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Perspective

# B-vitamins are potentially a cost-effective population health strategy to tackle dementia: Too good to be true?

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**Abstract**

**Introduction:** To respond to the threat of dementia to public health and the economy, we need to prioritize research resources on strategies that would be the most effective. In relation to the prevention of dementia, this article considers whether lowering plasma homocysteine by B-vitamin supplementation is one of the top priority and cost-effective treatments.

**Method:** A decision model was constructed to calculate the lifetime costs and quality-adjusted life years (QALYs) of providing B-vitamin treatment to people in the United Kingdom over 60 years with high levels (>13 μmol/L) of plasma homocysteine, which was compared to the lifetime costs and outcomes of not providing them with the treatment.

**Results:** Treatment with B-vitamins will save £60,021 per QALY gained and so is highly cost-effective.

**Discussion:** We anticipate that this provocative finding will be debated by scientists, clinicians, and policy makers and eventually be tested in future clinical trials.



*Keywords:* B-Vitamins; Homocysteine; Cost-effectiveness; Dementia; UK

## 1. Introduction

Dementia is an increasing threat to population health because of its association with the aging of the population, reduced quality of life, and premature mortality. It also poses substantial financial demands on the economy due to the increasing requirement for health and social care for people with dementia as well as substantial need for informal care. A recent report estimated the overall annual costs of dementia to society in the United Kingdom to be £26.8 billion, of which only £4.3 billion is spent on health care [1]. Considering also that a third of people in the UK born in 2015 will develop dementia in their lifetime [2] and the lack of an effective treatment for dementia [3], focusing on prevention of dementia certainly deserves to be high in health policy agenda [4]. Decision-makers urgently need evidence about the cost-effectiveness of the potential prevention strategies [3].

However, limited mental health budgets and underspending in research on dementia compared with public and private funds for research in cancer and cardiovascular disease [5] limits the possibility of providing evidence for all available prevention strategies in the short term. Therefore, we need to prioritize resources on strategies that would be the most worthwhile to focus future research on.

This article argues that B-vitamins are one of the top priority preventive treatments and aims to stimulate debate on this argument by investigating whether B-vitamins are potentially a cost-effective treatment, taking the situation in the United Kingdom as an example.

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### 1.1. The rationale to focus on B-vitamin–based treatment

Strategies for prevention, with the aim of decreasing the prevalence of dementia, are based on monitoring and controlling risk factors associated with dementia. These risk factors are broadly categorized as age, genetic factors, vascular and metabolic factors, lifestyle factors, diet and nutritional factors, and other factors (e.g., depression, occupational exposure) [3]. Among modifiable risk factors, high-plasma total homocysteine (tHcy) level, lower education attainment, and decreased physical activity were found in a recent meta-analysis to be particularly strong predictors of dementia [6]. Among these three strong predictors, tHcy is the only chemical risk factor biomarker for cognitive impairment and dementia [7]. Plasma tHcy concentrations can be screened relatively easily and are readily lowered by high-dose B vitamin supplementation [8]. Although there are no trials to test the effect of lowering tHcy on the incidence of dementia, a recent literature review showed that trials with high-risk subjects have shown positive results of B-vitamin treatment in modifying the dementia disease process [7]. The FACIT trial showed that folic acid supplementation could lower tHcy levels and delay age-related cognitive decline in people aged 50–70 years with high tHcy [9]. B-vitamin supplementation (a combination of vitamin B6, vitamin B12, and folic acid) in the VITACOG trial has been shown to be effective as a disease-modifying intervention in elderly with mild cognitive impairment by reducing elevated tHcy levels, by slowing whole brain atrophy [10] and regional brain atrophy [11], and by slowing further cognitive decline [12]. The VITAL trial showed a positive effect of B-vitamin treatment in slowing cognitive decline on the Alzheimer Disease Assessment Scale (ADAS-cog) [13] and on the Mini-Mental State Examination (Fig. 7 in ref. [7]) for patients with mild AD. B-vitamin supplements are available over-the-counter at very low cost, in contrast to long-term more expensive strategies that aim to increase education attainment or physical activity. B-vitamins, in the doses required, are considered without harm to health. Hence, we hypothesize that B-vitamin treatment has great potential to be cost-effective, and so, we performed a simulation exercise to investigate the potential cost-effectiveness of screening people above the age of 60 years in the United Kingdom and treating those with high levels of tHcy with B-vitamins. The aim of this exercise was to provoke discussion about cost-effective prevention of dementia and to stimulate further clinical trials on the impact of lowering tHcy levels.

## 2. Methods

To achieve the aim of the study, an explorative cost-effectiveness analysis was undertaken by following NICE recommendations for modeling and exploring uncertainty in technology appraisals [14]. A lifetime time-horizon was chosen in the analysis.

### 2.1. Stochastic decision model

A stochastic decision model was constructed in Excel to calculate the lifetime costs and outcomes of providing B-vitamin treatment to people over 60 years with high levels of tHcy, which was compared to the lifetime costs and outcomes of not providing them with the treatment. The model performed 10,000 iterations of all cost and effect parameters using prespecified distributions of input parameters and recording incremental costs and incremental quality-adjusted life years (QALYs) from each iteration. Input parameters were related to the target population, treatment effect, costs, and health outcomes (life years and QALYs). The incremental cost-effectiveness ratios (ICERs) were expressed as costs per QALY per treated person. The ICERs were plotted on cost-effectiveness planes to display the uncertainty in the results.

To populate the model, we used information from the literature about the potential target population, treatment effect and costs of dementia as well as life expectancy and quality of life of people over 60 years with and without dementia. When there was no information available in the literature, we made assumptions based on expert opinions. Furthermore, we used a relative standard error (i.e., standard error as percentage of the mean estimate) of 30% when standard errors of the mean were not available. This is considered to be the maximum relative standard error allowing for the report of a mean estimate. As an exception, for the utility (or else quality of life) parameters (with and without dementia), we used a relative standard error of 5% to restrict the cases where people attach higher utility to having dementia than not to having it, which is hardly realistic. Vitamins were assumed not to have negative impact on health and therefore, incremental QALYs can theoretically never become negative in our analysis. However, we allowed incremental QALYs to take negative values to incorporate extreme, close to unrealistic, cases in which treated patients would value the disutility of taking vitamins every day during the gained dementia-free years higher than having dementia in the same period. Moreover, the model assumed that people would receive B-vitamin treatment until dementia onset or death.

### 2.2. Parameters used in the model

The parameters used in the decision model are listed in Table 1 and discussed in detail in the subsequent sections. We defined a "high tHcy concentration" as $> 13$ μmol/L, as used by Pfeiffer et al [15]. The VITACOG trial showed that elderly people with mild cognitive impairment who had concentrations of tHcy above 13 μmol/L responded to B-vitamin treatment with a 53% reduction in the rate of whole brain atrophy [10], a 9-fold slowing of the rate of atrophy of specific brain regions involved in Alzheimer's disease [11], and a measurable clinical improvement as assessed by the Clinical Dementia Rating score [12].