International Journal of Nutrition and Food Sciences
2021; 10(6): 117-125
http://www.sciencepublishinggroup.com/j/ijnfs
doi: 10.11648/j.ijnfs.20211006.11
ISSN: 2327-2694 (Print); ISSN: 2327-2716 (Online)

Cognitive Health and Economic Benefits of Using Vitamin B Food Supplements Among the European Union's Aging Population

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To cite this article:
Christopher Shanahan. Cognitive Health and Economic Benefits of Using Vitamin B Food Supplements Among the European Union's Aging Population. *International Journal of Nutrition and Food Sciences*. Vol. 10, No. 6, 2021, pp. 117-125. doi: 10.11648/j.ijnfs.20211006.11

Received: June 23, 2021; **Accepted**: July 13, 2021; **Published**: November 23, 2021

Abstract: Giving the ageing of its citizens, and the expected rise in cognitive impairment that is likely to follow, the need for the mitigating tools to help manage the burden and the consequences of cognitive impairment grows daily in the European Union (EU). The total annual cost of managing the consequences of cognitive impairment among those age 65 and older in the EU was €265.17 billion in 2019 and is expected to reach €530.69 billion by 2030 given that more than 17 million European Union citizens will likely be inflicted by cognitive impairment of some type by 2030. This case study found that the total potential benefits for adults age 65 and older at risk of suffering from cognitive impairment from the daily utilization of Vitamin B at an effective intake level can yield over € 25 billion in health care cost savings per year between now and 2030 if all at-risk adults age 65 and older utilised Vitamin B supplements at effective intake levels. This finding is based on the meta analysis results of the qualified set of scientific studies where it is expected that the absolute risk reduction of a prevalent cognitive impairment event, given the supportive daily use of vitamin B food supplements is 9.5% relative risk reduction. This research and related case studies show that significant healthcare cost savings could be realised through a rigorous effort to identify high risk populations, such as seniors at risk of brain diseases that causes severe cognitive impairment, and inspire them to use an vitamin B food supplement that is shown through the scientific literature to have a significant health benefit to the user.

Keywords: Vitamin B, Economic Savings, Health Benefits, Europe, Cognitive Decline

1. Introduction

A common question among policymakers, public health experts, and consumers that is, in many ways, still unaddressed is whether health care costs can be avoided if more mitigating tools and measures were adopted and utilised. On the surface, it seems that the answer would be a logical yes, in that reducing the risk of diseases, such as those related to cognitive impairment, is a better option than playing the odds and having to pay for costly treatments and long-term care in the future.

The European Union (EU) is undergoing an undesired transformation that will bring increased health and economic burdens to the continent in the long run. Specifically, the EU is progressively burdened by the growing cost of health care in the country. This growth in health care costs is driven by the increasing average age of the EU's citizens. 96 million people in the EU were age 65 and older in 2019 [1, 2]. By 2030, this proportion of individuals age 65 and older will grow to over 25% of the EU population [1, 2]. Accordingly, the cost of health care is rising because the ratio of the older population (those individuals age 65 and older) relative to those younger is driving health care service demand. As the average age of the EU citizen grows, this population's burden on public health care systems grows.

One critical age-related set of conditions that has had a significant impact on the demand for specialised medical services and long-term professional dependency care is cognitive impairment. Cognitive decline is a normal process occurring while ageing, but certain conditions or diseases are responsible for non-normative cognitive decline and eventual progression to dementia, which also accelerates direct and indirect care costs. There are several distinct diseases that are classified under the umbrella term "dementia" including neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and vascular dementia. Based on a review of the most recent studies that monitored the prevalence of cognitive impairment in the EU and the most current population size estimates from the European commission, it is expected that 10.4 million individuals age 65 and older suffered from cognitive impairment in the EU in 2019 where each individual case requires additional medical and non-medical services that goes beyond what is required among those individuals with normal cognitive health [3-5].

Measuring the economic burden of cognitive impairment borne by Europeans as a whole, by each country and by each individual sufferer of cognitive impairment includes a mix of both direct medical costs and indirect non-medical costs related to supporting the individual sufferer's quality of life. Table 2 reports detailed description of the total and per case medical costs of cognitive impairment in the European Union by country. According to the Alzheimer's disease International, Médéric Alzheimer Foundation and author analysis, an individual with cognitive impairment spent an additional €26,830 in 2019 on direct and indirect healthcare costs. Specifically, twenty two percent (22%) of total healthcare costs attributed to cognitive impairment is spent on direct medical and paramedical goods and services including hospitalizations in medicine and surgery, city paramedicine, anti-Alzheimer drugs, and professional diagnosis; twenty one percent (21%) of total healthcare costs attributed to cognitive impairment is spent on direct care coverage by the medico-social sector such as nursing homes, long-term care units (USLD), specialised Alzheimer teams (ESA); and the remaining fifty seven percent (57%) of total healthcare costs attributed to cognitive impairment is spent on direct informal care such as help provided by the sick person's entourage such as personal hygiene care, walking, dressing, cleaning, etc.; and indirect professional costs including the at-home care costs, institutional costs, and accommodation costs for the caretaker [3]. It is expected that the overwhelming majority of these cognitive impairment health care costs is directly attributable to Alzheimer disease and related dementia conditions [3].

Accordingly, it is expected that the total annual cost of managing the consequences of cognitive impairment among those age 65 and older in the EU was €265.17 billion in 2019 and is expected to reach €530.69 billion by 2030 given current population growth rates and per unit cost growth at the typical rate of price inflation. Among those individuals with cognitive impairment, the cost of long-term care is the largest cost driver [3-5].

Table 1. *Total Prevalence of Dementia in the European Union by Country, Age 65 and Older - All Genders, Million People (% of Cohort Population, age 65 and Older), 2019-2030.*

Region/Countries	2019	2020	2025	2030	Compound Annual Growth Rate (2019-2030)
Total European Union (27 member states)	*9.8 (9.7%)*	*10.4 (10.2%)*	*13.8 (13.1%)*	*17.5 (15.4%)*	5.0%
Belgium	0.29 (12.6%)	0.31 (13.1%)	0.4 (15.9%)	0.5 (18.4%)	4.6%
Bulgaria	0.1 (6.2%)	0.1 (6.4%)	0.13 (7.4%)	0.15 (8.3%)	3.4%
Czechia	0.14 (6.2%)	0.15 (6.3%)	0.19 (7.2%)	0.24 (7.9%)	4.5%
Denmark	0.16 (12.7%)	0.17 (13.4%)	0.25 (16.8%)	0.34 (20.2%)	6.3%
Germany	2.42 (12.7%)	2.58 (13.4%)	3.41 (17.1%)	4.26 (20.6%)	4.8%
Estonia	0.02 (6.1%)	0.02 (6.3%)	0.02 (6.9%)	0.02 (7.4%)	2.9%
Ireland	0.09 (12.4%)	0.1 (12.9%)	0.13 (15%)	0.17 (16.8%)	5.4%
Greece	0.17 (6.4%)	0.18 (6.8%)	0.25 (8.7%)	0.32 (10.6%)	5.6%
Spain	1.21 (12.5%)	1.28 (12.9%)	1.65 (15%)	2.03 (16.9%)	4.4%
France	1.87 (12.5%)	1.99 (13%)	2.63 (15.5%)	3.33 (17.8%)	4.9%
Croatia	0.05 (6.3%)	0.05 (6.6%)	0.06 (8.2%)	0.07 (9.6%)	4.1%
Italy	0.8 (6.2%)	0.84 (6.4%)	1.02 (7.4%)	1.19 (8.3%)	3.4%
Cyprus	0.01 (6.1%)	0.01 (6.2%)	0.01 (6.7%)	0.02 (7.2%)	4.3%
Latvia	0.02 (6.3%)	0.02 (6.7%)	0.03 (8.3%)	0.04 (9.8%)	4.4%
Lithuania	0.04 (6.1%)	0.04 (6.2%)	0.04 (6.7%)	0.04 (7.1%)	1.5%
Luxembourg	0.01 (12.2%)	0.01 (12.4%)	0.01 (13.2%)	0.02 (13.9%)	2.7%
Hungary	0.12 (6.2%)	0.13 (6.4%)	0.16 (7.3%)	0.18 (8.2%)	3.6%
Malta	0.01 (8.3%)	0.01 (8.5%)	0.01 (9.7%)	0.02 (10.8%)	6.5%
Netherlands	0.47 (13.1%)	0.52 (14.1%)	0.85 (20.1%)	1.25 (26.4%)	8.5%
Austria	0.22 (12.7%)	0.24 (13.4%)	0.32 (17%)	0.42 (20.4%)	5.3%
Poland	0.44 (6.2%)	0.46 (6.4%)	0.59 (7.4%)	0.72 (8.3%)	4.3%
Portugal	0.3 (12.5%)	0.32 (12.9%)	0.4 (15.2%)	0.49 (17.2%)	4.2%
Romania	0.25 (6.3%)	0.27 (6.6%)	0.34 (8.2%)	0.42 (9.7%)	4.4%
Slovenia	0.03 (6.1%)	0.03 (6.2%)	0.03 (6.6%)	0.04 (7%)	2.9%
Slovakia	0.06 (6.3%)	0.07 (6.5%)	0.09 (7.8%)	0.12 (9%)	5.0%
Finland	0.17 (12.5%)	0.18 (13%)	0.25 (15.6%)	0.32 (17.9%)	5.4%
Sweden	0.3 (12.9%)	0.34 (13.8%)	0.52 (18.7%)	0.74 (23.6%)	7.7%
United Kingdom	1.74 (12.8%)	1.89 (13.5%)	2.72 (17.5%)	3.68 (21.4%)	6.4%

Source: Médéric Alzheimer Foundation (2017), Alzheimer's Disease International: World Alzheimer Report (2015), Paraponaris and Davin (2015), and Author analysis.

Table 2. *Total and Per Case Medical Costs of Cognitive Impairment in the European Union per Country, € Billion and € per Prevalent Case (In Parentheses), Forecast to 2030, Europe, 2019-2030.*

Region/Countries	2019	2020	2025	2030
Total European Union (27 member states)	*265.2 (26830)*	*285.3 (27132)*	*306.3 (28869)*	*328.1 (30395)*
Belgium	8.5 (28807)	9.1 (29095)	9.7 (30885)	10.4 (32460)
Bulgaria	1.7 (16975)	1.8 (17144)	1.9 (18199)	2 (19128)
Czechia	2.4 (16975)	2.5 (17144)	2.7 (18199)	2.9 (19128)
Denmark	4.7 (28807)	5.1 (29095)	5.6 (30885)	6.1 (32460)
Germany	70.5 (28807)	75.9 (29095)	81.4 (30885)	87.1 (32460)
Estonia	0.3 (16975)	0.3 (17144)	0.3 (18199)	0.3 (19128)
Ireland	2.7 (28807)	2.9 (29095)	3.1 (30885)	3.4 (32460)
Greece	2.8 (16975)	3.1 (17144)	3.4 (18199)	3.6 (19128)
Spain	35.3 (28807)	37.7 (29095)	40.2 (30885)	42.7 (32460)
France	54.3 (28807)	58.4 (29095)	62.6 (30885)	67 (32460)
Croatia	0.8 (16975)	0.8 (17144)	0.9 (18199)	1 (19128)
Italy	23.3 (28807)	24.5 (29095)	25.9 (30885)	27.2 (32460)
Cyprus	0.2 (16975)	0.2 (17144)	0.2 (18199)	0.2 (19128)
Latvia	0.4 (16975)	0.4 (17144)	0.5 (18199)	0.5 (19128)
Lithuania	0.6 (16975)	0.6 (17144)	0.7 (18199)	0.7 (19128)
Luxembourg	0.4 (28807)	0.4 (29095)	0.4 (30885)	0.4 (32460)
Hungary	2.1 (16975)	2.2 (17144)	2.3 (18199)	2.4 (19128)
Malta	0.2 (28807)	0.3 (29095)	0.3 (30885)	0.3 (32460)
Netherlands	13.7 (28807)	15.4 (29095)	17.2 (30885)	19.2 (32460)
Austria	6.5 (28807)	7 (29095)	7.6 (30885)	8.1 (32460)
Poland	7.5 (16975)	8 (17144)	8.5 (18199)	9.1 (19128)
Portugal	8.8 (28807)	9.4 (29095)	10 (30885)	10.6 (32460)
Romania	4.3 (16975)	4.6 (17144)	4.9 (18199)	5.2 (19128)
Slovenia	0.4 (16975)	0.5 (17144)	0.5 (18199)	0.5 (19128)
Slovakia	1.1 (16975)	1.2 (17144)	1.3 (18199)	1.4 (19128)
Finland	2.9 (16975)	3.1 (17144)	3.4 (18199)	3.6 (19128)
Sweden	8.9 (28807)	9.9 (29095)	10.9 (30885)	12.1 (32460)
United Kingdom	50.6 (28807)	55.4 (29095)	60.5 (30885)	65.9 (32460)

Source: Médéric Alzheimer Foundation (2017), Primary Research of Working Group and Author analysis.

There are a wide number of types of tests that physicians and medical practitioners use to assess changes in cognitive performance and help to identify severe cognitive diseases like Alzheimer's disease and other dementias. The Wechsler Adult Intelligence Scale (WAIS IV) is an intelligent quotient (IQ) test widely used in nutrition impact assessments that is designed to measure intelligence and cognitive ability in adults and older adolescents. It provided scores for Verbal IQ, Performance IQ, and Full Scale IQ, along with 4 secondary indices (Verbal Comprehension, Working Memory, Perceptual Organization, and Processing Speed) [6]. Another common test used in nutrition impact assessments is the Mini–Mental State Examination (MMSE) or Folstein test which is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment [7]. In clinical practice, MMSE is used as a diagnostic tool for dementia. Any score greater than or equal to 24 points (out of 30) indicates normal cognitive performance [7]. Below this benchmark, the scores can indicate severe (≤9 points), moderate (10–18 points) or mild (19–23 points) cognitive impairment [7]. The MMSE can be used to assess several mental abilities, including short- and long-term memory, attention span, concentration, language and communication skills, ability to plan, and the ability to understand instructions [7].

Another common test used is the Montreal Cognitive Assessment (MoCA) which is a brief cognitive screening tool for mild cognitive impairment [8]. The MoCA was created in 1996 as a screening tool for mild cognitive dysfunction, including early onset Alzheimer's. It assesses concentration, attention, memory, language, calculations, orientation, executive functions and visual skills [8]. A variant of the test is available for illiterate subjects or those with a lower standard of education. It comprises 30 points like the MMSE and takes 10 minutes to complete. A normal score is considered to be 26 and above. Anyone scoring lower than 26 would require further investigation of their cognitive skills [8]. The Activities of Daily Living (ADLs) tests are basic tasks that must be accomplished every day for an individual to thrive. Understanding how each category affects a person's ability to care for themselves can mean the difference between graceful and independent ageing and needing daily assistance [9, 10]. Other tests used to gauge cognitive performance and disability (memory, attention and/or executive functions) and found in nutrition impact assessments includes those of the Cambridge Neuropsychological Test Automated Battery (CANTAB), the Verbal Fluency Test (VFT), the Hopkins Verbal Learning

Test (HVLT), and the Boston Naming Test (BNT) among others [11-15]. Interestingly, some of these tests allow the researcher/clinician to distinguish between normal cognitive decline, mild cognitive decline and Alzheimer's disease (e.g. PAL test of the CANTAB battery) [38]. Cognitive tests used as assessment tools in nutritional interventions are expected to be sensitive enough to detect a small change within a non-pathological range; however this remains an area continuing research.

Three B vitamins—B6 (pyridoxine), folate (folic acid), and B12 (cobalamin)—have been extensively studied for their roles in cognitive health [34-36]. Many foods are natural sources of these vitamins: B6 is inherent in cereals, beans, poultry, fish, and some vegetables and fruits; food folate comes from fruits and vegetables, beans, and whole grains, while folic acid is the form used in fortified foods and food supplements; and B12 is derived from poultry, fish, red meat, eggs, and dairy products [16]. The interest in these vitamins for reducing cognitive decline stems from their role in metabolizing the amino acid homocysteine. The mechanisms connecting homocysteine levels with cognitive decline are unknown, but increased levels of serum homocysteine have been observed among individuals with cognitive decline [21, 33]. The analysis in this report is based on studies showing the direct effect on the mean differences of cognitive decline relative to baseline measurements, not on homocysteine as a marker of disease risk. According to EFSA, the generally recognised dietary reference daily adequate intake (AI) levels for B12 is 4.0 mcg and the daily average requirement levels (AR) for folic acid (B9) and B6 are 250 mcg and 1.5 mg [22-24]. However, the clinical research reviewed for this study reported intake levels of folic acid, B6, and B12 at ranges of 400 to 2000 mcg, 10 to 25 mg, and 25 to 1000 mcg, respectively.

This case study explores the possible health effect and economic benefit that could be expected from the daily use of Vitamin B6, B9 and B12 food supplements at effective intake levels as a means to inhibit cognitive decline as indicated on the performance of cognitive performance diagnostic tests by those target individuals at the highest risk of developing diseases that result in severe cognitive impairment. This will be done by determining the potential cost savings that could be realised given the usage of vitamin B food supplements that are scientifically shown to reduce the occurrence of disease-related cognitive decline episodes among adults age 65 and older in Europe. Specifically, this report will attempt to show that using vitamin B food supplements by subjects who are determined to be at a high risk of cognitive impairment can result in health care related cost savings.

First, a review of the scientific literature that tested the relationship between vitamin B food supplement utilization and markers of cognitive impairment was conducted. From this review, an overall change in the cognitive performance or odds of a mild cognitive impairment episode given the use of vitamin B food supplements had been deduced. Then, these impact variables are used as a critical input into a cost savings scenario analysis to determine the potential change in economic benefits—in terms of avoided direct and indirect medical and care costs—that could be realised if everybody in the specified high-risk population group were to use vitamin B food supplements at effective intake levels. These monetary benefits could be an element in reducing health care costs of vulnerable, high-risk populations, which are the greatest contributors to total health care costs in Europe.

2. Methods

The health economic analysis presented in this case study is based on the assessment of various health (and associated cost) scenarios and determines the difference between scenarios to derive the potential savings, or loss, that occurs if one scenario of prevalent cases of cognitive performance decline occurred versus another [18]. The benefits considered in this model are avoided direct medical expenditures related to avoided cognitive impairment-attributed medical care service utilisation and the avoided loss of opportunity costs in the forms of lost income to the sufferer and care givers. The result of these potential healthcare savings provides an economic indication of the monetary benefits the user of vitamin B food supplements can yield for all of society through medical cost reduction and increased productivity.

The volume of research assessing the cognitive impairment-related health benefits from using vitamin B food is substantial. From September to December of 2019, a rigorous systematic review of the scientific literature was conducted using Boolean logic-based searches on PubMed and Medline using the key words "vitamin B6", "pyridoxine", "vitamin B9", "folate", "folic acid", "B12", "cyanocobalamin", "cognitive", "memory", "risk", "disease", and other common synonyms of these keywords. The goal was to be as inclusive and exhaustive as possible at this first stage and 39 studies were identified. The heterogeneity of research design, sample population definitions, tested end points adopted by researchers in the field makes it difficult to compare and aggregate the findings of this body of literature. Thus, a detailed study selection exercise was conducted in order to identify a set of literature that explicitly tests for an association between vitamin B food use and cognitive performance and/or impairment. Prospective cohort observational studies were included in the set and qualitative articles, meta-analyses, and studies with concerns on research methodology and protocol quality were excluded. Also, only studies that included adult human subjects were considered for inclusion. After this selection exercise stage, 8 studies were qualified and included in the meta-analysis.

To determine the expected health effect (avoided prevalent case of cognitive impairment), a random-effects literature review approach was used [19]. This approach for deducing the true mitigating effect from a set of clinical/scientific research that varies by sample size, methodologies and study protocols, and patient population dynamics is based on weighting each study's contribution to the aggregated result based on its sample size (variance across studies) and study-specific determinants (variance caused by research protocol quality) [18]. This approach allows for a systematic and objective approach to weighing 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 vitamin B food supplement at effective intake levels. Absolute risk reduction estimates were estimated separately for studies that reported odds ratios and those studies that reported difference in cognitive test performance results and an average estimate of absolute risk reduction was calculated across the two study groups. Details on the studies included in the final analysis are reported in Table 3.

Table 3. *Vitamin B Literature Review: Description of the Qualified Studies.*

Ref #	Authors	Year	Dose Size of B6 (mg/day)	Dose Size of B9 (mcg/day)	Dose Size of B12 (mcg/day)	Sample Size	Treatment Duration (months)
25	Ma F et al.	2017	--	--	400	180	6
26	Kwok Tet al.	2017	--	--	1000	172-231	27
27	Dangour AD et al	2015	--	--	1000	184	12
28	van der Zwaluw NL et al.	2014	--	400	500	720-2556	24
29	Cheng D et al.	2016	10	800	25	104	3
30	Walker JG et al.	2011	--	400	100	900	12
31	Ford AH et al.	2010	25	2000	400	241	24
32	Eussen SJ et al.	2006	--	400*	1000	111	6

The scientific literature as it relates to the possible benefits of vitamin B food supplements on cognitive health is broad and multifaceted as represented by the 8 qualified studies, but the research literature does appear to be converging toward testing the link between the odds of a cognitive decline episode or the relative degree of decline between a non- or low user control group and a high-use or study group [25-32].

Based on the meta analysis results of the qualified set of scientific studies outlined above, it is expected that the relative risk reduction of a prevalent cognitive decline event, given the supportive daily use of vitamin B food supplements, is up to 9.5% according to the set of literature exploring the link between use of vitamin B food and the odds of a prevalent cognitive impairment event. The weighted expected absolute risk reduction from vitamin B food due to the use is 0.99% of all prevalent cases of cognitive impairment, or 100 users per potential benefactor. Furthermore, given an expected absolute risk reduction of 0.99%, the number of potential avoided prevalent cognitive impairment events among all European adults age 65 and older could be an estimated 0.9 million person cases in 2019 across the entire European region. By 2030, the number of potentially avoidable prevalent cases of severe cognitive decline could surpass 1.6 million cases if all eligible users used vitamin B food at effective intake levels. Table 4 provides detailed results of the health benefits systematic review and meta-analysis and Table 5 provides the aggregated results.

Table 4. *Vitamin B Literature Review: Detailed Systematic Review Results.*

Measurement & Author	Sample Size	Mean Difference, size effect	Favours Supplementation?	Statistically Significant	Significance of Findings Weight
Executive Function					
Ma F et al 2017	180	0.4	Yes	No	4%
Cheng D et al 2016	104	0.31	Yes	No	11%
van der Zwaluw NL et al 2014	720	0.12	Yes	No	4%
Walker JG et al 2011	900	0.08	Yes	No	5%
Ford AH et al 2010	241	0.03	Yes	No	2%
Eussen SJ et al 2006	111	-0.11	Yes	No	3%
Dangour et al 2015	184	-0.1	No	No	1%
Kwok et al 2017	231	-0.86	No	No	2%
Memory					
Cheng D et al 2016	104	0.39	Yes	No	11%
Ford AH et al 2010	241	0.16	Yes	No	2%
Kwok et al 2017	215	0.15	Yes	No	2%
van der Zwaluw NL et al 2014	2467	0.03	Yes	No	12%
Walker JG et al 2011	900	0.04	No	Yes	5%
Eussen SJ et al 2006	111	-0.21	No	No	4%
Dangour et al 2015	184	-0.32	No	Yes	1%
MMSE					
van der Zwaluw NL et al 2014	2556	0.1	Yes	No	22%
Ford AH et al 2010	241	0.06	No	No	2%
Response Time and Motor Speed					
Kwok et al 2017	172	0.22	Yes	Yes	1%
Dangour et al 2015	184	0.01	Yes	No	1%
Eussen SJ et al 2006	111	0.03	No	No	1%
van der Zwaluw NL et al 2014	731	-0.01	No	Yes	4%

Table 5. *Vitamin B Literature Review: Aggregated Meta-Analysis Results.*

Cumulative Sample Size	10,888
Mean Difference, size effect	0.061
Odds Ratio of Cognitive Decline Between Exposed Group versus Unexposed Group	0.895
Estimated Relative Risk of Cognitive Decline Between Exposed Group versus Unexposed Group	0.905
Attributable proportion	9.5%
Number Needed to Treat to Realise the Effect of One Individual	100.2
Observed Risk in 2019, Total European Union	10.5%

Table 6. *Total Potentially Avoidable Prevalent Cases and Expected Avoidable Cost of Cognitive Impairment given 100% Vitamin B utilization (in parentheses) in the European Union by Country, Age 65 and Older, Thousand Cases, (€ Million) 2019-2030.*

Region/Countries	2019	2020	2025	2030	Compound Annual Growth Rate (2019-2030)
Total European Union (27 member states)	928 (25,190)	989 (27,102)	1311 (37,845)	1659 (50,411)	5 (1.5)
Belgium	28 (808)	29 (865)	38 (1,181)	47 (1,540)	4.6 (1.3)
Bulgaria	10 (163)	10 (172)	12 (221)	14 (272)	3.4 (1.0)
Czechia	13 (225)	14 (241)	18 (329)	22 (429)	4.5 (2.5)
Denmark	15 (446)	17 (488)	24 (735)	32 (1,040)	6.3 (2.3)
Germany	230 (6,701)	245 (7,206)	323 (9,990)	404 (13,125)	4.8 (0.7)
Estonia	2 (28)	2 (30)	2 (37)	2 (45)	2.9 (1.4)
Ireland	9 (255)	9 (276)	13 (393)	16 (535)	5.4 (2.8)
Greece	16 (270)	17 (294)	23 (427)	30 (582)	5.6 (1.3)
Spain	115 (3,352)	122 (3,579)	156 (4,831)	193 (6,263)	4.4 (1.8)
France	177 (5,156)	189 (5,545)	250 (7,721)	316 (10,262)	4.9 (1.9)
Croatia	4 (76)	5 (81)	6 (107)	7 (136)	4.1 (0.5)
Italy	76 (2,209)	79 (2,332)	97 (2,983)	113 (3,682)	3.4 (0.9)
Cyprus	1 (17)	1 (18)	1 (24)	2 (32)	4.3 (3.0)
Latvia	2 (38)	2 (40)	3 (55)	4 (71)	4.4 (0.7)
Lithuania	3 (58)	3 (60)	4 (69)	4 (78)	1.5 (0.3)
Luxembourg	1 (34)	1 (35)	1 (43)	2 (52)	2.7 (1.6)
Hungary	11 (197)	12 (208)	15 (269)	17 (334)	3.6 (1.2)
Malta	1 (23)	1 (25)	1 (38)	2 (55)	6.5 (4.1)
Netherlands	45 (1,300)	50 (1,463)	80 (2,481)	119 (3,854)	8.5 (2.3)
Austria	21 (616)	23 (666)	31 (949)	39 (1,281)	5.3 (1.2)
Poland	42 (712)	44 (760)	56 (1,022)	69 (1,317)	4.3 (1.8)
Portugal	29 (834)	30 (889)	38 (1,188)	47 (1,519)	4.2 (1.4)
Romania	24 (408)	25 (437)	33 (595)	40 (766)	4.4 (0.8)
Slovenia	2 (42)	3 (44)	3 (55)	3 (66)	2.9 (1.8)
Slovakia	6 (104)	6 (112)	9 (157)	11 (210)	5.0 (1.9)
Finland	16 (275)	17 (297)	23 (425)	30 (576)	5.4 (2.3)
Sweden	29 (841)	32 (936)	49 (1,520)	71 (22,91)	7.7 (2.4)
United Kingdom	165 (4,802)	179 (5,263)	258 (7,968)	349 (11,332)	6.4 (2.0)

3. Results

After the expected potentially avoidable prevalent cases of cognitive impairment from the use of Vitamin B supplements is derived, the potential cost savings and cost-effectiveness of Vitamin B intake among a given high risk population can be calculated. The potential savings from reduced medical service and long-term care utilisation following the reduction in the number of prevalent cases of cognitive decline, *S*, that is realisable if the entire target population were to utilise a vitamin B food supplement regimen at effective intake levels can be expressed as $S=h*A$ where the term h is the expected per prevalent case cost of cognitive decline and A is the number of possible avoided prevalent cases of cognitive decline if everybody in the target population of adults age 65 and older used a vitamin B food regimen annually. The total potential cost savings between the extreme scenarios of non-use and 100% use is of specific interest, thus the removal of current users would be necessary to determine the proportion of health benefits that have already been realised by current Vitamin B users and the proportion of non-users yet to realise the health effects of Vitamin B. An easy way to do this is to observe the population's purchasing behavior through consumer research and identify only those who have purchased Vitamin B. The cumulative net savings achieved over consecutive years can also be calculated by summing the annual output over the indicated years while discounting future years to their present value.

Regarding total potential benefits *S*, had all adults age 65 and older utilised Vitamin B daily at effective intake levels, € 25,190 million in direct health care system and avoided indirect care cost savings can be realised in 2019 By 2025, € 37,845 million in health care system cost savings could be realised and by 2030, nearly € 50,411 million in savings could be obtained given 100% of the population of at risk adults age 65 and older utilised vitamin B6, B9, and/or B12 supplements. Of course, achieving 100% utilization among the entire target end user base (all adults in the EU age 65 and older) is hypothetical and has a low likelihood of occurring. However, even if a small portion of at risk adults utilised Vitamin B daily at effective intake levels, significant total health care cost savings could be realised. Table 6 reports the total potential benefits that could be realised from the use of Vitamin B food supplements at effective intake levels by year.

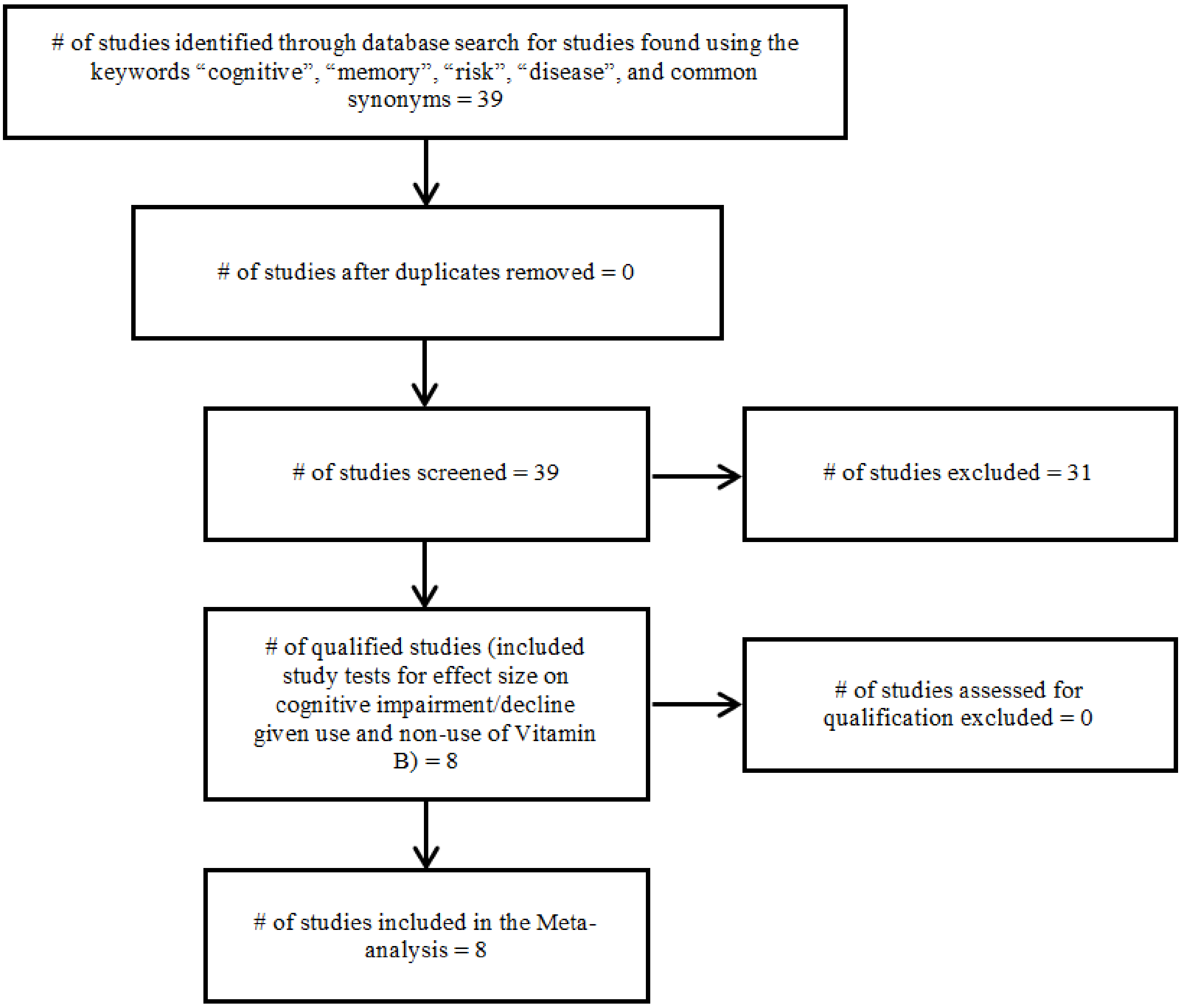

Figure 1. *Flow Diagram of the Systematic Review and Meta-Analysis Process for analyzing the Effect of Vitamin B on Cognitive Impairment.*

4. Discussion

It should be noted that the above equation is a generalised model that determines the total economic effect of using a given health-enabling nutrient 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 and costs that are related to the health condition of interest. However, for the purposes of this study, only the cost savings potential due to the hypothesised relationship between Vitamin B use and improvements of cognitive performance was assessed. In addition, 100% utilization is a hypothetical maximum utilization rate that is likely not feasible to achieve in practice. Thus, adding a multiplicative weight to S to adjust for a more achievable population utilization rate can be applied.

It should also be cautioned that the findings of this study requires further investigation due to the use of heterogeneous information to arrive at the expected outcomes reported in this study. Specifically, it is recognised that there is heterogeneity in the study populations, including factors caused by underlying disease state, levels of vitamin status of each individual in the study populations across the studies and the heterogeneity of interventions. In addition, the cost estimates used in this study mainly stem from avoiding the cost of treating and managing Alzheimer's disease. Future research should consider looking at the difference in healthcare costs between individuals who are diagnosed with mild cognitive impairment versus healthy individuals. The savings calculations in this analysis are defined as the medical expenditures and opportunity costs most likely to be associated with cognitive performance decline.

Furthermore, these estimates do not include a number of additional benefits that could be gained from the use of Vitamin B unrelated to cognitive health such as health benefits related to cognitive disease and related ailments. Since we are not focused on these potential other benefits, they have been ignored in this specific case study though it is possible to consider these other benefits in the general model. Also, this case study does not consider the population costs of utilising vitamin B food products that should be considered if looking to determine relative cost effectiveness. Finally, the current model does not follow individual people over time due to data availability limitations. 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 and cost/price inflation.

5. Conclusion

This case study demonstrated that there are possible health and economic benefits that could be expected from the daily use of Vitamin B6, B9 and B12 food supplements as a means to inhibit cognitive decline as indicated on the performance of cognitive performance diagnostic tests by those target individuals at the highest risk of developing diseases that result in severe cognitive impairment. The annual total cost of managing the consequences of cognitive impairment among those aged 65 and older in the EU was €265.17 billion in 2019 and is expected to reach €530.69 billion by 2030, given that more than 17 million EU citizens will likely be inflicted by cognitive impairment of some type [3-5]. This is based the meta analysis results of the qualified set of scientific studies reviewed in this case study where it is expected that the relative risk reduction of a prevalent cognitive impairment event, given the effective daily use of vitamin B food supplements, is 9.5%.

Giving the ageing of the EU's citizens, and the expected rise in cognitive impairment that is likely to follow, the need for mitigating tools to help manage the burden and the consequences of cognitive impairment grows daily. It is well understood that the consequences of the EU's growing elder population will increase the burden and dependency on public care systems and this in turn can lead to longer queues in publicly-funded hospitals and growing expenses related to retirement homes with long-term care. Growth in the demand for public options may lead to a compromise in medical service quality, medical service dissatisfaction, and an overall lack of care for some citizens. These factors are all multiplied by the fact that older EU citizens tend to have shrinking incomes and personal savings as they age. Seniors will increasingly struggle to afford the cost of medical services that goes beyond what public services are able to provide, especially if they suffer from a cognitive condition causing significant impairment. Clearly, reducing the risk of just some of these prevalent cases of cognitive impairment can yield significant savings.

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