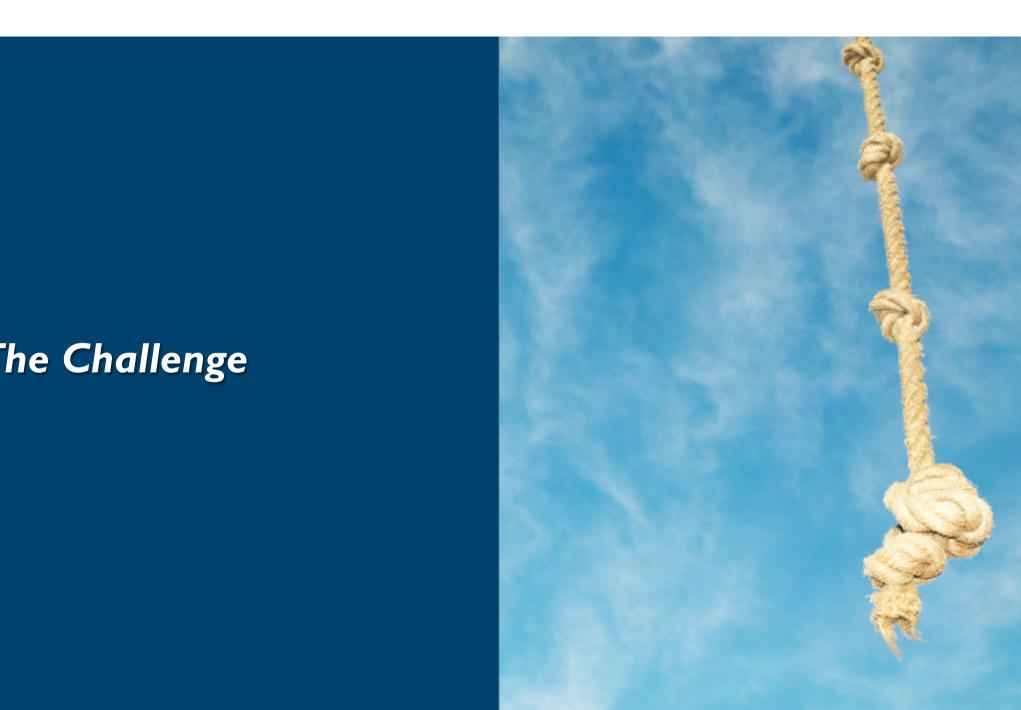


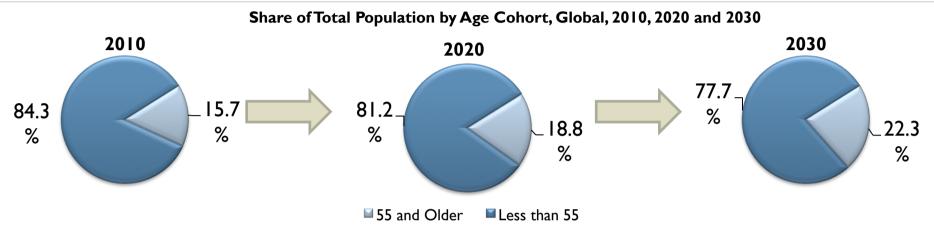
#### Contents

- The Challenge—The Global Burden of Non Communicable Diseases (NCDs) among Older Populations
- Overarching Methodology—From Health Benefits to Cost Savings
- The Benefits of Omega-3 Supplements Regarding CVD-attributed Health Outcomes
- The Global Burden of Osteoporosis-attributed Bone Fractures and the Benefits of Calcium + Vitamin D dietary/ food supplements
- Lutein & Zeaxanthin Supplements and the Management of the Severity of Age-related Macular Degenerationattributed Visual Acuity
- **Concluding Remarks**





## The Challenge—An Ageing World is Driving the Cost of Heath Care related on Noncommunicable Diseases Throughout the World



#### pact of the Ageing Population on Nations

**Growing cost of health care**: The cost of health care will rise as the proportion of the aged population grows relative to younger population due to demand growth.

**More burden on public care systems**: Long queues in publically-funded hospitals, retirement homes with long te care may lead to a compromise in quality, service dissatisfaction, and an overall lack of care.

**Shrinking incomes and personal savings:** Seniors will decreasingly struggle to afford the cost of medical insurance and post-retirement living costs, especially if they suffer from a age-related disease like CVD, osteoporosis, age-related eye disease or dementia.

What if certain dietary/food supplements could contribute to reducing overall healthcare expenditures?

### he Hypothesis

We hypothesised that if selected dietary/food supplements were taken at the same level as dictated by the clinical research, there would be cost savings to a given country's nealth care system from reduced medical expenses associated with those lower risks o disease events and less loss of productivity related to long-term disability.

In other words, using dietary/food supplements in certain cases to reduce disease-attributed adverse events would also reduce the associated medical costs of those events – and save the health care system money.

#### he Solution

The objective of this line of research is to determine the potential net economic savings that could be realised given ne usage of dietary/food supplements that are scientifically shown to reduce the occurrence of disease-related event among a targeted population.

he objectives of this evidence-based cost savings research are:

- To critically review the research literature which shows an association between dietary/food supplements intake and disease risk reduction to quantify the risk reduction; and then
- To determine the potential net health care cost savings from the use of certain dietary/food supplements as a result of avoided disease-related medical events.

#### Research Scope

The disease conditions and food supplement combinations this field of research examines over the years includes:



Omega-3 dietary/food supplements and CVD-attributed Health Outcomes



Calcium and Vitamin D Supplements and Osteoporosis-attributed Bone Fractures



Lutein & Zeaxanthin Supplements and the Management of the Severity of Age-related Macular Degeneration-attributed Visual Acuity

Nethodology—From lealth Benefits to Cost avings

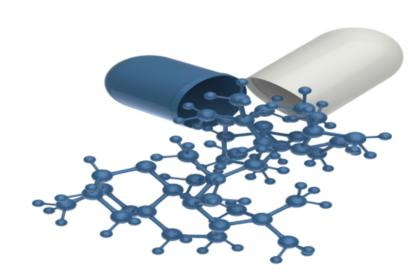


### Overarching Research Methodology—From Health Benefits to Cost Savings

Many dietary/food supplements products in the market today have significant bodies of scientific literature helping to back up their health efficacy claims

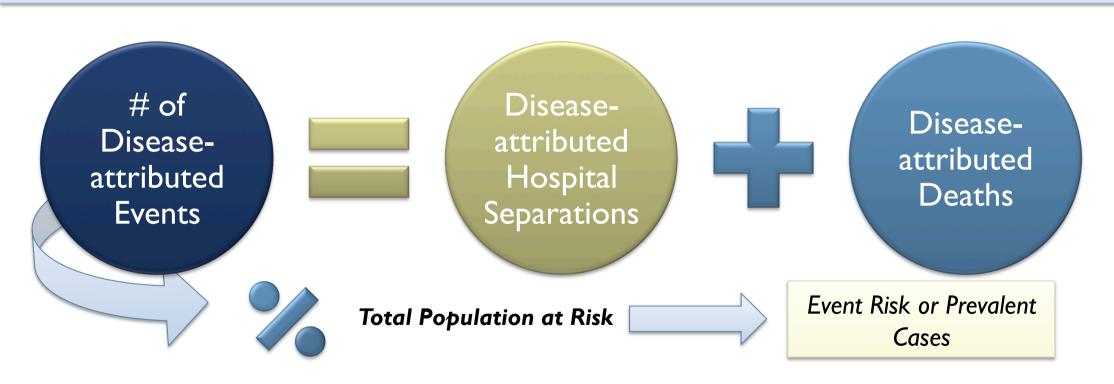
The studies with these bodies of science are typically aimed at identifying evidence for a **change in the risk** of the experiencing an disease-attributed adverse **event outcome** in a treatment population versus a control (placebo) population **Change in Risk** can be measured **directly** in a given

Change in Risk can be measured directly in a given study or a change in risk can be implied by a change in a correlated biomarker



#### Overarching Research Methodology—What is a Disease-attributed Event?

Event risk is the number of people relative to the total population who experienced a disease-attributed event or a ange in health status, in a set period of time, that necessitates the need for medical attention and contributes to a lo in quality of life.



Source: Frost & Sul

### Overarching Research Methodology—To Use or Not to Use dietary/food upplements

Net benefit gain, calculated as the difference between a target population's <u>expected</u> annual cost of a specified diseas under the control scenario and the treatment scenario will provide an economic reasoning for that person to adopt the specified dietary/food supplements regimen.



Source: Frost & Sul

supplements

population

## Overarching Research Methodology—Deducing Efficacy from the Scientific iterature (continued)

ealisable net benefits derived from the use of a given dietary/food supplements regimen is dependent on the **chang n the event rate weighted by Relative Risk Reduction factor**, which is derivable from the scientific literature

## Search Review of the scientific literature

# Qualify Identification of qualified studies and/ or Meta Analyses

Extract, Weight and Aggregate

Deduce overall expected impact of dietary
food supplements intervention

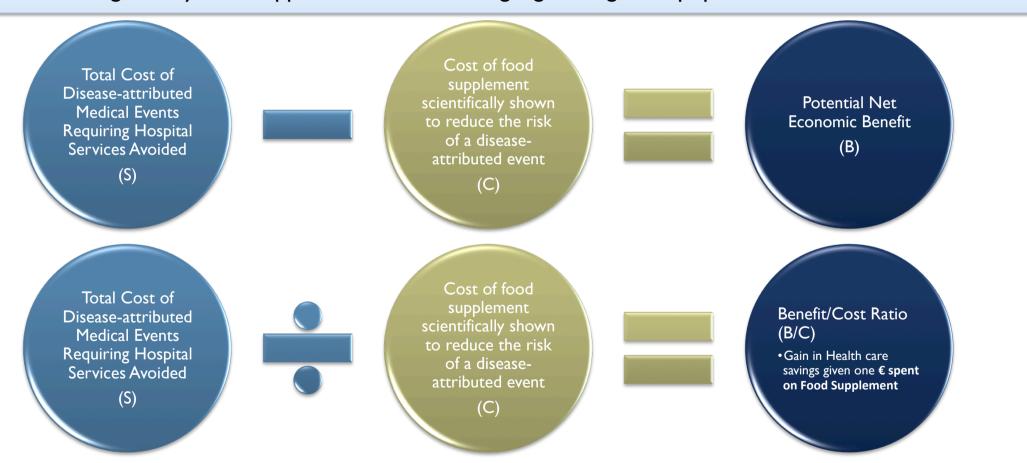
- Frost & Sullivan researched the scientific literature and built a database of studies that was expected to investigate a relationship between a given supplement's intake and the risk of specific diseases
- All findings were included in the database, independent of whether the findings were positive, negative, or null.

- For each study identified, the following filter question was used to develop a list of eligible studies:
  - 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 dietary/food supplements utilisation and the probability of a specific health condition event among a well-defined at-risk population?
- If a recent, independently produced, meta analysis was identified that explored the same hypothesis of interest, then the results of this study was used to deduce the RRR
- If not, then we conducted an objective random-effects meta analysis using meta analysis best practices.
- From this, the qualified studies' findings were weighted and aggregated in order to determine an overall expected impact of dietary/food supplements intervention on disease event occurrence.

Source: Frost & Sul

## Overarching Research Methodology—Determination of Health Care Cost Savings

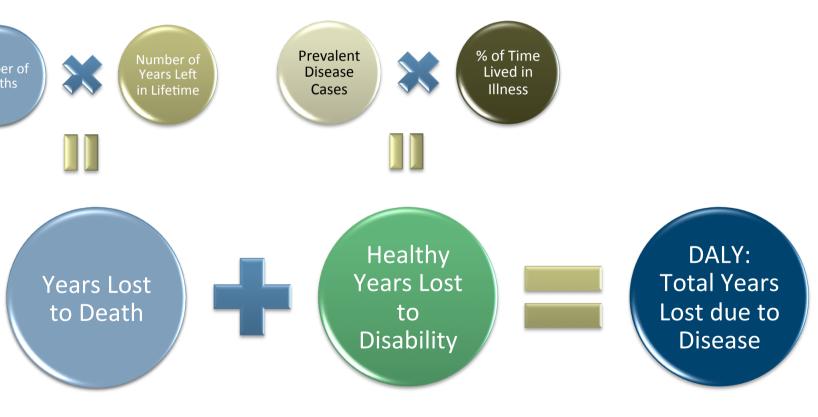
Once the expected risk reduction factor is derived from the literature review, the potential cost savings derived fron increasing dietary/food supplements intake among a given high risk population can be calculated.



Source: Frost & Sul

## Overarching Research Methodology—Using Disability-adjusted Life Years DALY) as a Proxy for per-Event Health Care Costs

Disability-adjusted Life Years (DALY) is a measure of the number of life years lost due to disease and it includes yea st due to premature death and years lost due to disease-attributed disability (morbidity) or where an individual lives physical or mental pain and is thus not able to contribute to society in the same degree as if they were healthy.



- Using a monetary measure of he care cost may actually lead to un comparisons of cost-effectivene
- Therefore, health economists of use a measure of time as a prox for the price of health care since is directly related to per-person productivity.
- DALYs allows health economists compare the cost effective of a given regimen in terms of time saved across countries that varie by economic performance. In o words, a human life is worth the same independent of which couthat human happens to be in.

The Benefits of Omega-3 upplements Regarding CVD-attributed Health Outcomes



#### he Burden of Cardiovascular Disease

Cardiovascular disease (CVD) is a significant burden on the health and wealth of the citizens of the World and the European Union (EU) specifically.

**Definition**—CVD is a set of conditions that causes the accumulation of plaque in the coronary arteries, thereby restricting blood flow to the heart and potentially resulting in angina, arrhythmia, myocardial infarction (MI), and heart failure [I]

**Prevalence**—It is expected that there will be over 38.4 million CVD-attributed medical events over the next 5 years (2016 to 2020) in the EU among adults age 55 and older [2]

Globally, over 30% of deaths are attributed to heart disease and stroke -  $\sim 18$  million deaths per year.

In terms of disability-adjusted life years, over 200 million life years were lost in 2015 due to CVD and over 26 million life years were lost in the European Union alone [3]



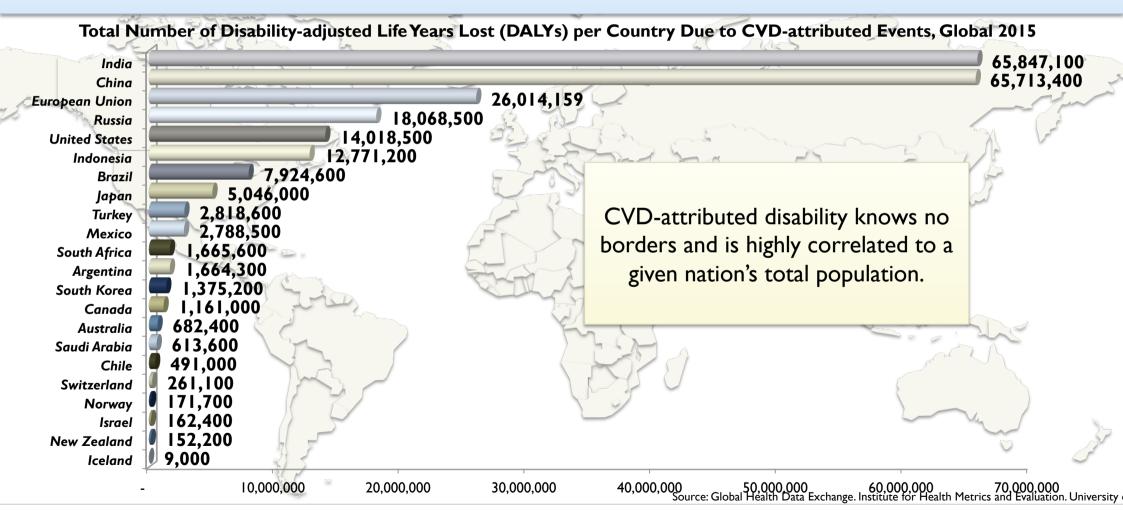
the purposes of this study, CVD is strictly defined as events associated with the following ICD /ISHMT codes: 0901 (Hypertensive diseases), 0902 (Angina pectoris), 0903 (Acute dial infarction), 0904 (Other ischaemic heart disease), 0907 (Heart failure), 0908 (Cerebrovascular diseases), and 0909 (Atherosclerosis).

rce: World Health Organization, Regional Office of Europe; Leal J, Luengo-Fernandez R, Gray A. Economic Costs. In: Nichols M, Townsend N, Scarborough P, Rayner M et al. European ascular Disease Statistics 2012. European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis; Frost & Sullivan analysis

oal Health Data Exchange. Institute for Health Metrics and Evaluation. University of Washington

#### he Burden of Cardiovascular Disease

The cost of CVD-attributed events, in terms of lost healthy life years lost, is over 200 million years per year globally



### The Benefits of Omega-3 dietary/food supplements

mega-3 EPA + DHA fatty acids are among the most extensively researched ingredients in food and beverages in terr of understanding the specific health benefits for users

There has been a significant amount of research in determining the underlying mechanism of action by which omega-3 might reduce CVD and it is likely that these compounds may have roles in regulating cell membrane properties or intracellular signal transduction [1].

The recommended daily intake of omega-3 food supplement is highly variable and depends on the individual user's health profile in terms of their cardiac function, blood pressure levels, blood triglyceride (TG) levels, and other health parameters. This has made it difficult for regulators, specifically the European Food Safety Authority's (EFSA) panel on Dietetic Products, Nutrition, and Allergies to set a standard intake level.

However, there is a proposed adequate daily intake of 250 mg for EPA + DHA for all adults for normal health and wellness [2].

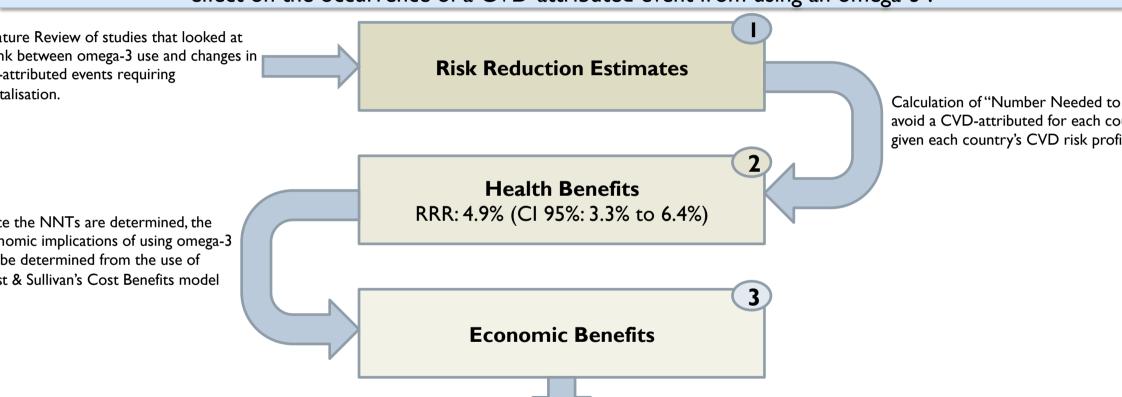
The typical amount level found in a single 1,000 mg non-concentrated omega-3 supplements capsule is 250 mg to 300 mg of EPA+DHA [2].



ton, P., Harris, W., & Appel, L. "Fish Consumption, Fish Oil, Omega-3 Fatty Acids, and Cardiovascular Disease." (Circulation) 106 (2002). nal. 2010. http://www.efsa.europa.eu/en/efsajournal/pub/1461.htm.

## he Benefits of Omega-3 Dietary/Food Supplements: Research Methodology

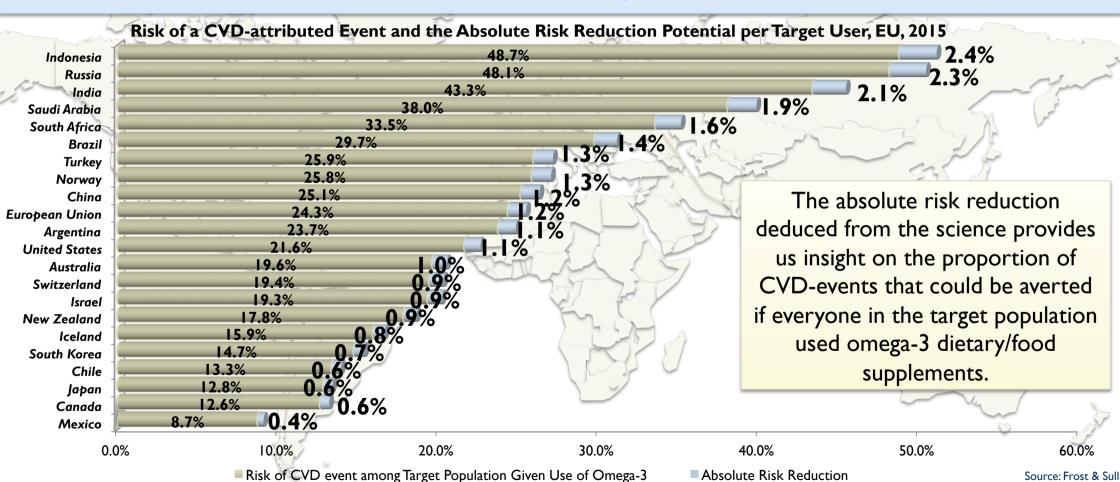
A new random-effects systematic review of the omega-3 literature was conducted in order to deduce the expected effect on the occurrence of a CVD-attributed event from using an omega-3.



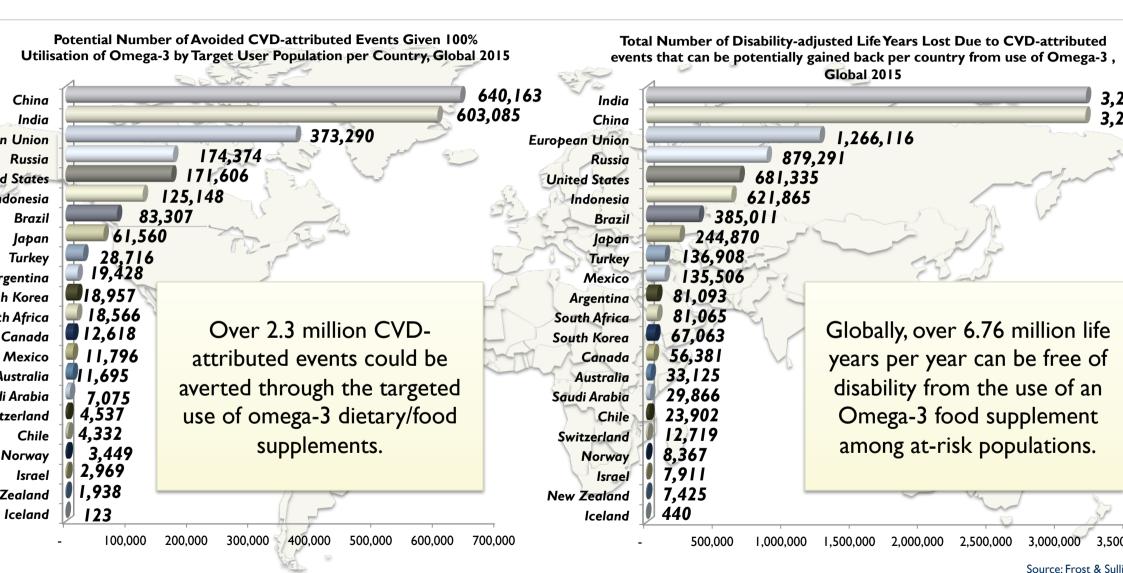
A greater understanding of the economic implications of the use of omega-3 as a means to reduce CVD event risl given the varying risk profiles of each EU country

### he Benefits of Omega-3 dietary/food supplements: Global and EU Benefits

The absolute risk reduction measure per country provides us guidance on how many at-risk people would need to use omega-3 order to realise an avoided, and costly, CVD-attributed event.



### The Benefits of Omega-3 dietary/food supplements (continued)



The Global Burden of Osteoporosis-attributed Sone Fractures and the Senefits of Calcium + Sitamin D dietary/food



#### he Burden of Osteoporosis

As osteoporosis becomes increasingly more prevalent, the importance of using regimen options known to decrease bone fracture risk becomes more apparent as a means to control the increasing financial burden of osteoporosis.

Osteoporosis is the most prevalent age related bone disease globally is characterised by accelerated bone loss, which results in brittle and weak bones that are easily fractured Prevalence of osteoporosis is especially higher in the European Union which varies from 15% to 21% of the total population of people age 55 and older depending on the country

Each osteoporosis-attributed fracture is estimated to cost EU Average: **€21,231 per** Fracture in the EU

In 2015, there will be 1.2 million disease—attributed bone fractures among people age 55 and over with osteopenia or osteoporosis in the EU who are at risk of experiencing a costly disease-attributed bone fracture which is more than any other region of the world

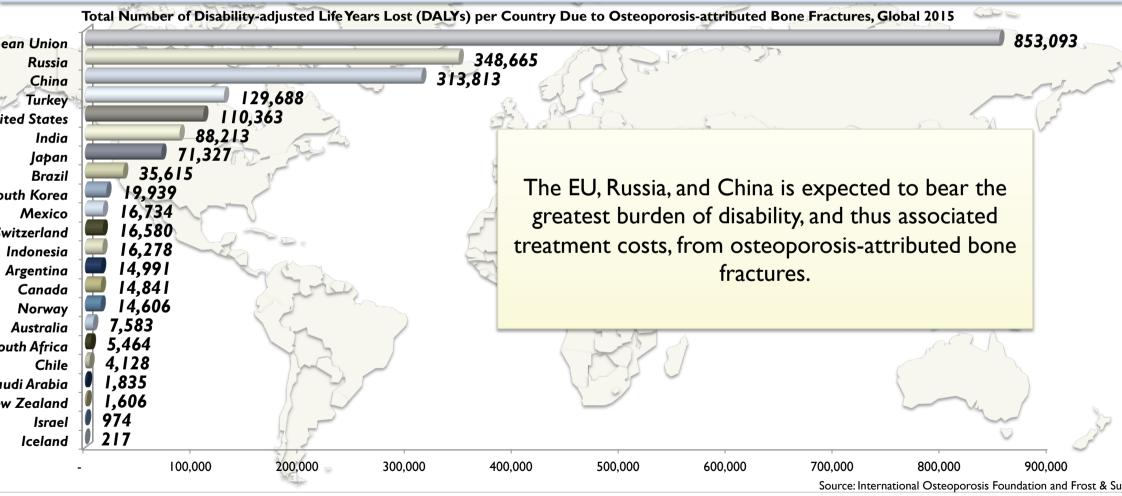
Globally, over 3.0 million osteoporosis-attributed bone fractures occurred in 2015 [1] As a consequence, over 2.0 million disability-adjusted life years will be lost globally due to osteoporosis-attributed bone fractures [2]



[1] J.A. Kanis, A. Odén, E.V. McCloskey, H. Johanss Wahl, C. Cooper, on behalf of the IOF Working Gepidemiology and Quality of Life. (2012) A system of hip fracture incidence and probability of fractu worldwide. Osteoporos Int. 2012 September; 23(2256. and Frost & Sullivan analysis [2] International Osteoporosis Foundation

#### he Burden of Osteoporosis (continued)

The cost of osteoporosis-attributed fractures, in terms of lost healthy life years lost, is over 2 million years per yea globally.



#### he Benefits of Calcium + Vitamin D

oproximately 70% of the target population globally are not realising the potential benefits of regular usage of a calciu + vitamin D food supplement and, thus, are at an increased risk of experiencing an osteoporosis-attributed bone fracture.

There has been a significant amount of research exploring the benefits of alcium + vitamin D utilisation among the elderly, where most of the research as focused on the correlation between use and the risk of an osteoporosis one fracture.

n 2014, Shanahan and de Lorimier determined that the relative risk reduction of an osteoporosis-attributed fracture event given the use of calcium + vitamin D, was a statistically significant 19.7% (95% CI: 21.1% to 18.3%) [1].

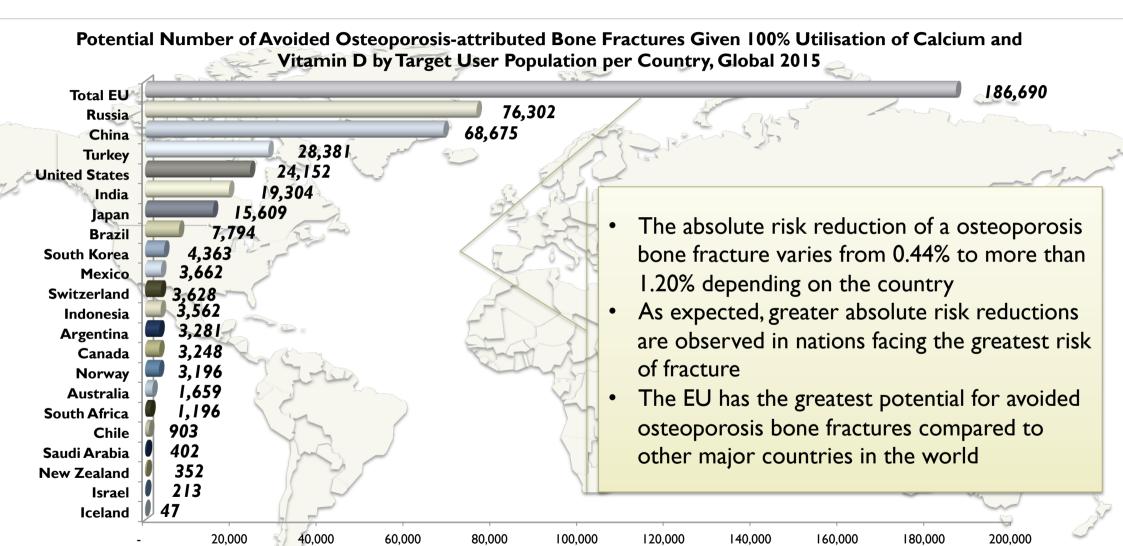
n 2015, researchers from the International Osteoporosis Foundation and National Osteoporosis Foundation (Weaver et al. 2015) conducted the most up-to-date meta-analysis of the connection between calcium + vitamin D upplement intake and the risk of a bone fracture which included 8 studies, 20,970 subjects, and 2,231 total fractures.

The authors show that the use of a calcium + vitamin D supplement resulted in statistically significant 15% reduced risk of total fractures (Relative Risk RR) = 0.85; 95% CI: 0.73-0.98) [2].



[1] Shanahan, C. and de Lorimier, R. (2014). Ta Complementary Medicines: Potential Health Cost Savings in Australia. Fro [2] Weaver CM et al. (2015) Calcium p supplementation and risk of fractures: an u analysis from the National Osteoporosi

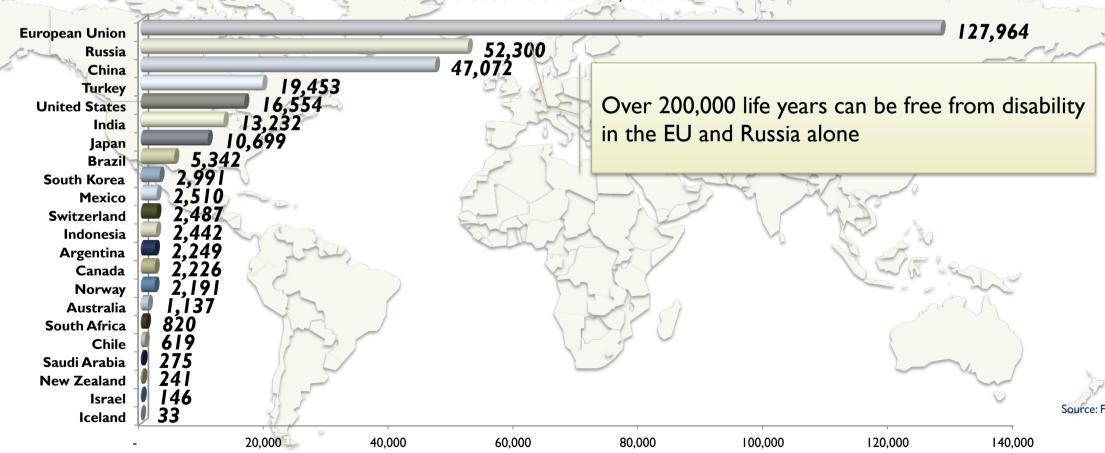
#### The Benefits of Calcium + Vitamin D (continued)



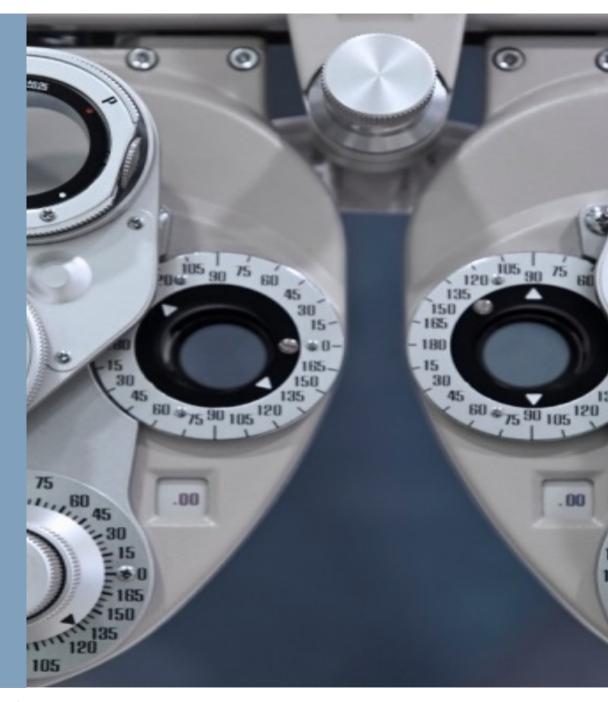
#### otential Economic Benefits from using Calcium and Vitamin D (continued)

Globally, over 300,000 life years per year can be free of disability from the use of calcium and vitamin D.

Total Number of Disability-adjusted Life Years Lost Due to Osteoporosis-attributed bone fractures that can be potentially gained back per country from use of Calcium and Vitamin D, Global 2015



utein & Zeaxanthin
upplements and the
Nanagement of the Severity
f Age-related Macular
Degeneration-attributed
Sisual Acuity



#### he Burden of Age-related Macular Degeneration

-related macular degeneration (AMD) is an eye disease that affects the central part of the retina known as the macu AMD can impair an individual's independence and ability to perform daily activities, which often leads to significant emotional distress and significantly impacts quality of life.

**Target Population:** In 2015, is expected that over 8.8 million cases of ADM occurred globally among people aged 55 and over [1]

Among this subset of AMD sufferers, 19.7% are diagnosed with severe age-related macular degeneration (AMD) which is characterised by a significant reduction in visual acuity (VA) (LogMAR Baseline of 1 or 6/60 vision in one or both eyes) or severe vision oss, which causes difficulty in daily activities, some emotional impact (for example worry), and some difficulty going outside the home without assistance (thus requiring ong-term care).



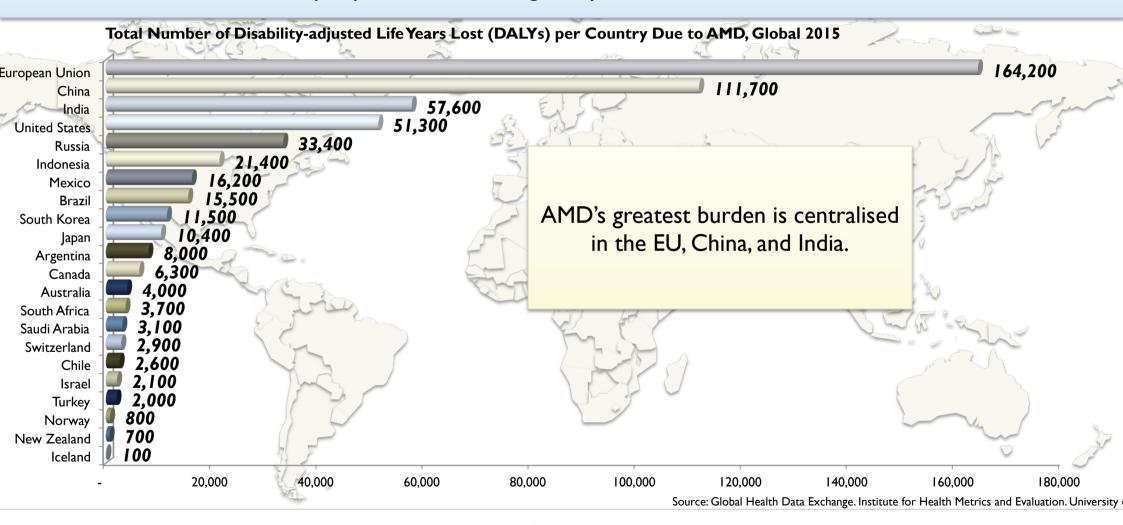
The LogMAR Baseline for mild AMD is 0.6 or 6/24 vision which is characterised by some vision problems that make it difficult to recognise faces or objects across a room As a consequence of AMD, over 500,000 DALYs are lost per year due to this disease globally and over 164,000 DALYs are lost in the EU alone [1]

The average cost of managing AMD in the EU was €8,278 per case and the total cost of Severe or Wet AMD in the EU was estimated at €4.9 billion in 2015.

[1] Global Health Data Exchange. Instit Metrics and Evaluation. University of W Frost & S

### he Burden of Age-related Macular Degeneration (continued)

Over 500,000 DALYs are lost per year due to AMD globally and over 164,000 DALYs are lost in the EU alone.



#### he Benefits of Lutein & Zeaxanthin Supplements

AMD patients who use lutein and zeaxanthin supplements witnessed less transitions to severe cases of AMD compared to a placebo group, implying that the group of lutein and zeaxanthin users would also bear less disease management costs.

Recent studies have revealed that increasing intake with lutein and/or zeaxanthin in AMD patients leads to an increase in macular pigment and improved visual acuity [1].

For example, Liu et al. (2014) conducted a detailed meta-analysis of eight randomised controlled trials (RCTs) of AMD patients (n=1,176 patients) that explored the relationship between lutein and zeaxanthin intake and its effect on visual acuity.

The researchers found that the groups of users with mild AMD of 10 to 20 mg of lutein and/or 0.6 to 10 mg of zeaxanthin — typically in an AREDS2 formulation — versus users of a placebo — had a baseline logMAR levels of VA by a statistically significant 0.04 basis points less than the placebo group This implies that there were significantly less transitions from mild to severe cases of AMD in the lutein & zeaxanthin groups compared to the placebo group.



#### The Benefits of Lutein & Zeaxanthin Supplements (continued)

alculation of the % Change in Number of Costly Severe ADM cases given use of Lutein and Zeaxanthin Supplements, Total EU

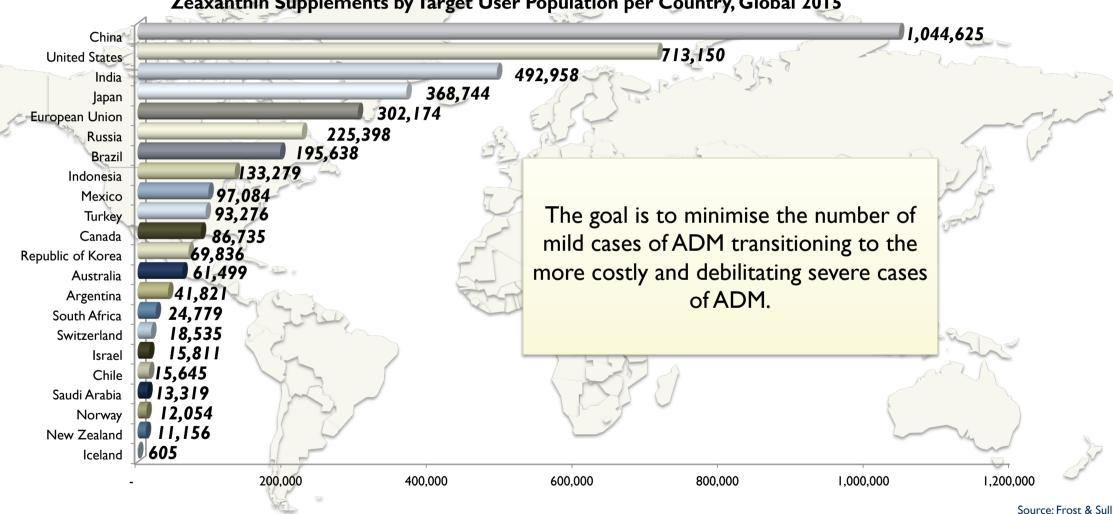
ер	Measure	Mild ADM	Severe ADM	Average ADM	Notes
A	Share of Population of AMD cases	79.6%	20.4%		Source: Global Health Data Exchange, Wong et al. 2014, and Frost & Sullivan analysis
В	LogMar Baseline Level	0.60	1.00	0.68	The average LogMAR baseline level is the sumproduct of the typical LogMAR baseline levels for mild and severe and the current prevalence of Mild and Severe AMD
С	Change in LogMar given use of lutein and zeaxanthin			-0.04	Source: Liu et al. 2014
D	Updated LogMar Baseline Level given use of lutein and zeaxanthin	0.60	1.00	0.64	The difference in average LogMAR baseline level and the updated LogMAR baseline level given use of lutein and zeaxanthin
E	Updated Share of Population of AMD cases given use of lutein and zeaxanthin	89.9%	10.1%		Calculated given the use of lutein and zeaxanthin
F	% change in number of costly severe ADM cases given use of lutein and zeaxanthin		-10.3%		Step A – Step F

- In order to determine the percent change in the number of costly seven ADM cases given use of lutein and zeaxanthin versus non-use we first must know what the current prevalence of Mild AMD and Severe AMD in each country/region of investigation which is used to find the average LogMAR baseline level for the given country/region.
- Applying the findings of Liu et al.
   (2014) and calculating the updated share of population of AMD cases given use of lutein and zeaxanthin provides the change in severe ADM cases needed to calculate the number of costly AMD transitions avoided.

Source: Frost & Sull

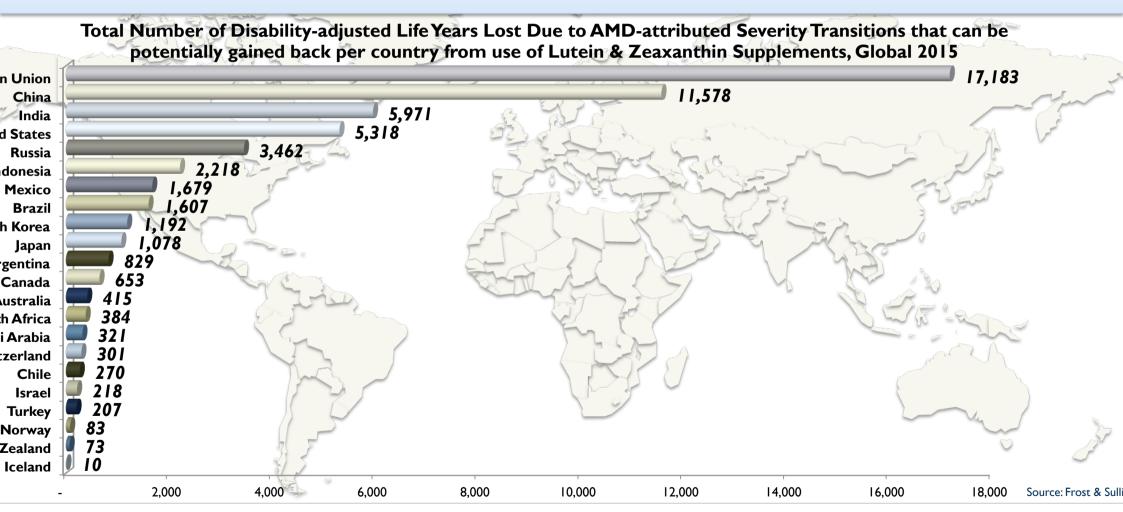
#### he Benefits of Lutein & Zeaxanthin Supplements (continued)





## otential Economic Benefits from using Lutein & Zeaxanthin Supplements continued)

Globally, over 55,000 life years per year can be free of AMD-attributed disability from the use of Lutein & Zeaxanthir



Concluding Remarks



#### Concluding Remarks—Research Caveats

The savings calculations in this analysis are conservatively defined as the medical expenditures most likely to be associated with each food supplement and its health benefits. These estimates do not include a number of additional benefits that can be gained from the use of a given food supplement.

The results from these five food supplement regimens may not be generalisable to all supplements.

Care should be taken if one sums the results of each food supplement regimer in order to determine an overall cost-savings effect.

Due to data availability limitations, the current model does not follow individual people over time.

The current model looks at each year as a separate independent scenario analysis and thus average costs and benefits are calculated on an annual basis, which is then adjusted by the time period and cost/price inflation Care should be taken if one compares the results of each food supplement regimen in terms of absolute savings or cost/benefit ratio



#### Concluding Remarks

These potential economic benefits can be realised by proactively identifying the population at greatest risk of speriencing a costly an age-related disease-attributed event and helping these high risk populations consider dieta food supplements as an important tool for enhancing their quality of life.

Giving the ageing of the world's population, and the expected rise in noncommunicable that is likely to follow, governments are already developing plans for the future

Also, there is already evidence that governments are considering and leveraging a more holistic approach to support aged care so that it covers financial, social, psychological, and health aspects. However, much more needs to be done This research shows that significant healthcare cost savings can be realised through a concerted effort to identify hig risk populations, such as seniors at risk of specific non-communicable diseases, and inspire them to use a food supplement that is shown through the scientific literature to have a significant health benefit to the user Because a significant portion of these benefits is in the form of saved consumer expenditures and informal post-treatment costs, the majority of this benefit would be conferred by the users of the given food supplement However, this research also demonstrates that is an approach that can be used by all relevant stakeholders, includin healthcare providers, employers, and policymakers as a means to total societal costs.

Understanding the link between smart prevention and health care cost savings will help key stakeholders, including patients, health care professionals, governments, insurance companies and employers, make better-informed decision on the best course of action that minimises current and future health care costs and maximises long term potentia benefits.

#### hank You!

#### hristopher Shanahan—Global Program Manager, Chemicals, Materials & Food



10+ years experience in agricultural, chemical, and natural resource markets. Expert in ingredients, chemicals, material, and agriculture markets with a focus on food & agriculture, organic polymers, energy, and natural resources

#### **Education**

Master of Science in Agricultural Economics, The Ohio State Universi