship between the intake of calcium and vitamin D and the relative risk of a disease event were preferred by the authors and studies were not selected on the basis of the magnitude, direction, or statistical significance of the reported findings. Forty-nine studies were identified in a search exercise conducted on PubMed using a combination of keywords including “calcium” and/or “vitamin D”; “osteoporosis” and/or “fracture”; and “risk reduction.” RCTs were preferred because they are designed to directly test for a cause-and-effect relationship between utilisation and osteoporosis-attributed bone fractures. As a result, seven RCT studies were identified as being eligible (Shanahan and de Lorimier, 2013). All seven studies included subjects aged 50 or older, and in four of the studies, the subjects were only women.

By updating the systematic review of Shanahan and de Lorimier (2013), the relative risk reduction of an osteoporosis-attributed fracture event given the use of calcium and vitamin D at preventive daily intake levels, was a statistically significant 19.7% (95% CI: 18.3% to 21.1%) after controlling for variance because of sample size, research methodologies and study protocols, and patient population differences within each study and among all studies. The control event rate or the risk of an osteoporosis-attributed bone fracture, as reported in the calcium and vitamin D literature was 10%. Consequently, it was found that 50 people would need to be treated with calcium and vitamin D in order to avoid one osteoporosis-attributed fracture event (Shanahan and de Lorimier, 2013). A description of the included studies and the results of the effect aggregation are shown in Table 2.3.

Table 2.3—Calcium and Vitamin D Literature Review: Description of the Eligible Studies and Expected Avoided Hospital Separation Results

Author	Year	Total sample (N)	TER[15]	CER[16]	Relative risk (RR)	Study weight
Jackson	2006	36,282	6.6%	7.3%	97.00%	22.55%
Chapuy (1992)	1992	3,270	9.8%	13.1%	74.50%	16.62%
Dawson-Hughes	1997	389	5.9%	12.9%	45.70%	6.15%
Porthouse	2005	3,314	4.4%	4.6%	96.20%	19.89%
Grant	2005	2,638	14.1%	14.7%	95.70%	14.49%
Larsen	2004	7,073	6.4%	7.9%	81.30%	20.30%
Chapuy (2002)	2002	583	6.6%	7.3%	59.20%	23.40%

Table 2.4—Calcium and Vitamin D Literature Review: Expected Avoided Hospital Separation Results

Metric	Measure (Confidence Interval (CI) 95%: Lower - Upper)
Risk of an Osteoporosis-Attributed Bone Fracture in the Control Group—Event Rate of Aggregated Scientific Findings, Risk(x)	10%
Weighted relative risk reduction of a osteoporosis-attributed bone fracture hospital separation RRR(x)	19.67% (95% CI: 18.3% to 21.1%)
Number of people needed to treat to avoid one osteoporosis-attributed bone fracture hospital separation, NNT(x), people	50
Expected number of avoided osteoporosis-attributed bone fracture hospital separations given 100% use of CM at daily preventive intake levels per year among target population, 2013[17]	36,058
Expected number of avoided losses in osteoporosis-attributed bone fracture quality-adjusted life years given 100% use of CM at daily preventive intake levels per year among target population, years, 2013	25,489

15 TER: % of subjects in treatment group who experienced event relative to number in the treatment group
16 CER: % of subjects in control group who experienced event relative to number in the control group
17 All Australian women aged 50 and over

Total possible medical cost avoidance and productivity gains can be over $1.7 billion and net benefits derived from the full utilization of calcium & vitamin D can be over $1.6 billion in 2015.

Economic Results

The following case study on calcium and vitamin D considers both health care cost savings derived from avoided bone fracture hospital separations and the gains in productive time of the entire population of Australian women aged 50 and over diagnosed with osteoporosis. Thus, the following equation is used to calculate net benefits:

1. $$B_t = Pop_t * (1 - c_t) * \Big(\big(h_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x)) + \bar{I}_t * L_{Pop} * D * b_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x)) \big) - d_t \Big)$$

where h_t is the expected per-person cost of a disease-attributed medical event in year t, $\bar{I}_t$ is the median per capita wage income for a member of the target population Pop_t, D is the change in disability-adjusted life years lost due to a osteoporosis-attributed bone fracture, L_{Pop} is the average remaining life expectancy, in years, per member of the target population, and d_t is the expected per-person cost of a given CM regimen utilisation per year t. b_t is a population weight that reflects the per cent of the target population that is currently in the labour force. This weight is applied because only that percentage of the population will actually be eligible in earning back the expected productivity gains. It is expected that 33.5% of Australian women aged 50 and older are in the work force based on estimates from the Australian Bureau of Statistics. Finally, c_t is the expected current per cent of calcium and vitamin D users in the target population. This subset of the target population is already realising the purported benefits of using calcium and vitamin D and should be removed in order to assess the yet-to-be-realised productivity gains. The following section reports the expected cost and benefit results for 2015 and detailed statistics for 2013 to 2020 are presented in the Appendix.

The results revealed that 50 people need to treat with calcium and vitamin D in order to avoid one bone fracture. Among all Australian women aged 50 and over with osteoporosis, this corresponds to 36,783 potentially-avoidable bone fractures in 2015. Given these avoided events and making projections on potential avoidances into the future, the avoided medical event expenditures, S, can be $866.7 million in 2015.

Table 2.5—Calcium and Vitamin D Cost Benefit Analysis: Summary Results[18]

Metric	Measure	Upper	Lower	Annual Average	Cumulative
	2015	95% Confidence Interval		2015 to 2020	
S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	$866,713,904	$927,439,374	$805,988,434	$921,779,244	$5,530,675,462
W: Gain in Productivity from Avoided Disease-attributed Events	$834,744,283	$893,229,833	$776,258,733	$900,363,388	$5,402,180,327
S + W: Total Benefit (Increase in Social Wealth)	$1,701,458,187	$1,820,669,207	$1,582,247,167	$1,822,142,631	$10,932,855,789
C: Total Cost of CM Consumption	$80,166,897	--	--	$80,205,823	$481,234,938
S-C: Net Benefit (Excludes Productivity)	$786,547,007	$847,579,659	$725,514,356	$841,573,421	$5,049,440,524
B: Net Benefit (Includes Productivity)	$1,621,291,290	$1,740,827,400	$1,501,755,180	$1,741,936,808	$10,451,620,851
B/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)	$21.22	$22.71	$19.74	$22.34	--

With respect to total productivity gains, *W*, among the target population of Australian women over the age of 50 with osteoporosis, $834.7 million in 2015 is potentially gained. The total economic benefits of calcium and vitamin D use in terms of avoided bone fractures, or *S + W*, can be $1,701.5 million in 2015. The cost of calcium and vitamin D use, *C*, would need to be $80.2 million in 2015 among the target population of Australian women aged 50 and over with osteoporosis. Subtracting out the cost of calcium and vitamin D consumption from total economic benefit can yield a net benefit, *B*, of $1,621.3 million in 2015. Table 2.5 details the final costs and benefits derived from calcium and vitamin D use among the target population.

With respect to the distribution of savings and gains among key stakeholders in 2015, 27.9% of the total net benefits (both savings in national health care expenditures and gains in productivity) is earned by the Commonwealth Government, 14.5% of net

18 Regarding the cost estimate forecasts, health care costs per person are expected to grow at an average annual growth rate of 3.5% from 2015 to 2020 based on the historical growth rate over the last 10 years. Growth in the targeted population is expected to occur at an average annual growth rate of 2.0 % during the forecast period, and it was assumed that growth in disease prevalence is equal to population growth. Calcium and vitamin D and magnesium retail prices are expected to grow at a compound annual growth rate of 2% per year. All future monetary figures on health care expenditures, productivity earnings, and CM spending were discounted at a 3% rate, according to normalisation best practices promoted by the World Health Organisation in order to control for inflationary effects (World Health Organisation, 2008).

More than one-half of the potential total benefits go to the individual and nearly 30% of potential total benefits can be realised by the Australian Government.

benefits is earned by the State and Territory governments, 6.4% would be distributed by private insurance companies and other sources of private funding, and 51.2% would be savings and productivity gains realised by individuals (AIHW Health Expenditure Database; author calculations). Table 2.6 provides the expected distribution of potentially-realisable net benefits to the primary stakeholders given the use of calcium and vitamin D among the target population.

Table 2.6— Calcium and Vitamin D Cost-Benefit Analysis: Distribution of Benefits, 2015[19]

Stakeholder	$
Commonwealth Government Health Care (HC) Expenditure Savings	$388,512,212
State, Territory, and Other Government HC Expenditure Savings	$217,789,608
Private Health Insurance Companies' HC Expenditure Savings (and Employers Indirectly through Health Insurance Benefit Plans)	$108,584,540
Individuals' HC Expenditure Savings	$151,827,544
Individual Wage Income Saved	$720,121,072
Commonwealth Government Income Tax Revenue Saved	$62,848,780
State and Territory Governments Tax Revenue Saved	$28,397,870
Commonwealth Government Company Tax Revenue Saved	$23,376,560
Share of Net Benefits (B) to Australian Commonwealth Government	27.9%
Share of Net Benefits (B) to State and Territory Government	14.5%
Share of Net Benefits (B) to Private Sector	6.4%
Share of Net Benefits (B) to Individuals	51.2%

19 Source: AIHW Health Expenditure Database; author calculations

Magnesium

Product Description

It is estimated that half the magnesium in the human body is found in bones, while a further third is located in muscles and soft tissues (Memorial Sloan-Kettering Cancer Centre, 2014). Magnesium is broadly distributed in the food supply in both plant and animal food forms. Foods particularly rich in magnesium include most green vegetables, legumes, peas, beans and nuts, certain shellfish, and spices. Magnesium plays an important role in promoting bone health through assisting in the metabolism of calcium (Nutrient Reference Value – Australia and New Zealand).

The recommended dietary intake of magnesium is 420 milligrams a day for male adults over the age of 31, while women over the ageof 31 are advised to consume at least 320 milligrams a day (Nutrient Reference Value – Australia and New Zealand).

Table 2.7—Magnesium: Product Description, 2013 and 2015

Metric	Measure
Expected median daily cost of CM per capita, 2013[20]	$0.25
Expected annual median cost of CM per capita, 2015[21]	$92.05
Current CM usage rates among target population[22]	10%
Cost of CM utilisation of the target population, 2015	$150.1 million

20 These estimates were based on the average retail price, per dose, of a selection of 9 top-selling magnesium products for sale in Australia through Internet sales channels.
21 This measure is calculated as the product of the expected median daily cost of magnesium per capita, at preventive intake levels, and for 365.25 days per year.
22 Source: Osteoporosis Australia, 2013; Brownie, 2005; author calculations

The relative risk reduction of an osteoporosis-attributed fractures event given the use of magnesium at preventive daily intake levels is a 5.2% reduction in risk.

Based on the review of the best-selling magnesium CM in leading brick-and-mortar, online, and mail-order retail establishments in Australia, the cost of a daily dose of magnesium is between $0.03 and $0.36. The median daily price will be $0.25 per day, or $92.05 annually, in 2013. Given this median price, the total expected average annual cost of consumption for 1.8 million people in the target population of women aged 50 or over with osteopenia or osteoporosis would be $150 million in 2015 and $900.7 million. Regarding the expected usage rates of magnesium CM among older Australian women, it is estimated that current utilisation rates are approximately 10% of the total population (Brownie, 2005; author calculations).[ii]

Clinical Research Review

For the purpose of this case study, the results of the systematic review analysis from Shanahan and de Lorimier (2013) was updated to determine the expected efficacy of magnesium on decreasing the risk of bone fractures attributed to osteoporosis. The objective was to identify a set of studies that tested for a causal relationship between magnesium supplement intake and the level of bone density, which is correlated to the relative risk of fracture. Shanahan and de Lorimier (2013) only included studies with similar protocols in an attempt to control for observable variance and were not selected on the basis of the magnitude or statistical significance of the reported findings.

Twelve studies were identified in a search exercise conducted on PubMed using the keyword combination “magnesium”; “osteoporosis” and/or “fracture”; and “risk reduction” (Shanahan and de Lorimier, 2013). No studies directly linked magnesium utilisation to bone fracture risk; however, twostudies linked magnesium dietary intake and its relation to bone mineral density (BMD) (Tucker et al., 1999; Ryder et al., 2005). In order to determine the change in fracture risk from changes in bone mineral density because of magnesium intake, Shanahan and de Lorimier (2013) used the FRAX online tool which takes factors such as sex, age, height, weight, and BMD at the femoral neck and obtained a value of 0.94 relative risk assuming a magnesium intake of 100 mg/day more than normal intake levels (WHO Fracture Risk Assessment Tool, World Health Organisation Collaborating Centre for Metabolic Bone Diseases, 2013; Shanahan and de Lorimier, 2013). Accordingly, the expected relative risk reduction of an osteoporosis-attributed fracture, given the use of magnesium CM at the preventive level of 100 mg per day, was 5.2% (95% CI: 1.8% to 7.1%) after controlling for variance due to sample size, research methodologies and study protocols, and patient population differences within each study and among all studies. In addition, the control event rate or the risk of an osteoporosis-attributed bone fracture, as reported in the magnesium literature was eight per cent. Therefore, 244 people must consume a magnesium CM at the daily preventive level of 100 mg in order to avoid one osteoporosis-attributed fracture (Shanahan and de Lorimier, 2013).

Table 2.8—Magnesium Literature Review: Expected Avoided Hospital Separation Results

Metric	Measure (Confidence Interval (CI) 95%: Lower - Upper)
Risk of an Osteoporosis-Attributed Bone Fracture in the Control Group—Event Rate of Aggregated Scientific Findings, Risk(x)	8%
Weighted relative risk reduction of an osteoporosis-attributed bone fracture hospital separation RRR(x)	5.2% (95% CI: 1.8% to 7.1%)
Number of people needed to treat to avoid one osteoporosis-attributed bone fracture hospital separation, NNT(x), people	244
Expected number of avoided osteoporosis-attributed bone fracture hospital separations given 100% use of CM at daily preventive intake levels per year among target population, 2013	7,472
Expected number of avoided losses in osteoporosis-attributed bone fracture quality-adjusted life years given 100% use of CM at daily preventive intake levels per year among target population, years, 2013	5,388

In 2015, 7,472 bone fractures can be avoided if the at-risk target population used magnesium at preventive intake levels.

Economic Results

The following case study on magnesium, like calcium and vitamin D, considers both health care cost savings derived from avoided bone fracture hospital separations and the gains in productive time of the entire population of Australian women aged 50 and over diagnosed with osteoporosis. Thus, the following equation is used to calculate net benefits:

1. $$B_t = Pop_t * (1 - c_t) * \Big(\big(h_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x)) + \bar{I}_t * L_{Pop} * D * b_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x)) \big) - d_t \Big)$$

where h_t is the expected per-person cost of a disease-attributed medical event in year t, $\bar{I}_t$is the median per capita wage income for a member of the target population Pop_t, L_{Pop} is the average remaining life expectancy, in years, per member of the target population, D is the change in disability-adjusted life years lost due to a osteoporosis-attributed bone fracture, and d_t is the expected per-person cost of a given CM regimen utilisation per year t.

b_t is a population weight that reflects the per cent of the target population that is currently in the labour force. This weight is applied because only that percentage of the population will actually be eligible in earning back the expected productivity gains. Thirty three per cent of Australian women aged 50 and over is in the work force (Australian Bureau of Statistics). Finally, c_t is the expected current per cent of magnesium users in the target population. This subset of the target population are already realising the purported benefits of using magnesium and should be removed in order to assess the yet-to-be-realised productivity gains. The following section reports the expected cost and benefit results for 2015 and detailed statistics for 2013 to 2020 are presented in the Appendix.

The calculated relative risk reduction of an osteoporosis-attributed bone fractures, given the use of magnesium CM at the preventive level of 100 mg per day, was 5.2% (95% CI: 1.8% to 7.1%). Consequently, *S* can be $199.6 million in 2015 for this target population.

Total possible medical cost avoidance and productivity gains can be over $372 million and net benefits derived from the full utilization of magnesium can be over $222 million in 2015.

Table 2.9—Magnesium Cost Benefit Analysis: Summary Results[23]

Metric	Measure	Upper	Lower	Average	Cumulative
	2015	95% Confidence Interval		2015 to 2020	
S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	$199,561,121	$268,197,801	$60,775,833	$212,239,930	$1,273,439,583
W: Gain in Productivity from Avoided Disease-attributed Events	$172,973,420	$232,465,576	$52,678,616	$186,570,831	$1,119,424,983
S + W: Total Benefit (Increase in Social Wealth)	$372,534,540	$500,663,377	$113,454,449	$398,810,761	$2,392,864,566
C: Total Cost of CM Consumption	$150,046,900	--	--	$150,119,757	$900,718,540
S – C: Net Benefit (Excludes Productivity)	$49,514,221	$130,229,439	-$113,694,207	$62,120,174	$372,721,043
B: Net Benefit (Includes Productivity)	$222,487,641	$355,524,035	-$46,515,670	$248,691,004	$1,492,146,026
B/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)	$2.48	$3.34	$0.76	$2.50	

Total productivity gains among the target population of Australian women aged 50 and over with osteoporosis, *W,* can yield gains of $173 million in 2015. The cost of magnesium use, *C*, will amount to $150.0 million in 2015 among the target population of Australian women in order to maximise the expected health benefits. Subtracting the cost of magnesium from total economic benefit (*S + W* = $373 million in 2015) can yield a net benefit, *B*, of $222.5 million in 2015. Table 2.9 details the final costs and benefits derived from magnesium use among the target population.

With respect to the distribution of savings and gains among key stakeholders in 2015, 35.8% of total net benefits (both savings in national health care expenditures and gains in productivity) is earned by the Commonwealth Government, 15.0% of net benefits is earned by the State and Territory governments, 6.9% would be distributed by private insurance companies and other sources of private funding, and 42.3% would be savings and productivity gains realised by individuals (AIHW Health Expenditure Database; author calculations). Table 2.10 provides the expected distribution of potentially-realisable net benefits to the primary stakeholders given the use of magnesium CM among the target population.

23 Regarding the cost estimate forecasts, health care costs per person are expected to grow at an average annual growth rate of 3.5% from 2015 to 2020 based on the historical growth rate over the last 10 years. Growth in the targeted population is expected to occur at an average annual growth rate of 2.0% during the forecast period, and it was assumed that growth in disease prevalence is equal to population growth. Calcium and vitamin D, and magnesium retail prices are expected to grow at a compound annual growth rate of 2% per year. All future monetary figures on health care expenditures, productivity earnings, and CM spending were discounted at a 3% rate, according to normalisation best practices promoted by the World Health Organisation in order to control for inflationary effects (World Health Organisation, 2008).

Table 2.10—Magnesium Cost Benefit Analysis: Distribution of Benefits, 2015[24]

Stakeholder	$
Commonwealth Government Health Care (HC) Expenditure Savings	$87,117,170
State, Territory, and Other Government HC Expenditure Savings	$51,210,868
Private Health Insurance Companies' HC Expenditure Savings (and Employers Indirectly through Health Insurance Benefit Plans)	$25,532,479
Individuals' HC Expenditure Savings	$35,700,603
Individual Wage Income Saved	$121,818,982
Commonwealth Government Income Tax Revenue Saved	$10,631,788
State and Territory Governments Tax Revenue Saved	$4,803,914
Commonwealth Government Company Tax Revenue Saved	$35,718,736
Share of Net Benefits (B) to Australian Commonwealth Government	35.8%
Share of Net Benefits (B) to State and Territory Government	15.0%
Share of Net Benefits (B) to Private Sector	6.9%
Share of Net Benefits (B) to Individuals	42.3%

Over 45% of the potential total benefits go to the individual and over 37% of potential total benefits can be realised by the Australian National Government if magnesium was used by the entire at-risk target population at preventive intake levels.

24 S Source: AIHW Health Expenditure Database; author calculations

Conclusion

With a growing number of Australians reaching retirement age, osteoporosis is expected to grow in prevalence. The consequences of osteoporosis include the cost of post-procedure care, loss of mobility and freedom, and a reduction in an individual's quality of life. Therefore, a regimen that provides some support in reducing the possible burden of this disease and is cost-effective ought to be considered. The prior case study implies that given the full utilisation of a calcium and vitamin D regimen at preventive daily intake levels among all Australian women aged 50 and older diagnosed with osteopenia or osteoporosis, $21.22 in possible health care cost savings and productivity gains are realisable per $1 spent on the complementary medicine. With respect to a magnesium regimen, $2.48 per $1 spent on magnesium complementary medicines may be realised if the target population was fully treated. Both cases demonstrate that using these complementary medicines is cost-effective as both CMs return on spending is positive. As fractures attributed to osteoporosis become more prevalent in Australia, the importance of capturing these positive economic returns will become increasingly critical to the long-term health of Australia's ageing populace and the economy as a whole.

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CHAPTER 3 THE ROLE OF COMPLEMENTARY MEDICINES ON ALLEVIATING THE BURDEN OF CARDIOVASCULAR DISEASE—THE CASE OF OMEGA-3 AND FOLIC ACID, B6 AND B12

Problem Statement

In this chapter, a review of two important CMs, omega-3 fatty acids and a folic acid, B6 and B12 regimen, was conducted with the objective of qualifying and quantifying the expected change in the risk of experiencing a severe hospital separation event attributed to a specified chronic cardiovascular disease (CVD) given the use of either omega-3 fatty acids or a folic acid, B6 and B12 combination product. These deduced risk variables are then used as an input into a cost-benefit scenario analysis that calculates the potential change in economic benefits and costs that could be realised if all Australians aged 55 and over, diagnosed with CVD were to use one of the CM regimens at preventive intake levels. If the resultant net benefits are positive after controlling for the cost of the CM regimen in question, then it can be argued that a CM regimen ought to be considered as an important component in combatting the damaging effects of rising health care costs attributed to chronic non- communicable diseases in Australia.

The term cardiovascular disease (CVD) covers all diseases and conditions of the heart and blood vessels (AIHW, 2014). The most prominent CVDs in Australia are coronary heart disease (CHD), stroke, heart failure, and rheumatic heart disease (AIHW, 2014). According to the Australian Bureau of Statistics 2011–12 National Health Survey, more than 3.7 million people (approximately 16% of the total population) had been diagnosed with some form of cardiovascular disease (Australian Bureau of Statistics, 2011-12). While the majority of these were attributed to hypertensive disease, approximately one million were related to heart, stroke, and vascular diseases such as heart attack and other ischaemic heart diseases; diseases of the arteries, arterioles, and capillaries; stroke and other cerebrovascular diseases (Australian Bureau of Statistics, 2011-12).

While the overall death rate from CVD has recently declined, the disease continues to be the major cause of death among Australians (AIHW, 2011). Nearly 44,000 deaths were attributed to CVD in 2011–12, accounting for nearly 1-in-3 deaths in Australia over that period (Australian Bureau of Statistics, 2012). CVDs are responsible for the death of one Australian nearly every 12 minutes (Heart Foundation Australia).

Death rates from CVD complications are heavily correlated to age (AIHW, 2011). The greatest mortality rates attributed to CVD occurred among those aged 85 and over (AIHW, 2011). CVD is not only more prevalent among Australian men when compared to women, it also accounts for a significantly higher death rate amongst men (AIHW, 2011). For example, men between the ages of 45 and 64 experienced CVD death rates three times higher than females in the same age group (AIHW, 2011). Aboriginal and Torres Strait Islander people, people in the lower socioeconomic groups, and those living in regional and remote Australia are generally more susceptible to CVD-related deaths than other Australians (AIHW, 2011).

Table 3.1— Burden of Cardiovascular Disease: All Adults Aged 55 and Older with CVD, 2013–2020

Metric	Measure	2013	2015	2015 to 2020
Total population aged 55 and older with CVD, people[25]	--	848,500	865,555	5,324,906
Total CVD-attributed hospital separations[26]	--	337,913	344,705	2,120,631
Risk of Hospital Separation Events[27]	16.2%	--	--	--
Total CVD-attributed deaths among target population, people[28]	--	40,876	40,917	245,808
Risk of Death Events[29]	4.9%	--	--	--
Discount on residual person years due to occurrence of CVD-attributed hospital separation (D)[30]	11.1%	--	--	--
Average remaining life expectancy per member of the target population, years (L)[31]	7	--	--	--
Mean claimed expenditures per person[32]		$31,397	$34,278	--

As the leading cause of death and a major contributor to the overall burden of disease, expenditures on CVD are higher than any other disease group in Australia. In 2015, it is estimated that approximately $11.8 billion will be spent on CVD conditions for the target population of all adults aged 55 and over with CVD (AIHW 2008; author calculations).

25 Source: Australian Health Survey 2011–12, Australian Bureau of Statistics; author calculations
26 Australian Hospital Data 2011–12, AIHW. Includes separations for ischaemic heart diseases (I20-I25), other forms of heart disease (I30-I52), cerebrovascular diseases (I60-I69), and diseases of the arteries, arterioles, and capillaries (I70-I79); also only includes those people aged 55 and over
27 Derived from the literature review conducted for this report
28 Source: Australian Bureau of Statistics, 2011–12; author calculations
29 Derived from the literature review conducted for this report
30 Source: Australian Institute of Health and Welfare 2011–12; author calculations
31 Source: Australian Institute of Health and Welfare 2011–12; Feldman and Johansson, 2013; author calculations
32 Calculated as the total claimed expenditures on CVD-attributed hospital separations divided by the total number of expected CVD-attributed hospital separations

Omega-3 Fatty Acids

Product Description

Omega-3 fatty acids are a class of polyunsaturated fatty acids that are mainly found in marine food sources, and are also available to a lesser degree in animal and plant foods (Memorial Sloan-Kettering Cancer Centre, 2014). Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are types of omega-3 fatty acids that are found in marine sources such as oily fishes and are associated with the reduction of risk of several health conditions, such as CVD. This is due to the ability of omega-3 fatty acids to integrate with and improve the stability of atherosclerotic plaques (Memorial Sloan-Kettering Cancer Centre, 2014). Atherosclerosis is a long-term condition in which fatty deposits of plaque build-up inside coronary arteries. This, in turn, results in arteries eventually becoming narrow to the point that the blood flow to the heart muscle is decreased or blocked, resulting in a CVD event such as chest pain (angina) and/or heart attack (American Heart Association, 2014).

Table 3.2—Omega-3: Product Description, 2013 and 2015

Metric	Measure
Expected median cost of CM per capita, 2013[33]	$0.27
Expected annual median cost of CM per capita, 2015[34]	$100.50
Current CM usage rates[35]	17.0%
Cost of CM utilization of the target population, 2015	$69.4 million

33 These estimates were based on the average retail price, per dose, of a selection of 20 omega-3 products for sale in Australia through Internet sales channels. The only omega-3 products considered were products produced from marine (fish and microalgae) feedstock. It was assumed that 1,000 mg of EPA and/or DHA was the amount that represented the preventive level of daily intake required to realise the purported health benefits.

34 This measure is calculated as the product of the expected median daily cost of omega-3 per capita, at preventive intake levels, and for 365.25 days per year.

35 Source: Source: Brownie, 2005; author calculations

The relative risk reduction of a cardiovascular disease-attributed hospital separation event, given the use of omega-3 fatty acids at preventive daily intake levels, is a 6.9% reduced risk.

The Australian Heart Foundation recommends that healthy adults consume approximately 500 milligrams of omega-3 (from marine sources) every day to reduce the risk of heart diseases, while Australians with a heart condition are recommended to consume one gram of omega-3 per day (National Heart Foundation Australia, 2008).

The scientific literature suggests that about one gram of EPA and DHA is sufficient to realise CVD-attributed health benefits. Based on the authors' review of the best-selling retail products currently sold through brick and mortar, online, and mail-order retailers, the price of a preventive level dose of omega-3 EPA and DHA per day ranges from as low as $0.05 to as high as $0.71 for one gram of EPA and DHA (author calculations). The median cost of a daily dose of omega-3 is approximately $0.27 per day. Given this daily cost requirement, the median annual expected cost of omega-3 dietary consumption for all Australian adults aged 55 and older with CVD would be $100.5 per person or $69.4 million in 2015 for the total target population.

Seventeen percent of Australians aged 55 and older are regular users of omega-3/fish oil complementary medicines.[ii] The remainder—83%—has not yet realised the potential CVD-attributed health benefits of using omega-3 EPA and DHA. Because avoided expenditures and net cost savings are a direct function of the total number of people in the target population using omega-3 complementary medicines, the calculation of avoided health care expenditures and net cost savings yet to be realised is simply a proportional adjustment of the total potential avoided expenditures and net cost savings.

Clinical Research Review

Spanning several decades, there has been a significant amount of scientific research conducted exploring the use of omega-3 and its impact on heart health. Various attempts at pooling the body of scientific literature using systematic review techniques to derive an overall level of expected efficacy has also resulted in mixed results. The greatest determinant to these alternative conclusions is a result of the study's inclusion selection process, the definition of an event, and the author's interpretation of the results. A good example of this debate is shown in the work of Rizos et al. (2012), which was a meta-analysis published in the Journal of the American Medical Association, which reported that there was "no effect" on cardiovascular event rates when using omega-3 CM. This study aggregated the raw clinical results of randomised trials and looked at all-purpose deaths, cardiac-attributed deaths, heart attacks, and/or strokes, separately (Rizos et al., 2012). Twenty studies were included, representing an aggregated sample of 68,680 people. The authors interpreted the results and concluded that there were no statistically-significant benefits derivable from the use of omega-3 on any of the event outcomes tested. However, the authors' interpretations of the results were, on the one hand, strictly due to the use of a stricter p-value of 0.006 instead of the generally acceptable p-value of 0.05 and, on the other hand, selective due to the authors solely focusing on the null and negative results to infer their conclusions. Nevertheless, the study does report statistically significant positive results in terms of reduced risk of a cardiac-attributed death and nearly statistically significant reductions in all-purpose and sudden cardiac death and heart attacks. In addition, the authors looked at each CVD event outcome independent of the other possible CVD-attributed event outcomes, which effectively reduced the sample size of each case study considerably, and consequently, added statistical insignificance by constraining the sample size.

It is generally recognised that there is an expected heart health benefit derived from the use of omega-3 and more research is required to settle the debate. In 2013, a literature review of the omega-3 scientific literature was conducted by Shanahan and de Lorimier that focused on published studies that tested for and quantified the effect of omega-3 use on the occurrence of a number of CVD-related events requiring medical treatment (as measured by hospital separations attributed to CVD) and CVD-attributed death to determine if there are potential health care cost savings realisable in the United States (Shanahan and de Lorimier, 2013). In that study, the authors deduced that the expected relative risk reduction was 6.9% after controlling for variance from sample size, research methodologies and study protocols, and patient population differences within each study and among all studies (Shanahan and de Lorimier, 2013). This implied that 133 people needed to be treated with an omega-3 CM at 1,000 milligrams of total EPA and DHA content to avoid one CVD event.

For the purpose of this study, an updated literature review was conducted to infer the expected size of a treatment effect on the occurrence of an event. A random-effects literature review approach was adopted based on the literature review process developed by Der Simonian and Laird (D-L approach) (Der Simonian & Laird, 1986). This approach allows for a systematic and objective approach to weighting each of the qualified reported effects and combining them to estimate an expected risk reduction factor that can be used to estimate the number of avoided events and avoided expenditures, if a given patient were to use a given CM at a given intake level. An overview of the random-effects model is described in the Appendix of this report.

The studies selected for the analysis tested for a direct causal relationship between the intake of an omega-3 CM regimen and the risk of a CVD event. The selected studies were similar in study protocol in an attempt to control likely variances. Specifically, from the various study methods found for omega-3 fatty acid use, randomised controlled trials (RCT) were preferred because they are designed to directly test for a cause-and-effect relationship between treatment and outcome. Studies were not selected on the basis of the magnitude, direction, or statistical significance of the reported findings.

In June 2014, an updated search exercise was conducted and 95 studies were found in the PubMed database based on the keywords “omega-3” or “polyunsaturated fatty acids”; “coronary heart disease” or “cardiovascular disease”; and “risk reduction” as filtering keywords. Eighteen RCT studies were identified as being eligible and were used to infer the efficacy. All 18 studies included individuals who had pre-existing CVD. The treatment groups received omega-3 as a mixture including EPA and DHA—except in one study that administered EPA alone—with dosage rates ranging from 0.6 to 3.4 g of EPA and DHA per day in capsule form. A treatment or placebo was given for various durations across the studies, ranging from one to five years. All 18 studies tested for a change in relative risk for CVD events given omega-3 use compared with a non-usage control group. Reported primary outcomes usually included total deaths, as well as deaths due to cardiovascular reasons, myocardial infarctions (MI), angina pectoris, intervention by implanted cardioverter/defibrillator, and hospital admission due to cardiovascular reasons, stroke, and other specified events. For the purpose of this study, each of these outcomes was considered as a CVD event, as each uses health care services. Hence, the size of the effect, if any, of omega-3 on the occurrence of these outcomes can be directly inserted into the cost model. A short description of each of the 18 studies included in the analysis and study result details used in the analysis are outlined in Table 3.3 and Table 3.4.

Table 3.3—Omega-3 Literature Review: Description of the Eligible Studies for Avoided CVD-attributed Hospital Separations

Author	Region	Year	Total sample (N)	TER[36]	CER[37]	Relative risk (RR)	Study weight
Leaf	USA	1994	551	0.00%	0.72%	0.00%	9.57%
Sacks	USA	1995	80	17.07%	28.21%	60.53%	0.69%
Leng	UK	1998	120	28.33%	30.00%	94.44%	0.85%
Von Schacky	Germany	1999	223	1.79%	6.31%	28.32%	4.81%
GISSI-prevenzione	Italy	1999	11,334	9.65%	10.73%	90.00%	9.48%
Nilsen	Norway	2001	300	32.00%	26.67%	120.00%	1.89%
Burr	UK	2003	3,114	11.46%	8.75%	130.96%	8.44%
Leaf	USA	2005	2,501	6.46%	6.09%	106.15%	8.69%
Raitt	USA	2005	200	48.00%	49.00%	97.96%	1.14%
Brouwer	Netherlands	2006	546	56.04%	57.14%	98.08%	2.63%
Svensson	Denmark	2006	206	60.19%	57.28%	105.08%	1.20%
Yokoyama	Japan	2007	18,645	4.61%	5.22%	88.41%	9.81%
GISSI-HF	Italy	2008	6975	67.17%	70.44%	95.36%	8.36%
Galan	France	2010	2,501	6.46%	6.09%	106.15%	8.69%
Einvik	Norway	2010	563	11.39%	12.77%	89.21%	4.59%
Rauch et al.	Germany	2010	3,453	10.39%	8.76%	118.59%	8.62%
Nodari	USA	2011	133	14.93%	39.39%	37.89%	1.04%
Risk and Prevention Study Collaborative Group	Italy	2013	12,513	9.93%	11.88%	83.55%	9.50%

Table 3.4—Omega-3 Literature Review: Expected Avoided Hospital Separation Results

Metric	Measure (Confidence Interval (CI) 95%: Lower - Upper)
Weighted relative risk of a CVD-attributed hospital separation RR(x)	0.951 (95% CI: 0.936 to 0.982)
Weighted relative risk reduction of a CVD-attributed hospital separation RRR(x)	4.9% (95% CI: 3.3% to 6.4%)
Number of people needed to treat to avoid one CVD-attributed hospital separation, NNT(x), people	127
Expected number of avoided CVD-attributed hospital separations given 100% use of CM at daily preventive intake levels per year among target population, 2013	6,677

Nearly 6,700 CVD-attributed hospital-separations could have been realised in 2013 had omega-3 been used by the entire target population at preventive intake levels.

36 TER: % of subjects in treatment group who experienced event relative to number in the treatment group
37 CER: % of subjects in control group who experienced event relative to number in the control group

The relative risk reduction of a cardiovascular disease-attributed death given the use of omega-3 fatty acids at preventive daily intake levels is a 14.1% reduced risk.

Table 3.4—Omega-3 Literature Review: Description of the Eligible Studies for Avoided CVD-attributed Deaths

Author	Year	Total sample (N)	TER[38]	CER[39]	Relative risk (RR)	Study weight
Leaf	1994	551	0.00%	0.72%	0.00%	8.63%
Sacks	1995	80	0.00%	2.56%	0.00%	4.50%
Von Schacky	1999	223	0.00%	0.90%	0.00%	7.98%
GISSI-prevenzione	1999	11,334	4.02%	5.15%	78.11%	8.77%
Nilsen	2001	300	5.33%	5.33%	100.00%	4.39%
Burr	2003	3,114	11.46%	9.01%	127.19%	7.59%
Leaf	2005	402	4.50%	4.46%	101.00%	5.41%
Raitt	2005	200	2.00%	5.00%	40.00%	4.40%
Brouwer	2006	546	2.20%	4.76%	46.15%	6.51%
Yokoyama	2007	18,645	0.31%	0.33%	93.48%	8.97%
GISSI-HF	2008	6975	17.54%	18.99%	92.39%	7.92%
Einvik	2010	563	1.77%	2.49%	71.18%	7.30%
Rauch et al.	2010	3804	1.46%	1.54%	94.84%	8.76%
Risk and Prevention Study Collaborative Group	2013	12,505	2.28%	2.19%	104.10%	8.88%

Table 3.5—Omega-3 Literature Review: Expected Avoided CVD-attributed Death Results

Metric	Measure (Confidence Interval (CI) 95%: Lower - Upper)
Weighted relative risk of a CVD-attributed death RR(y)	85.9% (95% CI: 84.4% to 87.4%)
Weighted relative risk reduction of a CVD-attributed death RRR(y)	14.1% (95% CI: 12.6% to 15.6%)
Number of people needed to treat to avoid one CVD-attributed death, NNT(x), people	160
Expected number of avoided CVD-attributed deaths given 100% use of CM at daily preventive intake levels per year among target population, 2013	2,375

38 TER: % of subjects in treatment group who experienced event relative to number in the treatment group
39 CER: % of subjects in control group who experienced event relative to number in the control group

Overall, it is expected that the relative risk reduction of a CVD event requiring the utilisation of medical services, given the preventive daily use of omega-3, is 4.9% (95% CI: 3.3% to 6.4%) and the relative risk reduction of a CVD death was 14.1% (95% CI: 12.6% to 15.6%) after controlling for variance due to sample size, research methodologies and study protocols, and patient population within and among all studies. This implies that 127 people would need to be treated with omega-3 in order to avoid one CVD event and 160 people would need to be treated to avoid one CVD-attributed death. Consequently, the number of potentially avoidable CVD-attributed hospital utilisation and deaths events in 2013 among all Australians aged 55 and older with CVD would have been 6,677 avoided hospital separations and 5,320 CVD-attributed deaths.

Economic Results

The following case study on omega-3 fatty acids considers both health care cost savings derived from avoided CVD-attributed hospital separations and the gains in productive time for the entire population of Australians aged 55 and over diagnosed with CVD. Thus, the following equation is used to calculate net benefits:

1. $$B_t = Pop_t * (1 - c_t) * \big(h_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x)) + \bar{I}_t * L_{Pop} * \big((Risk_{iy} - Risk_{iy} * (1 - RRR_y)) + D * b_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x))\big) - d_t\big)$$

where h_t is the expected per-person cost of a disease-attributed medical event in year t, $\bar{I}_t$ is the median per capita wage income for a member of the target population Pop_t, L_{Pop} is the average remaining life expectancy, in years, per member of the target population, D is the change in disability-adjusted life years lost due to an CVD medical event, and d_t is the expected per-person cost of a given CM regimen utilisation per year t. x indicates what the RRR is with respect to avoided CVD-attributed hospital separations and y is associated with the RRR of a CVD-attributed death. b_t is a population weight that reflects the per cent of the target population that is currently in the labour force. This weight is applied because only that percentage of the population will actually be eligible in earning back the expected productivity gains. It is expected that 41.8% of Australians aged 55 and over are in the work force based on estimates from Australian Bureau of Statistics. Finally, c_t is the expected current per cent of omega-3 users in the target population. This subset of the target population is already realising the purported benefits of using omega-3 and ought to be removed in order to assess yet-to-be-realised productivity gains. The following section reports the expected cost and benefit results for 2015 and detailed statistics for 2013 to 2020 are presented in the Appendix.

Total possible medical cost avoidance and productivity gains can be over $559 million and net benefits derived from the full utilisation of Omega-3 can be over $489 million in 2015.

Table 3.7—Omega-3 Cost Benefit Analysis: Summary Results

Metric	Measure	Upper	Lower	Average	Cumulative
	2015	95% Confidence Interval		2015 to 2020	
S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	$182,656,968	$241,596,819	$123,717,117	$194,261,798	$1,165,570,791
W: Gain in Productivity from Avoided Disease-attributed Events	$376,415,593	$435,627,609	$317,203,576	$405,218,012	$2,431,308,073
S + W: Total Benefit (Increase in Social Wealth)	$559,072,561	$677,415,454	$440,729,667	$599,479,811	$3,596,878,863
C: Total Cost of CM Consumption	$69,410,397	$69,410,397	$69,410,397	$69,444,100	$416,664,602
S – C: Net Benefit (Excludes Productivity)	$113,246,571	$174,025,999	$52,467,143	$124,817,698	$748,906,188
B: Net Benefit (Includes Productivity)	$489,662,163	$608,952,287	$370,372,039	$530,035,710	$3,180,214,261
B/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)	$8.05	$9.93	$6.32	$8.49	--

In 2013, 378,789 Australians aged 55 and older with CVD experienced a hospital separation event requiring the use of hospital services and a further 40,876 deaths were attributed to CVD (AIHW, 2011–2012; author calculations). In order to avoid one CVD-attributed hospital separation, 127 Australians aged 55 and older are expected to be treated with omega-3 fatty acids. This corresponds to 6,811 avoided medical events in 2015 or a total of 41,902 people avoiding CVD-attributed medical events during the forecast period. Consequently, the avoided medical event expenditures, S, can be $182.7 million in 2015. With respect to total productivity gains, W, the total quality-adjusted years gained back from avoided hospital separation events and deaths can yield productivity gains of $376.4 million in 2015.

Finally, the total economic benefit of omega-3 fatty acids use in terms of avoided CVD-attributed medical events and CVD-attributed deaths, or $S + W$, can amount to $559.1 million in 2015 and the cost of omega-3 fatty acids use, C, would need to be $69.4 million in 2015 among the target population of Australians aged 55 and older with CVD. Subtracting the cost of omega-3 fatty acids consumption from the total economic benefits can yield a net benefit, B, of $489.7 million in 2015. Table 3.7 details the final costs and benefits derived from omega-3 fatty acids among the target population.

With respect to the distribution of savings and gains among key stakeholders in 2015, 26.0% of total net benefits (both savings in national health care expenditures and gains in productivity) is earned by the Commonwealth Government, 10.4% of net benefits is earned by the State and Territory governments, 4.1% would be distributed by private insurance companies and other sources of private funding, and 59.5% would be savings and productivity gains realised by individuals (AIHW Health Expenditure Database; author calculations). Table 3.8 provides the expected distribution of potentially-

realisable net benefits to the primary stakeholders given the use of omega-3 fatty acids among the target population.

Table 3.8—Omega-3 Cost Benefit Analysis: Distribution of Benefits, 2015[40]

Stakeholder	$
Commonwealth Government Health Care (HC) Expenditure Savings	$81,877,610
State, Territory, and Other Government HC Expenditure Savings	$45,898,409
Private Health Insurance Companies' HC Expenditure Savings (and Employers Indirectly through Health Insurance Benefit Plans)	$22,883,818
Individuals' HC Expenditure Savings	$31,997,132
Individual Wage Income Saved	$300,403,814
Commonwealth Government Income Tax Revenue Saved	$43,796,260
State and Territory Governments Tax Revenue Saved	$12,483,941
Commonwealth Government Company Tax Revenue Saved	$19,731,578
Share of Net Benefits (B) to Australian Commonwealth Government	26.0%
Share of Net Benefits (B) to State and Territory Government	10.4%
Share of Net Benefits (B) to Private Sector	4.1%
Share of Net Benefits (B) to Individuals	59.5%

Over 60% of the potential total benefits go to the individual and over 26% of potential total benefits can be realised by the Commonwealth Government if Omega-3 was used by the entire at-risk target population at preventive intake levels.

40 Source: AIHW Health Expenditure Database; author calculations

Folic Acid, B6 and B12

Product Description

The three B-vitamin types that are primarily associated with having an impact on cardiovascular health, including CVD are; folate (folic acid), B6 (pyridoxine), and B12 (cyanocobalamin) (Memorial Sloan-Kettering Cancer Centre, 2014). These vitamins are widely distributed in the general food supply. For instance, vitamin B6 is found in a wide range of foods including meats, breakfast cereals (principally due to fortification), vegetables, and fruits. B12 is derived from poultry, fish, red meat, eggs, and dairy products (Memorial Sloan-Kettering Cancer Centre, 2014). Folate is found in food sources such as fruits and vegetables, beans, and whole grains, while folic acid is the form used in fortified foods and complementary medicines. In Australia, the recommended daily intake levels for folic acid and B12 for adults are 400 micrograms and 2.4 micrograms, respectively. Meanwhile, it is recommended that adults also consume between 1.3 to 1.7 milligrams of vitamin B6 daily (Nutrient Reference Value – Australia and New Zealand).

Table 3.9—Folic Acid, B6 and B12: Product Description, 2014–2020

Metric	Measure
Expected median daily cost of CM per capita, 2013[41]	$0.15
Expected annual median cost of CM per capita, 2015[42]	$55.02
Current CM usage rates[43]	9%
Cost of CM utilisation of the target population, 2015	$42 million

41 These estimates were based on the average retail price, per dose, of a selection of top-selling vitamin B homocysteine-blocker products for sale in Australia through Internet sales channels

42 This measure is calculated as the product of the expected median daily cost of a vitamin B homocysteine-blocker per capita, at preventive intake levels, and for 365.25 days per year.

43 Source: Brownie, 2005; author calculations

The consumer's cost for a daily dose of a combination product of folic acid, B6 and B12 regimen, sold as homocysteine blockers, through internet sales channels range from $0.03 to more than $0.35 for a daily dose in 2013 (author calculations). The mean daily cost to consumers will be approximately $0.15 in 2015. Given this $0.15-per-day requirement, the annual expected cost of folic acid, B6 and B12 for all Australians aged 55 and older with CVD will be $55.02 per person in 2015.

Nine percent of Australians age 55 and older with CVD are regular users of Vitamin B/B complex CM.[ii] As in the case of the omega-3 EPA and DHA CM, the folic acid, B6 and B12 case study makes the assumption that in the consumption scenario all Australians aged 55 and older with CVD use the selected folic acid, B6 and B12s at preventive daily intake levels from a base of zero usage among this population segment. In other words, the calculated difference between the two scenarios is the total potential net savings. However, a percentage of adults aged 55 and older are regular users of folic acid, B6 and B12 complementary medicines and thus already have a reduced risk of a costly CVD event and are realising its risk-reducing benefits.

Clinical Research Review

The interest in this combination of B vitamins—folic acid, B6 and B12 and their purported role in preventing CVD events—stems from their role in metabolising the amino acid, homocysteine. The scientific consensus on the specific mechanism of action is still unknown, but it is expected to be related to the damage to vascular endothelium caused by homocysteine (Memorial Sloan-Kettering Cancer Centre, 2014). For the purpose of this analysis, the authors are interested only in studies that tested for a direct effect on CVD event risk, not on homocysteine levels as a marker of disease risk.

In the Shanahan and de Lorimier (2014) health care cost savings study, the authors explored this relationship by conducting a systematic literature review that focused on published studies measuring the effect of B vitamin use on the occurrence of CVD-attributed deaths and events that require the use of medical services. Specifically, the authors collected a set of studies that were representative of the body of scientific understanding of the efficacy of a combination B-vitamin homocysteine blocker (Shanahan and de Lorimier, 2014). Studies that tested for a direct causal relationship between the intake of the CM and the relative risk of a disease event were preferred. Additionally, a concerted effort was adopted to ensure that the selected studies were similar in protocol in an attempt to control for inter- and intra-study variance. Studies were not selected on the basis of the magnitude, direction, or statistical significance of the reported findings.

Using a PubMed search, 104 studies were found based on the use of “vitamin B” or “B9” and/or “folic acid” and/or “B12” and/or “B6”; “coronary heart disease;” “cardiovascular disease” and related terms; and “risk reduction” as filtering keywords (Shanahan and de Lorimier, 2014). The search was conducted between February 1 and May 31, 2013. Seven RCT studies were identified that tested for the direct relationship between homocysteine blocker intake and the risk of a CVD-attributed disease event. The seven studies only included subjects who had pre-existing cardiovascular disease, such as a MI or stroke, thus, secondary prevention was the primary focus of the cost-savings analysis. The treatment groups received all three as a daily supplement, with dosage rates ranging by study, but averaging 29 mg (B6), 1.7 mg (folate), and 0.5 mg (B12). The experimental or placebo treatments were given for various durations across the studies, ranging from one to 7.3 years. Details of the included studies are outlined in Table 3.10.

Utilising a random-effects meta-analysis methodology, Shanahan and de Lorimier (2014) determined that the relative risk reduction of a CVD-related medical event, given the use of a folic acid, B6 and B12 regimen, was 3.3% (95% CI: 1.6% to 5.1%), after controlling for variance because of sample size, research methodologies and study protocols, and patient population differences within each study and among all studies. This translates to 4,689 events that could have been avoided had all Australians aged 55 and over with CVD used a folic acid, B6 and B12 regimen.

Table 3.10—Folic Acid, B6 and B12 Literature Review: Description of the Eligible Studies

Description of Eligible Studies

Author	Year	Total sample (N)	TER[44]	CER[45]	Relative risk (RR)	Study weight
Albert	2008	5,442	14.90%	14.30%	104.10%	17.07%
Bonaa	2006	1,880	21.50%	18.20%	117.60%	11.23%
Hankey	2010	8,164	15.10%	16.60%	90.50%	18.08%
Lonn	2006	5,522	18.80%	19.80%	95.10%	16.34%
Toole	2004	3,680	18.00%	18.60%	96.70%	14.85%
Schnyder	2002	553	15.40%	22.80%	67.80%	5.44%
Galan	2010	2,501	6.00%	6.50%	92.70%	16.99%

Table 3.11—Folic Acid, B6 and B12 Literature Review: Expected Avoided Hospital Separation Results

Metric	Measure (Confidence Interval (CI) 95%: Lower - Upper)
Weighted relative risk of a CVD-attributed hospital separation RR(x)	0.967 (95%CI: 0.949 to 0.985)
Weighted relative risk reduction of a CVD-attributed hospital separation RRR(x)	3.3% (95%CI: 1.6% to 5.1%)
Number of people needed to treat to avoid one CVD-attributed hospital separation, NNT(x), people	181
Expected number of avoided CVD-attributed hospital separations given 100% use of CM at daily preventive intake levels per year among target population	4,689

44 TER: % of subjects in treatment group who experienced event relative to number in the treatment group
45 CER: % of subjects in control group who experienced event relative to number in the control group

Total possible medical cost avoidance derived from the full utilisation of B vitamins can be over $140 million in 2015.

Economic Results

In the case of folic acid, B6 and B12, health care cost savings and wage income gains derived from avoided CVD-attributed hospital separations were considered in this case study. Thus, the following equation is used to calculate net benefits:

$$1.\quad B_t = Pop_t * (1 - c_t) * \Big(\big(h_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x) + \bar{I}_t * L_{Pop} * D * b_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x)) \big) - d_t \Big)$$

where h_t is the expected per-person cost of a disease-attributed medical event in year t, $\bar{I}_t$ is the median per capita wage income for a member of the target population Pop_t, L_{Pop} is the average remaining life expectancy, in years, per member of the target population, D is the change in disability-adjusted life years lost due to an CVD medical event, and d_t is the expected per- person cost of a given CM regimen utilisation per year t. b_t is a population weight that reflects the per cent of the target population that is currently in the labour force. This weight is applied because only that percentage of the population will actually be eligible in earning back the expected productivity gains. c_t is the expected current per cent of the folic acid, B6 and B12 regimen users in the target population. This subset of the target population is already realising the purported benefits of using folic acid, B6 and B12 and ought to be removed in order to assess the yet-to-be-realised productivity gains. The following section reports the expected cost and benefit results for 2015 and detailed statistics for 2013 to 2020 are presented in the Appendix.

Table 3.12—Folic Acid, B6 and B12 Cost-Benefit Analysis Summary Results

Metric	Measure	Upper	Lower	Average	Cumulative
	2015	95% Confidence Interval		2015 to 2020	
S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	$140,651,585	$215,569,281	$65,733,889	$149,587,668	$897,526,007
W: Gain in Productivity from Avoided Disease-attributed Events	$63,184,292	$96,839,239	$29,529,346	$68,151,199	$408,907,191
C: Total Cost of CM Consumption	$41,659,451	$41,659,451	$41,659,451	$41,679,679	$250,078,076
B: Net Benefit (Excludes Productivity)	$98,992,134	$175,499,765	$22,484,503	$107,907,988	$647,447,931
B: Net Benefit (Includes Productivity)	$162,176,426	$272,245,481	$52,107,371	$176,059,187	$1,056,355,122
B/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM, excludes productivity)	$3.38	$5.17	$1.58	$4.57	--

The expected number needed to treat with a folic acid, B6 and B12 regimen is 181 people in order to avoid one CVD-attributed hospital separation for all Australians aged 55 and older with CVD, which corresponds to 4,784 avoided CVD-attributed hospital

separations in 2015. As a result, the avoided CVD-attributed hospital separation expenditures, S, will amount to $140.7 million in 2015.

The cost of using a folic acid, B6 and B12 regimen, C, will be $41.7 million in 2015 among the target population of Australians aged 55 and older with CVD. Subtracting out the cost of folic acid, B6 and B12 consumption from the total economic benefit, S, can yield a net benefit, B, of $99.0 million in 2015. Including wage income gains, W, can increase potential net benefits to $162.2 million in 2015. Table 3.12 details the final costs and benefits derived from using a folic acid, B6 and B12 regimen among the target population.

With respect to the distribution of savings and gains among key stakeholders in 2015, 39.2% of total net health care savings is earned by the Commonwealth Government, 18.2% of net benefits is earned by the State and Territory governments, 8.6% would be distributed by private insurance companies and other sources of private funding, and 33.9% would be savings and productivity gains realised by individuals (AIHW Health Expenditure Database; author calculations). Table 3.13 provides the expected distribution of potentially-realisable net benefits to the primary stakeholders given the use of a folic acid, B6 and B12 regimen among the target population.

Table 3.13—Folic Acid, B6 and B12 Cost Benefit Analysis: Distribution of Benefits, 2015[46]

Stakeholder	$
Commonwealth Government Health Care (HC) Expenditure Savings	$63,048,323
State, Territory, and Other Government HC Expenditure Savings	$35,343,212
Private Health Insurance Companies' HC Expenditure Savings (and Employers Indirectly through Health Insurance Benefit Plans)	$17,621,256
Individuals' HC Expenditure Savings	$24,638,793
Individual Wage Income Saved	$44,426,972
Commonwealth Government Income Tax Revenue Saved	$6,477,066
State and Territory Governments Tax Revenue Saved	$1,846,260
Commonwealth Government Company Tax Revenue Saved	$10,433,994
Share of Net Benefits (B) to Australian Commonwealth Government	39.2%
Share of Net Benefits (B) to State and Territory Government	18.2%
Share of Net Benefits (B) to Private Sector	8.7%
Share of Net Benefits (B) to Individuals	33.9%

46 Source: AIHW Health Expenditure Database; author calculations

Conclusion

This set of case studies demonstrates that there are significant health care cost savings and productivity gains to be earned by the health care system that can be realised through a concerted effort in identifying high-risk populations and motivating them to use CM with substantiated efficacy. In terms of the ratio of avoided health care costs and gains in productivity due to using omega-3 fatty acids CMs, $8.05 can be saved and/or gained back per $1.00 spent on omega-3 fatty acids in 2015. With respect to the folic acid, B6 and B12, $3.38 can be saved and/or gained back per $1.00 spent on the CM in 2015. These potential economic benefits can be realised through a concerted effort in identifying Australians who are at the greatest risk of experiencing a costly, yet preventable, event.

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CHAPTER 4 LUTEIN AND ZEAXANTHIN UTILISATION AND THE ECONOMIC BENEFITS DERIVED FROM EFFECTIVE AGE-RELATED MACULAR DEGENERATION MANAGEMENT

In Australia, AMD is the most common cause of blindness contributing to 50% of all blindness. It is estimated that over 180,000 Australians above the age of 55 (3.1%) have some form of AMD.

Problem Statement

Visual impairment is a critical health issue amongst the current generation of older Australians because it can affect physical, functional, emotional, and social wellbeing, which, in turn, could significantly reduce quality of life. Besides uncorrected refractive error, cataracts (~15%) and age-related macular degeneration (AMD) are the leading causes of vision loss in older Australians (Vision 2020 Australia, 2010). AMD progressively destroys the macula (the central portion of the retina), impairing central vision and affecting quality of life (Vision 2020 Australia, 2010). Generally, AMD can be classified into early (typically not visually impairing) and late (visually impairing) stages. Late AMD can be further divided into 'wet' (neovascular) and 'dry' (atrophic) forms.

Table 4.1—Burden of Age-related Macular Degeneration: All Australians 55 and over with Age-related Macular Degeneration, 2013 and 2015

Metric	Measure	2013	2015	2015 to 2020
Total population aged 55 and over with age-related macular degeneration, people[47]	--	164,612	167,921	--
Total age-related macular degeneration-attributed hospital separations[48]	--	8,196	8,360	51,434
Risk of age-related macular degeneration-attributed hospital separation[49]	5.0%	--	--	--
Discount on residual person years due to occurrence of age-related macular degeneration-attributed hospital separation (D)[50]	0.29	--	--	--
Average remaining life expectancy per member of the target population, years (L)[51]	5	--	--	--
Mean claimed expenditures per person[52]	--	$37,448	$38,197	--

47 Source: Australian Health Survey (Vision problems among older Australians 2005), Australian Bureau of Statistics; author calculations

48 Australian Hospital Data 2011–12, AIHW. Includes separations for H35.30 Degeneration of Macula and posterior pole; author calculations

49 Calculated as total AMD-attributed hospital separations divided by the total population aged 55 and older with AMD

50 Source: Australian Institute of Health and Welfare 2011–12; author calculations

51 Source: Australian Institute of Health and Welfare 2011–12; Feldman and Johansson, 2013; author calculations

52 Calculated as total claimed expenditures on AMD-attributed hospital separations divided by the total number of expected AMD-attributed hospital separations

Visual impairment from AMD is estimated to have cost the Australian economy approximately $5 billion in 2010.

In Australia, AMD is the most common cause of blindness contributing to 50% of all blindness (Vision 2020 Australia, 2010). Over 180,000 Australians above the age of 55 (3.1%) are estimated to have some form of AMD (AIHW, 2005). The economic impact of vision loss due to AMD in Australia was estimated at $5 billion in 2010 (Vision 2020 Australia, 2010). The socio-economic impacts of AMD include low employment rates, higher use of social services, social isolation, emotional distress, and an early need for nursing home care.

In this chapter, a review of the lutein and zeaxanthin scientific literature was conducted with the aim of qualifying and quantifying the expected change in the risk of an AMD-related hospital separation event given the use of lutein and zeaxanthin at preventive intake levels. This deduced risk variable was then used as an input into a cost-benefit scenario analysis in order to calculate the potential change in economic benefits and costs—in terms of avoided AMD hospital separation costs and productivity losses—that could be realised if all Australians aged 55 and over diagnosed with AMD were to use lutein and zeaxanthin at preventive intake levels. If the resultant net benefit is positive after controlling for the cost of lutein and zeaxanthin consumption for the entire at-risk population, then it can be argued that a lutein and zeaxanthin regimen ought to be considered an important component in combatting the damaging effects of AMD's prevalence in Australia.

Lutein and Zeaxanthin

Product Description

Lutein and zeaxanthin are provitamin A carotenoid pigments that accumulate in both the lens and retinal macula (Memorial Sloan-Kettering Cancer Centre, 2014). These compounds are not naturally produced by the human body and intake is primarily through consumption of leafy vegetables such as spinach, cabbage, and kale; as well as yellow and orange fruits such as mangoes, papayas, peaches, and oranges (Memorial Sloan-Kettering Cancer Centre, 2014). According to the Joint Expert Committee on Food Additives (JECFA), the acceptable daily intake (ADI) level for Lutein is up to 2 mg per kg of body weight (Fryirs, Eisenhaur, and Duckworth, 2008). However, less than two per cent of Australians aged 55 and older are expected to be regular users of lutein and zeaxanthin products according to author calculations. This implies that more than 98% of the entire target population is not currently realising the potential benefits from regular use. Because avoided expenditures and net cost savings are a direct function of the total number of people in the target population using these complementary medicines, the calculation of avoided health care expenditures and net cost savings yet to be realised is simply a proportional adjustment of the total potential avoided expenditures and net cost savings (Shanahan and de Lorimier, 2013).

The price of a daily dose of lutein and zeaxanthin ranges from as low as $0.11 to as high as $0.61 for one daily dose based on a review of best-selling products in leading brick-and-mortar, online, and mail-order retail establishments in Australia. The median price per daily dose is $0.31. Thus, the annual expected cost of lutein and zeaxanthin dietary consumption for all Australians aged 55 and older at risk of an AMD event was $113.86 per person in 2013.

Less than 2% of Australians aged 55 and older are expected to be regular users of lutein and zeaxanthin products. This implies that more than 98% of the entire target population are not currently realising the potential benefits from regular use.

Table 4.2—Lutein and Zeaxanthin: Product Description, 2014–2020

Metric	Measure
Expected median daily cost of CM per capita at preventive intake levels, 2013	$0.31
Expected annual median cost of CM per capita at recommended daily intake levels, 2013[53]	$113.86
Current CM usage rates[54]	3%
Cost of CM utilisation of the target population, 2015	$18.4 million

53 This measure is calculated as the product of the expected median daily cost of lutein and zeaxanthin per capita, at preventive intake levels, and for 365.25 days per year.
54 Source: Brownie, 2005; author calculations

Clinical Research Review

Lutein and zeaxanthin have an antioxidant property that potentially prevents damage to DNA and protein molecules (Memorial Sloan-Kettering Cancer Centre, 2014). In dry AMD, the concentration of pigments in the central part of the macula declines with age. Some studies have demonstrated that increasing dietary consumption with lutein and/or zeaxanthin in AMD patients leads to an increase in macular pigment and improved visual acuity. Other studies test for a direct link between the high dietary intake of lutein and zeaxanthin with the decreased risk of AMD.

Overall, the state of the science of the AMD-related health benefits from using lutein and zeaxanthin is young. This is reflected in the number of studies conducted over the years looking at this subject and the heterogeneity of research design, sample population definitions, and tested end points adopted by researchers in the field. This makes the relative comparability and aggregation of the studies difficult regarding the determination of an overall expected effect.

In 2013, the authors of this report conducted a literature review of published lutein and zeaxanthin studies with the aim of identifying eligible studies that tested for and quantified the effect of lutein and zeaxanthin utilisation on AMD-attributed medical events that require medical treatment and post-procedural care (Shanahan and de Lorimier, 2013). The results of the conducted PubMed search identified more than 25 studies based on keyword combinations such as “lutein” and/or “zeaxanthin”; “macular degeneration”; and “risk reduction.” In all, five studies were identified as eligible for analysis including one RCT, three case-controlled, and a cohort epidemiological study.

Each of these studies tested for a direct relationship between lutein and zeaxanthin use and the risk of an AMD-attributed medical event. However, due to the remaining variance in study protocol, the use of a random-effects review process is not possible. The remaining 20 studies tested for relationships between lutein and zeaxanthin use and cataract or other age-related eye disease event risks or tested for risk biomarkers. Accordingly, the last year’s findings determined that 157 people (95% CI: 77 to 5,461) would need to be treated with lutein and zeaxanthin to avoid one age-related macular degeneration event. For the purposes of this analysis, the same relative risk reduction measures were used to calculate the possible net benefits in the case of the Australian populace. The included studies and the deduction to the relative risk reduction are shown in Table 4.3 and Table 4.4, respectively.

Table 4.3—Lutein and Zeaxanthin Literature Review: Description of the Eligible Studies

Author	Total sample (N)	AMD relative risk (RR) for lutein and zeaxanthin, top versus bottom quintile or tertile	Confidence Interval (CI) 95%: Upper - Lower	Study weights based on sample size variance
Chew (AREDS2)	4,203	0.90**	0.76 to 1.07	43.30%
SanGiovanni	1,772	0.65*	0.45 to 0.93	18.30%
Seddon	820	0.60*	0.40 to 1.00	8.40%
Seddon	876	0.57*	0.35 to 0.92	9.00%
Tan	2,035	0.77***	0.13 to 0.92	21.00%
Estimated relative risk		0.77	0.50 to 0.99	

** Odds ratio*

*** Hazard ratio compared to no treatment*

**** Relative risk of top tertile versus bottom tertile*

Table 4.4—Lutein and Zeaxanthin Literature Review: Expected Avoided Hospital Separation Results

Metric	Measure (Confidence Interval (CI) 95%: Lower - Upper)
Weighted relative risk of a AMD-attributed hospital separation RR(x)	0.78 (95% CI: 0.50 to 0.99)
Weighted relative risk reduction of a AMD-attributed hospital separation RRR(x)	22.4% (95% CI: 1.0% to 50%)
Number of people needed to treat to avoid one AMD-attributed hospital separation, NNT(x), people	157
Expected number of avoided AMD-attributed hospital separations given 100% use of CM at daily preventive intake levels per year among target population	1,068

The relative risk reduction of an AMD-attributed hospital separation given the use of lutein and zeaxanthin at preventive daily intake levels is a 23% reduced risk.

One example of a study that directly tested a link between AMD event risk and lutein and zeaxanthin utilisation is Seddon et al. (1994). Here, the authors conducted a case-controlled study that matched 356 people in the United States with advanced AMD and the relative risk of AMD was estimated according to various indicators, including dietary components. In comparing the highest and lowest quintiles of lutein and zeaxanthin intake, the authors found a statistically-significant reduction in the risk of an AMD-attributed event among the higher intake cohort (odds ratio 0.57, 95% CI: 0.35 to 0.92) (Seddon et al., 1994).

Another example that tested for a direct link is San Giovanni et al. (2007) which was another case-controlled study of 4,519 subjects in the United States, most of whom had some degree of AMD (San Giovanni et al., 2007). Data on dietary intake was analysed and tested versus AMD incidence. A statistically-significant reduction in neovascular AMD incidence (odds ratio 0.65; 95% CI: 0.45 to 0.93) was identified in comparing the highest and lowest quintiles of lutein and zeaxanthin intake.

Tan et al. (2008) conducted a population-controlled cohort study of diet and AMD incidence in 3,654 Australian patients (Tan, Wang, Flood, Rochtchina, Smith, & Mitchell, 2008). Participants in the highest tertile of dietary lutein and zeaxanthin intake had a relative risk for incident AMD of 0.35 (95% CI: 0.13 to 0.92).

Seddon et al. (2010) compared 545 subjects with AMD to 275 subjects without AMD in a case-controlled study (Seddon, Reynolds, & Rosner, 2010). In comparing the highest and lowest tertile of lutein intake, the odds ratio for overall risk of AMD was 0.6 (95% CI: 0.4 to 1.0).

Finally, the most recent study included in this analysis is the Age-Related Eye Disease Study II (AREDS2), a RCT trial with 4,203 subjects at risk for progression to advanced AMD (Chew et al., 2013). In this study, the subjects took a daily dose of lutein (10 mg) and zeaxanthin (2 mg) and eye examinations were conducted over a median of 5 years to assess progression to advanced AMD. The primary analysis compared subjects who supplemented with the AREDS formulation and lutein plus zeaxanthin to those who supplemented with the AREDS formulation only. The hazard ratio for progression to advanced AMD was 0.90 for the lutein plus zeaxanthin group (98.7% CI: 0.76 to 1.07). However, secondary analyses in AREDS2 suggest that lutein and zeaxanthin utilisation may result in even lower hazard ratios for AMD. Only the primary result was used for the present analysis in order to maintain consistency with analyses of other complementary medicines in this study.

1,068 AMD-related hospital separation events can be avoided in 2015 if the at-risk target population used lutein and zeaxanthin.

Economic Results

The following lutein and zeaxanthin cost estimate forecasts assume that the expected compound annual growth rates of AMD-attributed health care costs will be 3.5% from 2015 to 2020 based on the historical nominal health care cost growth in Australia over the last 10 years. Growth in the targeted population is expected to occur at an average annual growth rate of two per cent during the forecast period, and it was assumed that growth in disease prevalence is equal to population growth. Lutein and zeaxanthin CM retail prices are expected to grow at a compound annual growth rate of two per cent per year. All future monetary figures on health care expenditures, productivity earnings, and CM spending were taken at a three per cent discount rate, which is the standard discount rate promoted by the World Health Organisation (World Health Organisation, 2008).

The following case study on lutein and zeaxanthin considers both health care cost savings derived from avoided AMD hospital separations and the gains in productivity time for the entire population of Australians aged 55 and over diagnosed with AMD. Thus, the following equation was used to calculate net benefits:

$$2.\quad B_t = Pop_t * (1 - c_t) * \Big(\big(h_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x) + \bar{I}_t * L_{Pop} * D * b_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x) \big) - d_t \Big)$$

where h_t is the expected per-person cost of a disease-attributed medical event in year t, $\bar{I}_t$ is the median per capita wage income for a member of the target population Pop_t, L_{Pop} is the average remaining life expectancy, in years, per member of the target population, D is the change in disability-adjusted life years lost due to an AMD medical event, and d_t is the expected per- person cost of a given CM regimen utilisation per year t. b_t is a population weight that reflects the per cent of the target population that is currently in the labour force. This weight is applied because only that percentage of the population will actually be eligible in earning back the expected productivity gains. It is expected that 41.8% of Australians age 55 and over are in the work force based on estimates from Australian Bureau of Statistics. Finally, c_t is the expected current per cent of lutein and zeaxanthin users in the target population. This subset of the target population are already realising the purported benefits of using lutein and zeaxanthin and ought to be removed in order to assess the yet-to-be-realised productivity gains.

The total possible medical cost avoidance and productivity gains can be over $50 million and the net benefits derived from the full utilisation of lutein and zeaxanthin can be over $32 million in 2015.

The following section reports the expected cost and benefit results for 2015 and detailed statistics for 2013 to 2020 are presented in the Appendix.

Table 4.5— Lutein and Zeaxanthin Cost-Benefit Analysis: Summary Results

Metric	Measure	Upper	Lower	Average	Cumulative
	2015	95% Confidence Interval		2015 to 2020	
S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	$25,723,045	$56,866,016	$740,590	$27,357,319	$164,143,917
W: Gain in Productivity from Avoided Disease-attributed Events	$25,463,284	$281,458,810	$3,665,557	$27,464,949	$164,789,693
S + W: Total Benefit (Increase in Social Wealth)	$51,186,330	$187,281,217	$2,439,043	$54,822,268	$328,933,610
C: Total Cost of CM Consumption	$18,375,631	$18,375,631	$18,375,631	$18,384,553	$110,307,320
S-C: Net Benefit (Excludes Productivity)	$7,347,414	$42,878,500	-$21,155,125	$8,972,766	$53,836,597
B: Net Benefit (Includes Productivity)	$32,810,699	$266,615,353	-$50,934,862	$36,437,715	$218,626,290
B/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)	$2.79	$10.19	$0.13	$3.02	

One-hundred-fifty-seven people would be need to be treated with lutein and zeaxanthin in order to achieve one avoided hospital separation, corresponding to 1,068 avoided hospital separations among all Australians aged 55 and over with AMD in 2015. Subsequently, the avoided medical event expenditures, S, will amount to $25.7 million in 2015. With respect to total productivity gains W, a yield of $25.5 million can be achieved in 2015.

Finally, the total economic benefit of lutein and zeaxanthin use in terms of avoided hospital separations, or $S + W$, can amount to $51.2 million in 2015. The cost of lutein and zeaxanthin use, C, will be $18.4 million in 2015 among the target population of Australians aged 55 and over with AMD. Subtracting out the cost of lutein and zeaxanthin consumption from the total economic benefit can yield a net benefit, B, of $32.8 million in 2015. Table 4.5 details the final costs and benefits derived from lutein and zeaxanthin among the target population.

Table 4.6—Lutein and Zeaxanthin Cost-Benefit Analysis: Distribution of Benefits, 2015[55]

Stakeholder	$
Commonwealth Government Health Care (HC) Expenditure Savings	$11,530,584
State, Territory, and Other Government HC Expenditure Savings	$6,463,738
Private Health Insurance Companies' HC Expenditure Savings (and Employers Indirectly through Health Insurance Benefit Plans)	$3,222,661
Individuals' HC Expenditure Savings	$4,506,062
Individual Wage Income Saved	$17,628,919
Commonwealth Government Income Tax Revenue Saved	$2,570,143
State and Territory Governments Tax Revenue Saved	$732,608
Commonwealth Government Company Tax Revenue Saved	$4,531,615
Share of Net Benefits (B) to Australian Commonwealth Government	36.4%
Share of Net Benefits (B) to State and Territory Government	14.1%
Share of Net Benefits (B) to Private Sector	6.3%
Share of Net Benefits (B) to Individuals	43.2%

Regarding the distribution of savings and gains among key stakeholders in 2015, 36.4% of total net benefits (both savings in national health care expenditures and gains in productivity) will be earned by the Commonwealth Government, 14.1% of net benefits will be earned by the State and Territory governments, 6.3% would be distributed between private insurance companies and other sources of private funding, and 43.2% would be savings and productivity gains realised by individuals (AIHW Health Expenditure Database; author calculations). Table 4.6 provides the expected distribution of potentially-realisable net benefits to the primary stakeholders given the use of lutein and zeaxanthin among the target population.

55 Source: AIHW Health Expenditure Database; author calculations

Conclusion

It should be reaffirmed that the state of the science of the AMD-related health benefits from using lutein and zeaxanthin is still young and more standardised clinical research should be undertaken that minimises the heterogeneity of research design, sample population definitions, and tested end points adopted by researchers in the field. However, there is enough evidence to show that the use of lutein and zeaxanthin CM do enhance the health and wellness of sufferers of AMD and, subsequently, can result in potential medical cost savings of $2.79 in avoided health care costs attributed to age-related macular degeneration per every $1.00 spent on the regimen in 2015. This is a significantly positive return on an individual's health investment. The key source of these potential savings and gains is tied to expected post-AMD-event reduced vision, which results in an overall lower quality of life. AMD limits an individual's freedom, mobility, and the seemingly simple ability to perform daily activities. In addition, intangible costs not captured in the analysis, such as significant physical and emotional distress of AMD sufferers, are additional burdens to consider in assessing overall quality of life. It is estimated that nearly five per cent of all people aged 55 and older with AMD will require costly post-AMD event services at a cost of over $38,197 per person in 2015. Nearly half of these costs will be borne by the AMD sufferer and it will cost the Commonwealth Government over $11 million in the form of health care expenditures and lost tax revenue. Therefore, any means to help reduce these costs, including the adoption of scientifically-substantiated CM that are shown to have a health benefit, ought to be considered as a viable device to reduce the societal and economic burden of this disease.

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CHAPTER 5 THE USE OF ST. JOHN'S WORT AND PRODUCTIVITY GAINS POTENTIAL FROM MAJOR DEPRESSION MANAGEMENT

In 2013, 698,270 Australians aged 20 and over experienced some type of a major depressive episode.

Problem Statement

Clinical depression is a medical condition that significantly affects the way someone feels, causing a persistent lowering of their mood (SANE Australia, 2014). Depression is often accompanied by a range of other physical and psychological symptoms that can interfere with the way a person is able to function in their everyday life. In 2012, there were 2,535 suicides in Australia (ABS, Causes of Death, 2012). Given that an estimated 80% of suicides are preceded by mental illnesses, the majority of which is depression. Men are three times more likely to die by suicide than women (Australian Bureau of Statistics, 2012).

Depression is the leading cause of non-fatal disability in Australia, representing a significant disease burden. The range of depressive disorders, which include perinatal depression, are associated with substantial losses to the economy in terms of lost worker productivity and the high utilisation of health and social services which impact the government directly. Depression costs the Australian economy approximately $12.6 billion per year and accounts for up to six million working days of lost productivity (Beyondblue, 2011) Additionally, there are significant personal and social costs to individuals and their families which are associated with depression.

In Australia, significant levels of depression affect approximately 20% of adults during their lifetime, with almost twice as many women diagnosed with the disorder than men. It is expected that 259,006 Australian men aged 20 and over and 439,264 Australian females aged 20 and over experienced a major depressive episode in 2013, a combined total of 698,270 Australians (Australian Hospital Data 2011–12, AIHW, and author estimates). Within the definition of being diagnosed with major depression, there are various classes that vary by severity of symptoms—mild, moderate, and severe (AIHW, 1998). Major depression severity is measured using various qualitative scoring schemes which are derived from diagnostic tests administered by mental health professionals (AIHW, 1998).

The most commonly used test is the Hamilton Depression Rating Score, or HAM-D score, which is a qualitative assessment based on 21 questions, of which the first 17 are used in building the score (Hamilton, 1960). Severe major depression is measured on the HAM-D scale as a score greater than or equal to 19, moderate major depression is measured on the HAM-D scale as a score from 18 to 14, and mild major depression is indicated by a HAM-D score of 14 or less (Hamilton, 1960). According to the Australian Bureau of Statistics, 21% of all people with a mental disorder, which is primarily made up of major depression, had a severe disorder, 33% had a moderate disorder, and the remainder had a mild disorder (ABS, 2009). Using these shares as a proxy for quantifying the breakdown of major depression cases by severity and applying it to known number of people in Australia diagnosed with major depression, 146,637 people had severe major depressive episodes which likely required hospitalisation. Moderate major depression inflicted 230,429 Australians in 2013 and 321,204 Australians over the aged 20 had mild major depression in 2013.

According to the Australian Institute of Health and Welfare, 191,786 disability-adjusted life years were lost in 2013 due to major depressive episodes (AIHW, 2012). Also, an average $10,391 per year is lost in personal wage income due to major depression (AIHW, 2012). See Table 5.1 for detailed statistics on the state of major depression in Australia.

Table 5.1—Burden of Major Depression: All Australians Aged 20 and over with Major Depression, 2013–2020

Metric	Metric	2013	2015	2015 to 2020
Total population that will experience a moderate major depression episode, people[56]	--	230,429	235,061	1,446,097
Discount on residual person years among people with moderate major depression[57]	0.14	--	--	--
Discount on residual person years among people with mild major depression[58]	0.35	--	--	--
Change in the discount on residual person years from a successful diagnosis transition from mild to moderate major depression	0.21	--	--	--
Average remaining life expectancy per member of the target population, years (L)[59]	7	--	--	--
Medium Personal Wage Income[60]	--	$49,482	$51,481	--
Per cent of the target population in the workforce[61]	68.4%	--	--	--
Mean personal wage incomes lost per change in disabled life year from mild to moderate severity of major depression[62]	--	$10,391	$11,345	--

56 Source: Australian Bureau of Statistics, 2009; author calculations
57 Source: Australian Institute of Health and Welfare 2011–12
58 Source: Australian Institute of Health and Welfare 2011–12
59 Source: Australian Institute of Health and Welfare 2011–12; Feldman and Johansson, 2013; author calculations
60 Source: Australian Bureau of Statistics, 2014; author calculations
61 Source: Australian Bureau of Statistics, 2014; author calculations
62 Calculated as the product of median personal wage income and change in the discount on residual person years from a transition from moderate to mild major depression

The following case study makes the case that significant productivity gains through the use of St. John's wort can be realised by those Australians suffering from moderate major depression and not currently using an antidepressant, gains that have a demonstrable and substantial effect on the risk of costly disease-attributed events. Explicitly, this case study examines the current state of the scientific literature demonstrating that the use of St. John's wort can potentially yield a significant enhancement in the quality of life of the average Australian aged 20 and over with diagnosed moderate major depression by means of lowering the severity of the disease symptoms to mild major depression and, consequently, enhances their earnings potential. This is not to say that other regimens such as antidepressants are ineffective, but rather that St. John's wort is a viable option for those suffering from moderate major depression. Thus, a proactive targeting of potential users of St. John's wort regimens ought to be considered as a means to increase societal health and wealth if efficacy is comparable and is safe to use.

St. John's Wort

Product Description

St. John's wort is a natural and widely available herb with a long history of being used to treat a range of disorders such as depression, anxiety, and sleep disorders (Memorial Sloan-Kettering Cancer Centre, 2014). The herb has been studied extensively and has shown evidence of neuroprotective properties and the ability to relieve neuropathic pain (Memorial Sloan-Kettering Cancer Centre, 2014). Studies also suggest that St. John's wort may be a cost-effective option for mild to moderate cases of depression. While St John's wort is available in Australia without prescription, the TGA has issued advice that the strength of active ingredients may vary between preparations and also that drug interactions with other medicines are possible. It is recommended that up to 900 mg of St John's wort per day is necessary to substantially reduce symptoms of non-melancholic depression (Black Dog Institute, 2012). As with other antidepressant medication, the herbal remedy may take up to four weeks to exert an effect.

It is expected that four per cent of Australians over the aged 20 in Australia are regular users of St. John's wort (Pirotta et al., 2014). Regular users are defined as using the given CM on a daily basis. Furthermore, a review of the retail St. John's wort CM on the market revealed that the cost of a daily dose of St. John's wort ranges from $0.38 to $0.60, the median cost being $0.50 per day. Using this figure, the expected cost of supplementing all Australians aged 20 and over diagnosed with major depression would be $185.2 per person in 2015, for a total of $40.1 million for the entire target population in 2015.

Table 5.2—St. John's Wort: Product Description, 2013 and 2015

Metric	Measure
Expected median daily cost of CM per capita, 2013[63]	$0.50
Expected annual median cost of CM per, 2015[64]	$185.2
Current CM usage rates[65]	4%
Cost of CM utilisation of the target population, 2015	$40.1 million

Clinical Research Review

The inferred enhancement in mental well-being given the use of St. John's wort is backed by several decades of focused clinical research. In 2009, the Cochrane Collaboration, a not-for-profit and independent network of health care practitioners, researchers, and other key industry stakeholders, with the stated mission of providing credible and accessible health information for the health care industry, conducted a detailed systematic review of the efficacy of St. John's wort with respect to the successful diagnosis transition from a moderate to mild case of major depression (The Cochrane Collaboration, 2014; Linde, Berner, and Kriston, 2009). In this systematic review, 18 randomised controlled trials encompassing 3,064 study participants were identified and analysed using system review of best practices that tested the "Response to Treatment" rates, where a positive response is indicated by a 50% reduction from a baseline HAM-D score of 18 points or greater or reduction to a score of 10 or less (Linde, Berner, and Kriston, 2009). The authors determined that the intake of St. John's wort resulted in a mean response-to-treatment risk ratio of 1.28 (95% CI: 1.22 to 2.87) (Linde, Berner, and Kriston, 2009). Translating this deduced mean response-to-treatment risk ratio to a relative risk reduction factor that can be used in the cost-benefit model, Frost & Sullivan took the inverse of the study's findings to determine the relative risk reduction of not experiencing a positive treatment response in the St. John's wort treatment group versus the placebo group. This yielded a relative probability increase of a successful diagnosis transition from moderate to mild major depression of 24.0% (95% CI: 14.8% to 33.1%).

63 These estimates were based on the average retail price, per dose, of a selection of 9 top-selling St. John's wort products for sale in Australia through Internet sales channels.
64 This measure is calculated as the product of the expected median daily cost of St. John's wort per capita, at preventive intake levels, and for 365.25 days per year.
65 Source: http://www.ncbi.nlm.nih.gov/pubmed/24969102

Table 5.3—St. John's Wort Literature Review: Description of the Eligible Studies

Author	Year	Total sample (N)	TER[66]	CER[67]	Relative risk (RR)[68]	Study weight
Witte	1995	97	0.71	0.51	59.5%	5.2%
Hansgen	1996	108	0.66	0.22	43.4%	5.5%
Schrader	1998	159	0.56	0.15	51.6%	5.8%
Laakmann	1998	98	0.49	0.33	75.8%	5.2%
Phillip	1999	153	0.63	0.47	69.2%	5.4%
Montgomery	2000	247	0.45	0.46	102.3%	5.9%
Volz	2000	140	0.66	0.49	66.7%	5.5%
Shelton	2001	200	0.27	0.19	90.3%	6.0%
Bracher	2001	218	0.59	0.44	73.8%	5.9%
Kalb	2001	72	0.62	0.43	66.2%	4.7%
Lecrubier	2002	375	0.53	0.42	82.0%	6.2%
HDTSG	2002	229	0.41	0.48	114.6%	5.9%
Uebelhack	2004	140	0.59	0.06	43.9%	5.9%
Bjerkenstedt	2005	109	0.41	0.38	95.9%	5.3%
Fava	2005	88	0.38	0.21	78.7%	5.2%
Moreno	2005	46	0.20	0.42	138.7%	4.4%
Kasper	2006	324	0.65	0.32	50.9%	6.0%
Gastpar	2006	261	0.54	0.39	75.4%	6.0%

Table 5.4—St. John's Wort Literature Review: Expected Successful Diagnosis Transitions from Moderate to Mild Major Depression Results

Metric	Measure (Confidence Interval (CI) 95%: Lower - Upper)
Weighted relative probability of a successful diagnosis transition from moderate major depression to mild major depression, RR(x)	0.76 (95% CI: 0.67 to 0.85)
Weighted relative probability increase of a successful diagnosis transition from moderate major depression to mild major depression, RRR(x)	24.0% (95% CI: 14.8 to 33.1%)
Number of people needed to treat to gain one successful diagnosis transition from moderate major depression to mild major depression, NNT(x), people	6
Expected number of successful transitions from moderate major depression to mild major depressions given 100% use of CM at daily preventive intake levels per year among the target population	39,060

66 TER: % of the population that did experience a successful transition from a diagnosis of moderate major depression to mild major depression given the use of St. John's wort at preventive intake levels
67 CER: % of the population that did experience a successful transition from a diagnosis of moderate major depression to mild major depression given the use of a placebo
68 The relative risk reduction is calculated at (1-TER)/(1-CER)

The relative risk reduction of not experiencing a positive depression treatment response given the use of St John's Wort at preventive daily intake levels is 24.0%.

Economic Results

For the purpose of this case study on St. John's wort, health care costs per person are expected to grow at an average annual rate of 3.5% from 2015 to 2020 based on observed historical growth rates. Growth in the target population and disease prevalence are expected to occur at an average annual rate of two per cent during the forecast period. In addition, it is expected that 68.4% of Australians age 20 and over are in the work force based on estimates from Australian Bureau of Statistics. St. John's wort retail prices are expected to grow at a compound annual rate of two per cent per year. All future monetary figures on health care expenditures, productivity earnings, and CM spending were at a three per cent discount rate, which is in line with health economic methods promoted by the World Health Organisation to reflect the present value of estimated future expenditures and net savings and control for inflationary effects (World Health Organisation, 2008).

The following case study on St. John's wort only considers the gains in productive time of the entire population of Australians aged 20 and over diagnosed with moderate major depression because the body of science solely looks at a change in quality of life. Thus, the following equation is used to calculate net benefits:

1. $B_t = \bar{I}_t * D * L_{Pop} * Pop_t * b_t * (1 - c_t) * (Risk_{ix} - Risk_{ix} * (1 - RRR_x) - Pop_t * (1 - c_t) * d_t$

where $\bar{I}_t$is the median per capita wage income for a member of the total target population Pop_t, L_{Pop} is the average remaining life expectancy, in years, per member of the target population, D is the change in disability-adjusted life years lost between moderate and mild forms of major depression, and d_t is the expected per-person cost of a given CM regimen utilisation per year t. b_t is a population weight that reflects the per cent of the target population that is currently in the labour force. This weight is applied because only that percentage of the population will be actually earning the productivity gains. Finally, c_t is the expected current per cent of St. John's wort users in the target population. This subset of the target population is already realising the purported benefits of using St. John's wort and ought to be removed from the population in order to assess the yet-to-be-realised productivity gains. The following section reports the expected cost and benefit results for 2015 and detailed statistics for 2013 to 2020 are presented in the Appendix.

Given a relative risk reduction of 24.0% from the previous section, the expected number of people with moderate major depression needed to treat with St. John's wort in order to gain one successful diagnosis transition from moderate to mild major depression is six people treated, corresponding to potentially 39,845 successful diagnosis transitions in 2015. Successful transitions to be gained in 2015 are reported in Table 5.5.

Total productivity gains in 2015, alone, can be over $255 million from the full utilisation of St. John's wort in the target population.

Table 5.5—St. John's Wort Cost-Benefit Analysis: Summary Results

Metric	Measure	Upper	Lower	Average	Cumulative
	2015	95% Confidence Interval		2015 to 2020	
W: Gain in Productivity	$295,746,413	$375,128,349	$167,930,117	$339,801,380	$2,038,808,278
C: Total Cost of CM Consumption	$40,058,431	$40,058,431	$40,058,431	$40,077,882	$240,467,290
B=W-C: Net Benefit	$255,687,982	$336,504,313	$125,562,105	$299,723,498	$1,798,340,989
W/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)	$7.38	$9.36	$4.19	$8.05	--

With respect to total productivity gains, *W,* 39,845 disability-adjusted years can be gained back through St. John's wort-induced successful transitions in 2015 among the target population of Australians aged 20 and older with moderate major depression. Multiplying each quality-adjusted year gained from successful transitions by the change in median wage income of $11,345 per year and weighting the number of gained quality-adjusted years by the anticipated employment rate of 68.4% can yield productivity gains of $295.7 million in 2015. The resultant productivity gains from possible successful diagnosis transitions are reported in Table 5.6.

The cost of St. John's wort use, *C*, will amount to $40.1 million in 2015 among the target population of Australians aged 20 and older with moderate major depression. Subtracting out this cost of St. John's wort consumption from total productivity gains can yield a net benefit, *B*, of $255.7 million in 2015.

Table 5.6— St. John's Wort Cost Benefit Analysis: Distribution of Benefits, 2015[69]

Stakeholder	$
Individual Wage Income Saved	$224,687,593
Commonwealth Government Income Tax Revenue Saved	$49,563,615
State and Territory Governments Tax Revenue Saved	$9,946,935
Commonwealth Government Company Tax Revenue Saved	$11,548,270
Share of Net Benefits (B) to Australian Commonwealth Government	20.7%
Share of Net Benefits (B) to State and Territory Government	3.3%
Share of Net Benefits (B) to Individuals	76.0%

Regarding the distribution of savings and gains among key stakeholders in 2015, 20.7% of the total net benefits are earned by the Commonwealth government. Meanwhile, 3.3% of net benefits are earned by the State and Territory governments through increased wage income and company tax revenue and 76.0% would be productivity

69 Source: AIHW Health Expenditure Database; author calculations

gains realised by individuals (AIHW Health Expenditure Database; author calculations). Table 5.6 provides the expected distribution of potentially-realisable net benefits for the primary stakeholders given the use of St. John's wort among the target population.

Conclusion

In conclusion, this analysis demonstrates that there are significant productivity gains to be earned back (in the form of increased personal wage income and tax revenue) by the average sufferer of moderate major depression. A concerted effort is needed to identify the populations at high risk of major depression-attributed episodes and motivate them to use St. John's wort as a means to help maximise their quality of life by helping to ease the severity of major depression to a milder form. In the above case study, the use of St. John's wort yields potential net benefits in successful diagnosis transitions from moderate to mild forms of major depression, which in turn, would yield a lower risk of experiencing a costly major depression-attributed medical episode. The majority of this benefit would be conferred to the final consumer of St. John's wort, but derived benefits to other stakeholders would also be realised, such as gained tax revenue from higher productivity. In terms of the ratio of gains in productivity, $7.38 can be gained per $1 spent on St. John's wort, a demonstration of the cost-effectiveness of St. John's wort.

A St. John's wort regimen ought to be an important tool for preventing costly events and productivity losses due to major depression. This should be considered as an option for consumers, general practitioners, employers, and policymakers as a means to reduce personal and societal costs. Understanding this link will help these key stakeholders make recommendations on the best course of action to help minimise current and futures costs and maximise benefits.

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CHAPTER 6 APPENDIX

The Economic Model

This report explores the possible direct economic benefits derived from using various complementary medicine regimens through the avoided hospital separation expenditures associated with disease events. It further calculates the additional indirect benefits through the increased quality and quantity of remaining life years. Specifically, this report outlines a systematic approach to understanding and evaluating the scientific literature for each of the CM regimens explored in the study, and shows how to translate health benefits derived from the use of CM into economic net benefits in terms of avoided health care costs and/or gains in productivity.

In order to determine the number of adverse avoidable events between the two states, or the change in event risk, the relative risk of these events occurring between the two states is required. Relative risk reduction (*RRR*) is a measure of expected efficacy of the regimen under study and this measure, in turn, can be used to determine the number of people who would need to take a given CM regimen to prevent one disease event and/or death (Barratt et al. 2004). It can be shown that the number of people who would need to utilise the preventive regimen in order to prevent one disease event, is simply the inverse of the difference between observed risk of the control state (subscript *i*) and the observed risk of the treatment state (subscript *j*), or:

1. $\Delta Risk = Risk_{ie} - Risk_{ie} * (1 - RRR_e)$

e indicates the type of event outcome where $e = x$ for avoided hospital utilisation events X and $e = y$ for avoided disease-attributed death events Y.

The potential savings to health care providers through reduced medical service utilisation following disease events, S_t, that are realisable if the entire target population were to sufficiently utilise a given CM regimen can be expressed as:

2. $S_t = h_t * Pop_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x))$

The term h_t is the expected per-person cost of a disease-attributed medical event in year t and Pop_t is the total number of people in the target population in year t yet to realise the benefits of using a given CM regimen. In addition, a percentage of the target population already uses a given CM regimen and, therefore, these people should be removed from the population under analysis. An easy way to do this is to observe the population's purchasing behaviour through consumer research and identify only those who have not bought any a given CM regimen. In this analysis, all population data is adjusted downward by current CM supplement utilisation weights in order to calculate only the net benefits yet to be realised.

Avoided medical expenditures are not the only potential benefits of using of a given CM regimen. Prevention of disease events can also result in enhanced quality and quantity of life. Calculation of these terms requires knowledge of two factors: quality of life and expected residual life.

If the possible net

If the possible net health care cost savings is positive, then the CM regimen in question should be considered an effective means to help reduce overall disease-related individual lifetime costs and total social health care costs.

An individual's quality of life is known to correlate with earning potential. If a person is healthy, then that person is able to enjoy life, be more productive, and contribute more to society than a sick person who is in pain, immobile, and/or physically or mentally limited. Given the negative impact of disease events on quality of life, it naturally follows that prevention of disease events through the consumption of a given CM regimen also reduces the risk of compromised earning potential.

To estimate the enhanced quality of life gained from avoided disease-attributed events, the average difference in quality of life for individuals who experience disease events versus disease-free individuals can be estimated. The concept of disability-adjusted life years lost (D) is based on the premise that the onset of disease can negatively impact a person's quality of life and personal productivity. In terms of monetary impact, a healthy year is naturally worth more than a sick year. D is defined as a life quality weight that reflects the discount of that year in terms of degree of illness. If D = 1, then the individual is deceased over the entire year (Sassi, 2006). If D = 0, the individual is considered in optimal health during the entire year (Sassi, 2006). The continuum between 0 and 1 reflects the transition from optimal health to increasingly worse health, leading up to death, for some or all of the year. D can be estimated from the Australian Institute of Health and Welfare's 2003 report on the burden of disease and injury.

An individual's lifespan or residual life years naturally impacts that person's personal earning capacity and, therefore, plays into the calculation of W. To estimate the total number of disability-adjusted life years, one must first determine the expected number of life years remaining for a given target population, the expected number of life years remaining for the subset of the population that experience a disease event, and the mean number of years lost due to the onset of disease. These statistics, reported by the Australian Institute of Health and Welfare, were used for the purposes of this report's analysis and is reported in each case studies' respective chapter (AIHW, Breg et al., 2007).

Because interest is in the 'gain' or change in disability-adjusted life years given the use of a given CM regimen, the total number of avoided events as calculated in equation (1) determines the changes in quality-adjusted life years, measured as person years in year t, between the control and treatment scenarios among those who are still alive. The gain in years from avoided disease-attributed events can then be matched with a median wage income estimate by age cohort to calculate the gain in productivity, as measured in gained earnings. In addition, a separate NNT can be calculated for death risk when a mortality rate for a given disease is available. Thus, the gain in productivity, W, from avoided events and deaths can be calculated as followed:

3. $$W_t = \bar{I}_t * L_{Pop} * Pop_t \Big((Risk_{ix} - Risk_{ix} * (1 - RRR_x)) + D * (Risk_{iy} - Risk_{iy} * (1 - RRR_y)) \Big)$$

where $\bar{I}_t$ is the median per capita wage income for a member of the target population Pop_t and L_{Pop} is the average remaining life expectancy, in years, per member of the target population. Note that L_{Pop} serves as a proxy for capturing residual future gains in productivity savings.

Finally, the total cost of a given CM regimen, assuming 100% utilisation by the entire observed population can be represented by:

4. $C_t = Pop_t * d_t$

where Pop_t is the same total number of people in the target population in year t that are at risk of experiencing an adverse outcome and have yet to realise the benefits of using a given CM regimen and d_t is the expected per-person cost of a given CM regimen utilisation per year t. Note that the entire target population must take the given CM regimen in order for the total number of avoided events to be realised.

Thus, combining the terms outlined in equations 2, 3, and 4, in the same fashion as shown in Figure 2, the model used to estimate the total potential net economic benefits yet to be realised from the use of a given CM in Australia is as follows:

5. $B_t = Pop_t * \Big(h_t * (Risk_{ix} - Risk_{ix} * (1 - RRR_x)) + \bar{I}_t * L_{Pop} * \Big((Risk_{ix} - Risk_{ix} * (1 - RRR_x)) + D * \big(Risk_{iy} - Risk_{iy} * (1 - RRR_y)\big)\Big) - d_t\Big)$

Overall, if the possible net health care cost savings is positive, then the CM regimen in question should be considered as an effective means to help reduce overall disease-related individual lifetime costs and total social health care costs. Of course, the prior cost-benefit analysis makes the assumption that the entire target population started from a base of zero CM regimen utilisation. In other words, the calculated net savings is actually the total potential net savings.

List of Common Variables and Equations Health Economics Research

1. Total sample size per study = **N**
2. Number of events occurring in the treatment group per study = **EE**
3. Number of events occurring in the control group per study = **CE**
4. Observed event rate (observed disease prevalence in the target population) = **ER**
5. Treatment group event rate—**TER = EE / N**
6. Control group event rate—**CER = CE / N**
7. Relative risk—**RR = TER/CER**
8. Absolute risk reduction—**ARR = CER – TER**
9. **Relative risk reduction—RRR = ARR/CER**

List of Abbreviations

AMD	Age-related macular degeneration
ARED	Age-related eye disease
B	billion
B12	Vitamin B12 - cyanocobalamin
B6	Vitamin B6 - pyridoxine
B9	Vitamin B9 – folate/folic acid
BMD	Bone mineral density
CBA	Cost-benefit analysis
CVD	Cardiovascular disease
CI	Confidence interval
CTT	Cholesterol Treatment Trialists
DHA	Docosahexaenoic acid
DPA	Dual photon absorptiometry
DXA	Dual-energy X-ray absorptiometry
EPA	Eicosapentaenoic acid
ESRD	End-stage renal disease
FRAX	Fracture Risk Assessment Tool
g	gram
HbA1c	Glycated hemoglobin
IU	International unit
M	million
mcg	microgram
mg	milligram
MI	Myocardial infarction
NNT	Number needed to treat
OR	Odds ratio
PUFA	Polyunsaturated fatty acids
RCT	Randomised controlled trials
RR	Relative risk
RRR	Relative risk reduction
UL	Tolerable Upper Intake Level

Detailed Figures

Chapter 2—Osteoporosis Detailed Results

Table A.1—Burden of Osteoporosis—Detailed Statistics and Forecast: All Women Aged 50 and Over with Osteopenia or Osteoporosis, 2013–2020

Metric	Number of People in Target Population, People	Number of People Experiencing Events, People	Cost per Person Experiencing Event	I: Median Income per Person per Residual Year, $ per Person Year Period
2013	1,819,596	102,602	$28,411	$30,857
2014	1,837,792	103,613	$29,686	$31,474
2015	1,856,170	104,634	$31,018	$32,104
2016	1,874,732	105,666	$32,410	$32,746
2017	1,893,479	106,708	$33,865	$33,401
2018	1,912,414	107,760	$35,385	$34,069
2019	1,931,538	108,823	$36,973	$34,750
2020	1,950,854	109,896	$38,632	$35,445
2015 to 2020 - Annual Average	1,903,198	107,248	$34,714	$33,752

Table A.2—Osteoporosis: Expected Avoided Hospital Separations Given the Use of 'Calcium and Vitamin D' and 'Magnesium', Detailed Results and Forecast, All Women Aged 50 and Over with Osteopenia or Osteoporosis, 2013–2020

Metric	Calcium and Vitamin D	Magnesium
	Avoided Hospital Separations	Avoided Hospital Separations
2013	36,058	7,472
2014	36,419	7,547
2015	36,783	7,622
2016	37,151	7,698
2017	37,523	7,775
2018	37,898	7,853
2019	38,277	7,932
2020	38,660	8,011
2015 to 2020 - Annual Average	37,715	7,815

Table A.3—Osteoporosis: Total Benefits Given the Use of Calcium and Vitamin D Complementary Medicines, Detailed Results and Forecast, All Women Aged 50 and Over with Osteopenia or Osteoporosis, 2013–2020

Metric	S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	W: Gain in Productivity from Avoided Disease-attributed Events	S + W: Total Benefit (Increase in Social Wealth)
2013	$825,607,886	$786,521,072	$1,612,128,958
2014	$845,911,245	$810,274,008	$1,656,185,253
2015	$866,713,904	$834,744,283	$1,701,458,187
2016	$888,028,142	$859,953,560	$1,747,981,703
2017	$909,866,541	$885,924,158	$1,795,790,699
2018	$932,241,989	$912,679,067	$1,844,921,057
2019	$955,167,695	$940,241,975	$1,895,409,670
2020	$978,657,190	$968,637,283	$1,947,294,473
2015: 95% Confidence Interval Upper	$927,439,374	$893,229,833	$1,820,669,207
2015: 95% Confidence Interval Lower	$805,988,434	$776,258,733	$1,582,247,167
2015 to 2020 - Annual Average	$921,779,244	$900,363,388	$1,822,142,631

Table A.4—Osteoporosis: Cost of Complementary Medicine Utilisation and Net Benefits Given the Use of Calcium and Vitamin D, Detailed Results and Forecast, All Women Aged 50 and Over with Osteopenia or Osteoporosis, 2013–2020

Metric	d: Cost of CM Product Per Person Per Year at Preventive Intake Levels, $ Per Person	C: Total Cost of CM	S-C: Net Benefit (Excludes Productivity)	B = S+W-C: Net Benefit (Includes Productivity)	(S+W)/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)
2013	$54.6	$80,135,773	$745,472,113	**$1,531,993,185**	$20.12
2014	$55.7	$80,151,334	$765,759,911	**$1,576,033,919**	$20.66
2015	$56.9	$80,166,897	$786,547,007	**$1,621,291,290**	$21.22
2016	$58.0	$80,182,463	$807,845,679	**$1,667,799,240**	$21.80
2017	$59.2	$80,198,033	$829,668,508	**$1,715,592,666**	$22.39
2018	$60.3	$80,213,605	$852,028,384	**$1,764,707,452**	$23.00
2019	$61.5	$80,229,181	$874,938,514	**$1,815,180,490**	$23.62
2020	$62.8	$80,244,759	$898,412,431	**$1,867,049,714**	$24.27
2015: 95% Confidence Interval Upper	--	--	$847,579,659	**$1,740,827,400**	$22.71
2015: 95% Confidence Interval Lower	--	--	$725,514,356	**$1,501,755,180**	$19.74
2015 to 2020 - Annual Average	--	$80,205,823	$841,573,421	**$1,741,936,808**	$22.34

Table A.5—Osteoporosis: Total Benefits Given the Use of Magnesium Complementary Medicines, Detailed Results and Forecast, All Women Aged 50 and Over with Osteopenia or Osteoporosis, 2013–2020

Metric	S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	W: Gain in Productivity from Avoided Disease-attributed Events	S + W: Total Benefit (Increase in Social Wealth)
2013	$190,096,448	$162,980,738	$353,077,187
2014	$194,771,302	$167,902,756	$362,674,059
2015	$199,561,121	$172,973,420	$372,534,540
2016	$204,468,730	$178,197,217	$382,665,947
2017	$209,497,027	$183,578,773	$393,075,800
2018	$214,648,981	$189,122,852	$403,771,832
2019	$219,927,631	$194,834,362	$414,761,993
2020	$225,336,094	$200,718,360	$426,054,453
2015: 95% Confidence Interval Upper	$268,197,801	$232,465,576	$500,663,377
2015: 95% Confidence Interval Lower	$60,775,833	$52,678,616	$113,454,449
2015 to 2020 - Annual Average	$212,239,930	$186,570,831	$398,810,761

Table A.6—Osteoporosis: Cost of Complementary Medicine Utilisation and Net Benefits Given the Use of Magnesium, Detailed Results and Forecast, All Women Aged 50 and Over with Osteopenia or Osteoporosis, 2013–2020

Metric	d: Cost of CM Product Per Person Per Year at Preventive Intake Levels, $ Per Person	C: Total Cost of CM	S-C: Net Benefit (Excludes Productivity)	B = S+W-C: Net Benefit (Includes Productivity)	(S+W)/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)
2013	$92.0	$149,988,646	$40,107,803	**$203,088,541**	$2.35
2014	$93.9	$150,017,770	$44,753,533	**$212,656,289**	$2.42
2015	$95.8	$150,046,900	$49,514,221	**$222,487,641**	$2.48
2016	$97.7	$150,076,035	$54,392,695	**$232,589,912**	$2.55
2017	$99.6	$150,105,176	$59,391,851	**$242,970,624**	$2.62
2018	$101.6	$150,134,322	$64,514,658	**$253,637,510**	$2.69
2019	$103.7	$150,163,475	$69,764,156	**$264,598,518**	$2.76
2020	$105.7	$150,192,633	$75,143,461	**$275,861,821**	$2.84
2015: 95% Confidence Interval Upper			$130,229,439	**$355,524,035**	$3.34
2015: 95% Confidence Interval Lower			-$113,694,207	**-$46,515,670**	$0.76
2015 to 2020 - Annual Average		$150,119,757	$62,120,174	**$248,691,004**	$2.50

Chapter 3—Cardiovascular Disease Detailed Results

Table A.7— Burden of Cardiovascular Disease—Detailed Statistics and Forecast: All Adults Aged 55 and Over with Cardiovascular Disease, 2013–2020

Metric	Number of People in Target Population, People	Number of People Experiencing Events, People	Number of Disease-attributed Hospital Separations, People	Number of Disease-attributed Deaths, People	Cost per Person Experiencing Event	I: Median Income per Person per Residual Year, $ per Person Year Period
2013	848,500	378,789	337,913	40,876	$31,397	$37,448
2014	856,985	382,189	341,292	40,896	$32,806	$38,197
2015	865,555	385,622	344,705	40,917	$34,278	$38,961
2016	874,210	389,089	348,152	40,937	$35,816	$39,740
2017	882,953	392,591	351,634	40,958	$37,424	$40,535
2018	891,782	396,128	355,150	40,978	$39,104	$41,346
2019	900,700	399,700	358,701	40,999	$40,859	$42,173
2020	909,707	403,308	362,288	41,019	$42,692	$43,016
2015 to 2020 - Annual Average	887,484	394,407	353,438	40,968	$38,362	$40,962

Table A.8—Cardiovascular Disease: Expected Avoided Medical Events Given the Use of Omega-3 Fatty Acids and Folic Acid, B6 and B12, Detailed Results and Forecast, All Adults Aged 55 and Over with Cardiovascular Disease, 2013–2020

Metric	Omega-3 Fatty Acids		Folic Acid, B6 and B12
	Avoided Hospital Separations	Avoided Deaths	Avoided Hospital Separations
2013	6,677	2,375	4,689
2014	6,744	2,396	4,736
2015	6,811	2,418	4,784
2016	6,879	2,439	4,832
2017	6,948	2,461	4,880
2018	7,017	2,483	4,929
2019	7,088	2,506	4,978
2020	7,159	2,528	5,028
2015 to 2020 - Annual Average	6,984	2,473	4,905

Table A.9—Cardiovascular Disease: Total Benefits Given the Use of Omega-3 Fatty Acid Complementary Medicines, Detailed Results and Forecast, All Adults Aged 55 and Over with Cardiovascular Disease, 2013–2020

Metric	S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	W: Gain in Productivity from Avoided Disease-attributed Events	S + W: Total Benefit (Increase in Social Wealth)
2013	$173,994,016	$355,216,490	$529,210,507
2014	$178,272,879	$365,661,226	$543,934,105
2015	$182,656,968	$376,415,593	$559,072,561
2016	$187,148,870	$387,488,822	$574,637,692
2017	$191,751,237	$398,890,422	$590,641,659
2018	$196,466,786	$410,630,186	$607,096,972
2019	$201,298,300	$422,718,199	$624,016,499
2020	$206,248,630	$435,164,851	$641,413,481
2015: 95% Confidence Interval Upper	$241,596,819	$435,627,609	$677,415,454
2015: 95% Confidence Interval Lower	$123,717,117	$317,203,576	$440,729,667
2015 to 2020 - Annual Average	$194,261,798	$405,218,012	$599,479,811

Table A.10—Cardiovascular Disease: Cost of Complementary Medicine Utilisation and Net Benefits Given the Use of Omega-3 Fatty Acid, Detailed Results and Forecast, All Adults Aged 55 and Over with Cardiovascular Disease, 2013–2020

Metric	d: Cost of CM Product Per Person Per Year at Preventive Intake Levels, $ Per Person	C: Total Cost of CM	S-C: Net Benefit (Excludes Productivity)	B = S+W-C: Net Benefit (Includes Productivity)	(S+W)/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)
2013	$98.5	$69,383,450	$104,610,567	**$459,827,057**	$7.63
2014	$100.5	$69,396,922	$108,875,957	**$474,537,183**	$7.84
2015	$102.5	$69,410,397	$113,246,571	**$489,662,163**	$8.05
2016	$104.6	$69,423,875	$117,724,995	**$505,213,817**	$8.28
2017	$106.6	$69,437,355	$122,313,882	**$521,204,304**	$8.51
2018	$108.8	$69,450,838	$127,015,948	**$537,646,133**	$8.74
2019	$110.9	$69,464,324	$131,833,976	**$554,552,175**	$8.98
2020	$113.2	$69,477,812	$136,770,817	**$571,935,669**	$9.23
2015: 95% Confidence Interval Upper			$174,025,999	**$608,952,287**	$9.76
2015: 95% Confidence Interval Lower			$52,467,143	**$370,372,039**	$6.35
2015 to 2020 - Annual Average		$69,444,100	$124,817,698	**$530,035,710**	$8.49

Table A.11—Cardiovascular Disease: Total Benefits Given the Use of Folic acid, B6 and B12 Complementary Medicines, Detailed Results and Forecast, All Adults Aged 55 and Over with Cardiovascular Disease, 2013–2020

Metric	S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	W: Gain in Productivity from Avoided Disease-attributed Events	S + W: Total Benefit (Increase in Social Wealth)
2013	$133,980,841	$59,534,133	$193,514,974
2014	$137,275,699	$61,332,064	$198,607,763
2015	$140,651,585	$63,184,292	$203,835,877
2016	$144,110,490	$65,092,458	$209,202,948
2017	$147,654,457	$67,058,250	$214,712,707
2018	$151,285,577	$69,083,409	$220,368,987
2019	$155,005,994	$71,169,728	$226,175,722
2020	$158,817,903	$73,319,054	$232,136,957
2015: 95% Confidence Interval Upper	$215,569,281	$96,839,239	$312,408,520
2015: 95% Confidence Interval Lower	$65,733,889	$29,529,346	$95,263,234
2015 to 2020 - Annual Average	$149,587,668	$68,151,199	$217,738,866

Table A.12—Cardiovascular Disease: Cost of Complementary Medicine Utilisation and Net Benefits Given the Use of Folic acid, B6 and B12, Detailed Results and Forecast, All Adults Aged 55 and Over with Cardiovascular Disease, 2013–2020

Metric	d: Cost of CM Product Per Person Per Year at Preventive Intake Levels, $ Per Person	C: Total Cost of CM	S-C: Net Benefit (Excludes Productivity)	B = S+W-C: Net Benefit (Includes Productivity)	(S+W)/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)
2013	$53.9	$41,643,277	$92,337,564	**$151,871,697**	$4.65
2014	$55.0	$41,651,363	$95,624,336	**$156,956,400**	$4.77
2015	$56.1	$41,659,451	$98,992,134	**$162,176,426**	$3.38
2016	$57.2	$41,667,540	$102,442,950	**$167,535,408**	$5.02
2017	$58.4	$41,675,631	$105,978,826	**$173,037,076**	$5.15
2018	$59.5	$41,683,723	$109,601,854	**$178,685,263**	$5.29
2019	$60.7	$41,691,817	$113,314,177	**$184,483,905**	$5.42
2020	$62.0	$41,699,913	$117,117,990	**$190,437,044**	$5.57
2015: 95% Confidence Interval Upper			$175,499,765	**$272,245,481**	$5.17
2015: 95% Confidence Interval Lower			$22,484,503	**$22,396,074**	$1.58
2015 to 2020 - Annual Average		$41,679,679	$107,907,988	**$176,059,187**	$4.57

Chapter 4—Age-related Macular Degeneration Detailed Results

Table A.13— Burden of Age-related Macular Degeneration—Detailed Statistics and Forecast: All Adults Aged 55 and Over with Age-related Macular Degeneration, 2013–2020

Metric	Number of People in Target Population, People	Number of Disease-attributed Hospital Separations, People	Cost per Person Experiencing Event	I: Median Income per Person per Residual Year, $ per Person Year Period
2013	164,612	8,196	$23,882	$37,448
2014	166,258	8,278	$24,954	$38,197
2015	167,921	8,360	$26,073	$38,961
2016	169,600	8,444	$27,244	$39,740
2017	171,296	8,529	$28,466	$40,535
2018	173,009	8,614	$29,744	$41,346
2019	174,739	8,700	$31,079	$42,173
2020	176,486	8,787	$32,474	$43,016
2015 to 2020 - Annual Average	172,175	8,572	$29,180	$40,962

Table A.14—Age-related Macular Degeneration: Expected Avoided Medical Events Given the Use of Lutein and Zeaxanthin, Detailed Results and Forecast, All Adults Aged 55 and Over with Age-related Macular Degeneration, 2013–2020

Metric	Lutein and Zeaxanthin
	Avoided Hospital Separations
2013	1,047
2014	1,057
2015	1,068
2016	1,079
2017	1,089
2018	1,100
2019	1,111
2020	1,122
2015 to 2020 - Annual Average	1,095

Table A.15—Age-related Macular Degeneration: Total Benefits Given the Use of Lutein and Zeaxanthin Complementary Medicines, Detailed Results and Forecast, All Adults Aged 55 and Over with Age-related Macular Degeneration, 2013–2020

Metric	S: Avoided Cost of Disease-attributed Medical Events Requiring Hospital Services	W: Gain in Productivity from Avoided Disease-attributed Events	S + W: Total Benefit (Increase in Social Wealth)
2013	$24,503,067	$23,992,269	$48,495,337
2014	$25,105,647	$24,716,836	$49,822,483
2015	$25,723,045	$25,463,284	$51,186,330
2016	$26,355,627	$26,232,276	$52,587,902
2017	$27,003,765	$27,024,490	$54,028,255
2018	$27,667,841	$27,840,630	$55,508,471
2019	$28,348,249	$28,681,417	$57,029,666
2020	$29,045,390	$29,547,596	$58,592,986
2015: 95% Confidence Interval Upper	$56,866,016	$56,291,762	$113,157,778
2015: 95% Confidence Interval Lower	$740,590	$733,111	$1,473,702
2015 to 2020 - Annual Average	$27,357,319	$27,464,949	$54,822,268

Table A.16—Age-related Macular Degeneration: Cost of Complementary Medicine Utilisation and Net Benefits Given the Use of Lutein and Zeaxanthin Detailed Results and Forecast, All Adults Aged 55 and Over with Age-related Macular Degeneration, 2013–2020

Metric	d: Cost of CM Product Per Person Per Year at Preventive Intake Levels, $ Per Person	C: Total Cost of CM	S-C: Net Benefit (Excludes Productivity)	B = S+W-C: Net Benefit (Includes Productivity)	(S+W)/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)
2013	$113.9	$18,368,497	$6,134,570	**$30,126,840**	$2.64
2014	$116.1	$18,372,063	$6,733,583	**$31,450,419**	$2.71
2015	$118.5	$18,375,631	$7,347,414	**$32,810,699**	$2.79
2016	$120.8	$18,379,199	$7,976,428	**$34,208,703**	$2.86
2017	$123.2	$18,382,768	$8,620,997	**$35,645,487**	$2.94
2018	$125.7	$18,386,337	$9,281,504	**$37,122,134**	$3.02
2019	$128.2	$18,389,907	$9,958,342	**$38,639,759**	$3.10
2020	$130.8	$18,393,478	$10,651,912	**$40,199,507**	$3.19
2015: 95% Confidence Interval Upper			$42,878,500	**$96,754,660**	$6.16
2015: 95% Confidence Interval Lower			-$21,155,125	**-$18,484,251**	$0.08
2015 to 2020 - Annual Average		$18,384,553	$8,972,766	**$36,437,715**	$3.02

Chapter 5—Major Depression Detailed Results

Table A.17—Burden of Major Depression—Detailed Statistics and Forecast: All Adults Aged 20 and Over with Major Depression, 2013–2020

Metric	Number of People in Target Population, People	Average Annual Lost Wages per Person Experiencing a Transition from mild to moderate major depression	I: Median Income per Person per Residual Year, $ per Person Year Period
2013	230,429	$10,391	$49,482
2014	232,733	$10,858	$50,472
2015	235,061	$11,345	$51,481
2016	237,411	$11,854	$52,511
2017	239,785	$12,386	$53,561
2018	242,183	$12,942	$54,632
2019	244,605	$13,523	$55,725
2020	247,051	$14,130	$56,840
2015 to 2020 - Annual Average	241,016	$12,697	$54,125

Table A.18—Major Depression: Expected Successful Transitions from Moderate to Mild Severity of Major Depression Given the use of St. John's wort Complementary Medicines, Detailed Results and Forecast, All Adults Aged 20 and Over with Moderate Major Depression, 2013–2020

Metric	St. John's wort
	Successful Transitions from Moderate to Mild Severity of Major Depression
2013	39,060
2014	39,451
2015	39,845
2016	40,244
2017	40,646
2018	41,053
2019	41,463
2020	41,878
2015 to 2020 - Annual Average	40,855

Table A.19— Major Depression: Net Benefit and Cost Results Given the Use of St. John's wort Complementary Medicines, Detailed Results and Forecast, All Adults Aged 20 and Over with Moderate Major Depression, 2013–2020

Metric	W: Gain in Productivity from Avoided Disease-attributed Events	d: Cost of CM Product Per Person Per Year at Preventive Intake Levels, $ Per Person	C: Total Cost of CM	B = S+W-C: Net Benefit (Includes Productivity)	(S+W)/C: Benefit Cost Ratio Expressed in $ ($ gain per $1 spent on CM)
2013	$265,548,043	$181.6	$40,042,879	**$225,505,165**	$6.63
2014	$280,240,756	$185.2	$40,050,654	**$240,190,102**	$7.00
2015	$295,746,413	$188.9	$40,058,431	**$255,687,982**	$7.38
2016	$312,109,995	$192.7	$40,066,209	**$272,043,786**	$7.79
2017	$329,378,969	$196.6	$40,073,989	**$289,304,980**	$8.22
2018	$347,603,433	$200.5	$40,081,770	**$307,521,662**	$8.67
2019	$366,836,251	$204.5	$40,089,553	**$326,746,698**	$9.15
2020	$387,133,217	$208.6	$40,097,338	**$347,035,880**	$9.65
2015: 95% Confidence Interval Upper	$375,128,349			**$336,504,313**	$9.36
2015: 95% Confidence Interval Lower	$167,930,117			**$125,562,105**	$4.19
2015 to 2020 - Annual Average	$339,801,380		$40,077,882	**$299,723,498**	$8.05

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The Australian Self Medication Industry (ASMI) is the peak body representing companies involved in the manufacture and distribution of consumer health care products in Australia. Since its establishment in 1974, the Association has focussed its efforts on supporting the progress and development of the Self Care products industry, including both over-the-counter (OTCs) and complementary medicine products.

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Frost & Sullivan (Australia) Pty. Ltd.
Level 9, Suite 1
189 Kent Street (ADC House)
Sydney, NSW 2000 Australia
Tel: +61 (0) 2 8247 8900

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Silicon Valley
331 E. Evelyn Ave. Suite 100
Mountain View, CA 94041
Tel 650.475.4500
Fax 650.475.1570

San Antonio
7550 West Interstate 10,
Suite 400,
San Antonio, Texas 78229
Tel 210.348.1000
Fax 210.348.1003

London
4 Grosvenor Gardens
London SW1W 0DH
Tel +44 (0)20 7343 8383
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