



*Rutgers Catalyst: Healthy Aging Symposium*  
*October 18, 2018*

# **Micronutrient Supplementation and the Aging Brain**

## ***Can Supplements Prevent Age-Related Cognitive Decline?***

**Joshua W. Miller, PhD**  
**Professor and Chair**  
**Dept. of Nutritional Sciences**  
**School of Environmental and Biological Sciences**  
**Rutgers, The State University of New Jersey**

# 7 WAYS TO CUT YOUR ALZHEIMER'S DISEASE RISK

Research suggests that certain diet and exercise habits may lower Alzheimer's disease risk by more than half.

## Steps to Prevent Alzheimer's

#1

### Avoid saturated fats and trans fats.

Dairy products, meats, and certain oils (coconut and palm oils – listed on labels as "partially hydrogenated oils") contain saturated fat. Many snacks, pastries, and fried foods are filled with trans fats.



#2

### Eat a healthy diet.

Vegetables, legumes (beans, peas, and lentils), fruits, and whole grains should be staples in your diet.



#3

### Go nuts for nuts.

One ounce of nuts or seeds – a small handful – is a great source of vitamin E.



#4

### Make vitamin B12 a priority.

Eat fortified foods or take a supplement to get at least the recommended daily allowance (2.4 mcg per day for adults).



#5

### Choose your multivitamin wisely.

Avoid multivitamins with iron and copper, and take iron supplements only when directed by your doctor.



#6

### Cook with caution.

Avoid aluminum cookware, which has been linked to Alzheimer's-related dementia. Instead choose stainless steel or cast iron pots and pans.



#7

### Keep moving.

Get at least 40 minutes of aerobic exercise three times a week – such as brisk walking, running, or cycling.



Help improve Memory

Vitamin B12



PLAN B POSITIVE ACTION ON ALZHEIMER'S

# HOMOCYSTEINE AND B VITAMINS



Link Found between Vitamin D Deficiency and Dementia

[www.alzheimers.net](http://www.alzheimers.net)



## VITAMIN D & DEMENTIA



# Press Release – July 16, 2014



## Taking B vitamins won't prevent Alzheimer's disease

[HEALTH \(/NEWS-LISTING?CATEGORY=249\)](#)

[RESEARCH \(/NEWS-LISTING?CATEGORY=228\)](#)

Taking B vitamins doesn't slow mental decline as we age, nor is it likely to prevent Alzheimer's disease, conclude Oxford University researchers who have assembled all the best clinical trial data involving 22,000 people to offer a final answer on this debate.

**Clarke et al, Am J Clin Nutr, 2014**

Effects of homocysteine lowering with B vitamins on cognitive aging: meta-analysis of 11 trials with cognitive data on 22,000 individuals<sup>1-5</sup>

*Robert Clarke, Derrick Bennett, Sarah Parish, Sarah Lewington, Murray Skeaff, Simone JPM Eussen, Catharina Lewerin, David J Stott, Jane Armitage, Graeme J Hankey, Eva Lonn, David Spence, Pilar Galan, Lisette C de Groot, Jim Halsey, Alan D Dangour, Rory Collins, and Francine Grodstein on behalf of the B-Vitamin Treatment Trialists' Collaboration*

# Do Supplements Prevent Cognitive Decline?

**Answer...**

**Probably, but...**

**The devil is in the **details****



# B Vitamins, Homocysteine, and Vascular Disease

## Vitamin Deficiencies

Folate (vitamin B9)  
Vitamin B12 (cobalamin)  
Vitamin B6 (pyridoxine)



## Homocysteine

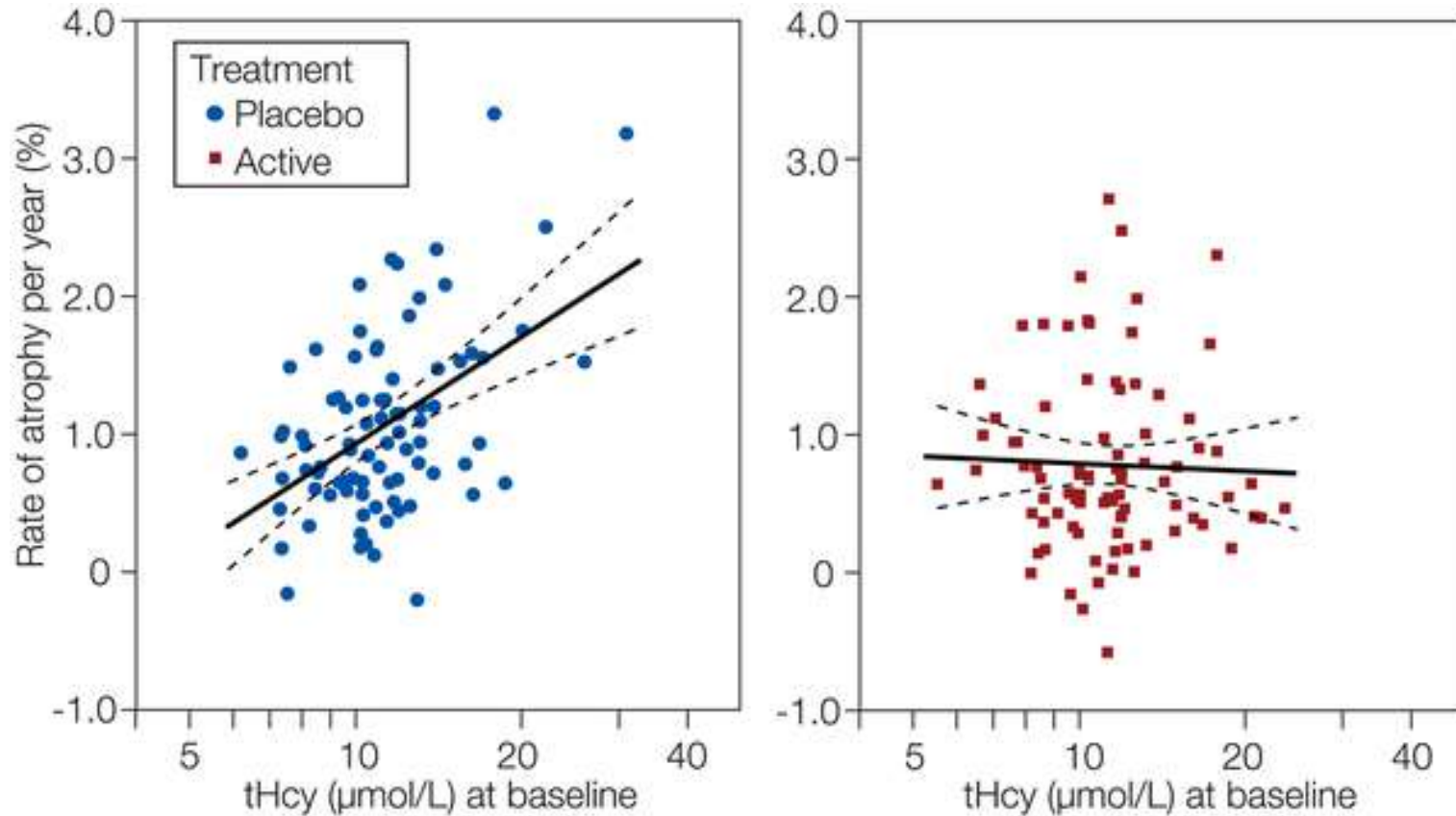
Increased in Blood



## Increased Risk of Vascular Disease and Dementia

Heart Attacks  
Strokes  
Brain Atrophy  
Cognitive Decline

# Effect of B Vitamin Supplements on Brain Atrophy in Older Adults with MCI



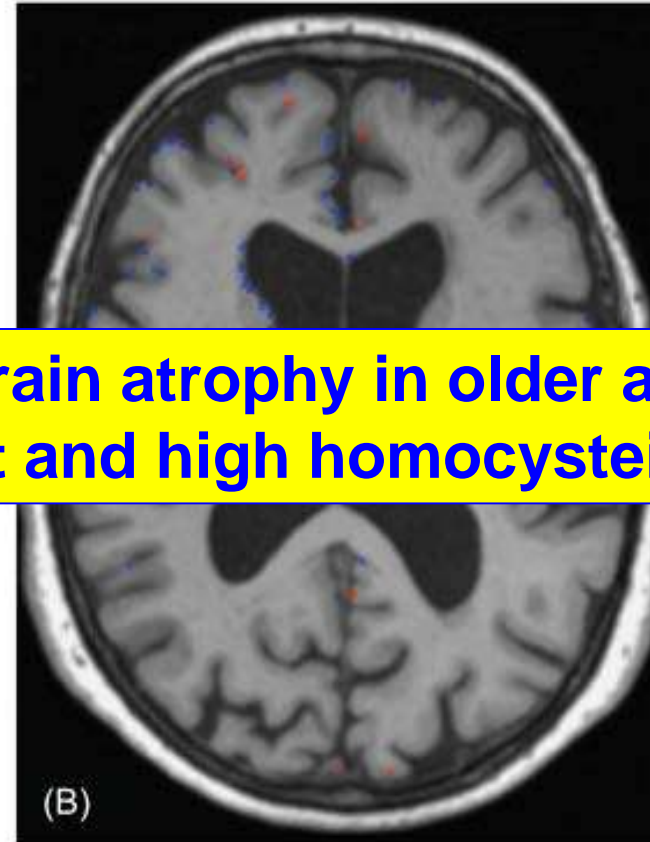
# Effect of B Vitamin Supplements on Total Brain Atrophy

Placebo



$\Delta$ Hcy: 22 to 30  $\mu$ mol/L  
Atrophy Rate: 2.5%/yr

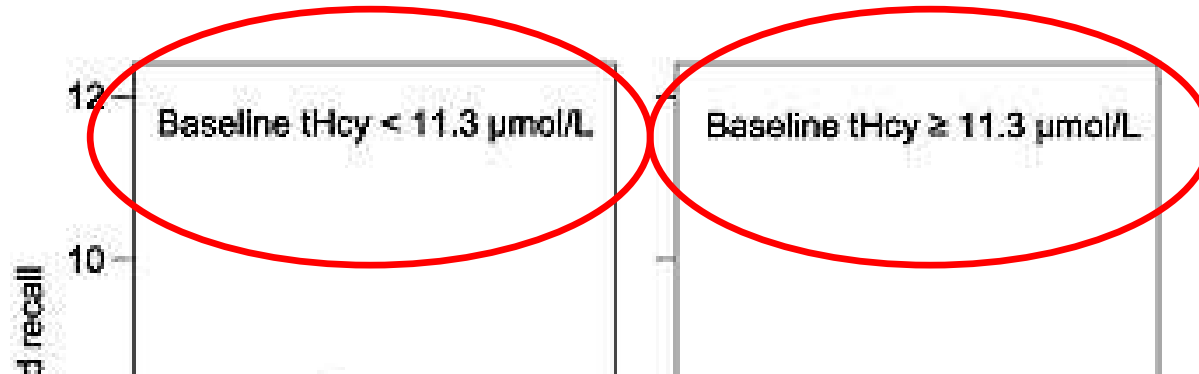
B Vitamins



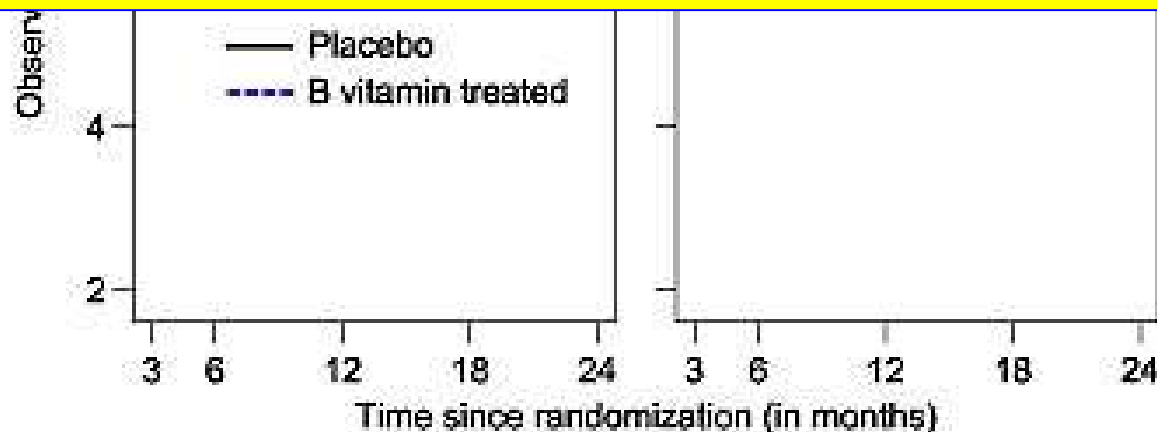
$\Delta$ Hcy: 24 to 12  $\mu$ mol/L  
Atrophy Rate: 0.46%/yr

**B vitamin supplements slow brain atrophy in older adults with mild cognitive impairment and high homocysteine.**

# Effect of B Vitamin Supplements on Delayed Recall (Short-Term Memory)



**B vitamin supplements slow cognitive decline in older adults with mild cognitive impairment and high homocysteine.**





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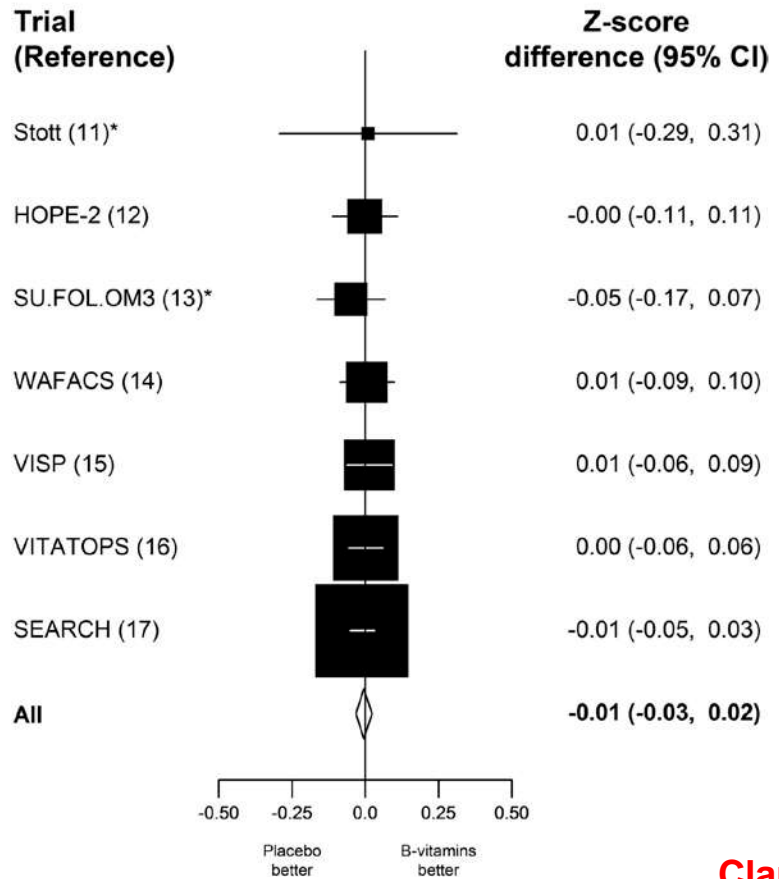
Effects of homocysteine lowering with B vitamins on cognitive aging: meta-analysis of 11 trials with cognitive data on 22,000 individuals<sup>1-5</sup>

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# Effects of B Vitamins and Homocysteine Lowering on Global Cognitive Function

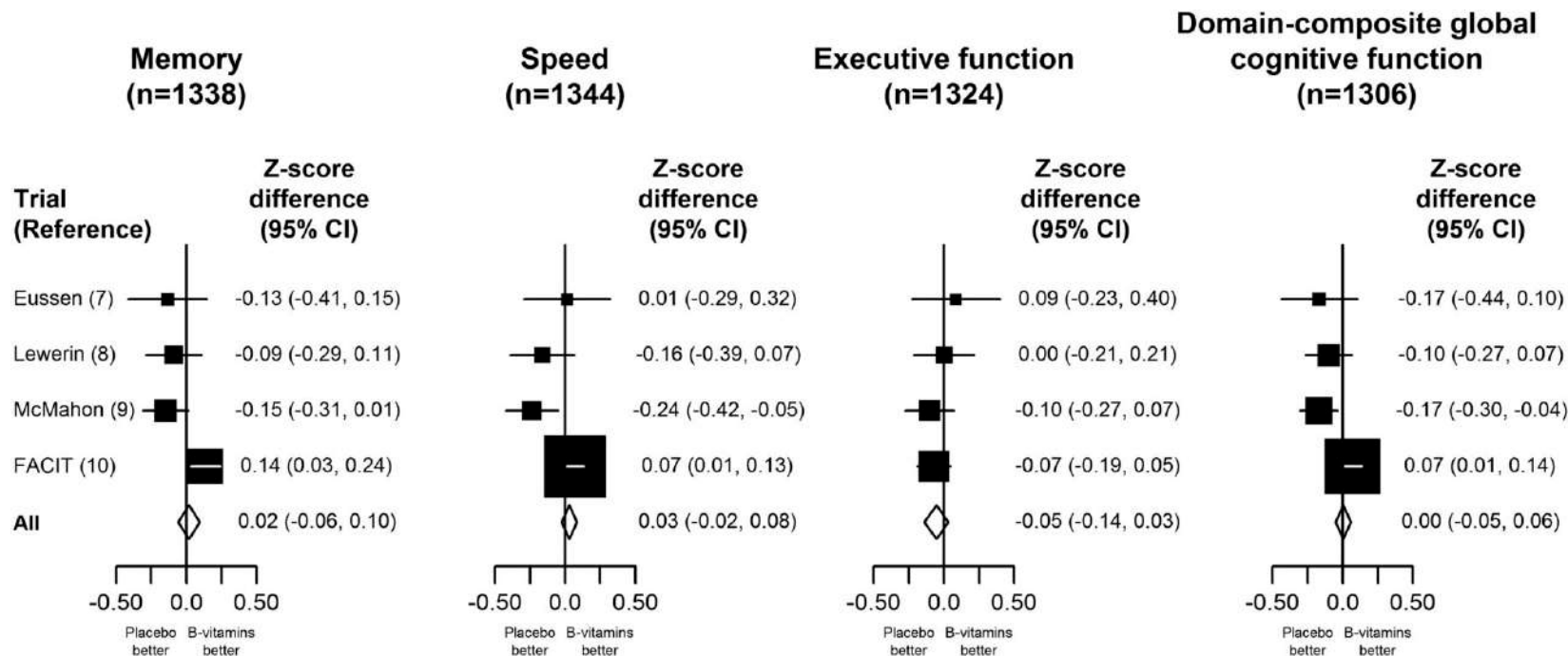
## Meta-Analysis of RCTs

MMSE-type global cognitive function score (n=20431)

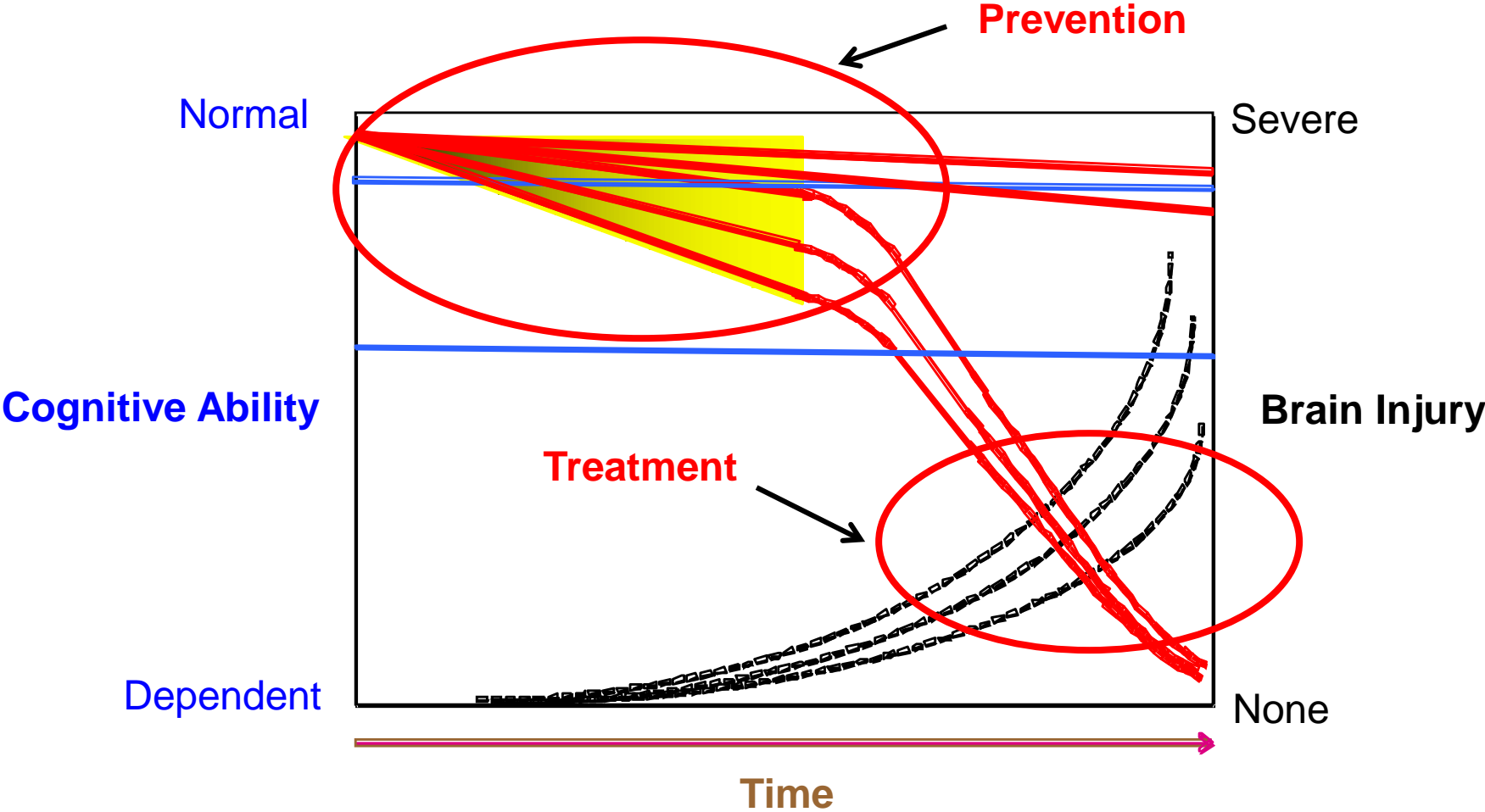


# Effects of B Vitamins and Homocysteine Lowering on Domains of Cognitive Function

## Meta-Analysis of RCTs



# Trajectories of Cognitive Change



*Special Article*

## **Assessing the association between homocysteine and cognition: reflections on Bradford Hill, meta-analyses, and causality**

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Andrew McCaddon and Joshua W. Miller

*Hyperhomocysteinemia is a recognized risk factor for cognitive decline and incident dementia in older adults. Two recent reports addressed the cumulative epidemiological evidence for this association but expressed conflicting opinions. Here, the evidence is reviewed in relation to Sir Austin Bradford Hill's criteria for assessing "causality," and the latest meta-analysis of the effects of homocysteine-lowering on cognitive function is critically examined. The meta-analysis included 11 trials, collectively assessing 22 000 individuals, that examined the effects of B vitamin supplements (folic acid, vitamin B<sub>12</sub>, vitamin B<sub>6</sub>) on global or domain-specific cognitive decline. It concluded that homocysteine-lowering with B vitamin supplements has no significant effect on cognitive function. However, careful examination of the trials in the meta-analysis indicates that no conclusion can be made regarding the effects of homocysteine-lowering on cognitive decline, since the trials typically did not include individuals who were experiencing such decline. Further definitive trials in older adults experiencing cognitive decline are still urgently needed.*

# Change in Cognition in Healthy Older Adults

## You can't prevent something that isn't happening...

**Table 2** Changes in cognitive domain scores of elderly people (only participants with baseline and 2-year data)

	Unadjusted mean (SD)		Change (95% CI)	Model 1, p value	Model 2, p value
	Baseline	2 y			
<b>Episodic memory (n = 2,467)<sup>a</sup></b>					
Placebo	0.04 (0.69)	0.13 (0.75)	0.08 (0.05 to 0.12)	0.27	0.42
B vitamins	0.05 (0.69)	0.16 (0.75)	0.11 (0.07 to 0.14)		
<b>Attention and working memory (n = 759)</b>					
Placebo	0.02 (0.86)	-0.04 (0.88)	-0.06 (-0.12 to 0.01)	0.38	0.37
B vitamins	-0.01 (0.84)	-0.10 (0.82)	-0.09 (-0.16 to -0.02)		
<b>Information processing speed (n = 731)</b>					
Placebo	0.08 (0.75)	0.06 (0.79)	-0.02 (-0.06 to 0.01)	0.65	0.51
B vitamins	0.04 (0.75)	0.01 (0.77)	-0.03 (-0.07 to 0.00)		
<b>Executive functioning (n = 720)</b>					
Placebo	0.04 (0.54)	0.10 (0.68)	0.06 (-0.00 to 0.12)	0.20	0.26
B vitamins	-0.01 (0.52)	0.13 (0.66)	0.13 (0.07 to 0.19)		

Abbreviation: CI = confidence interval.

Differences between the 2 groups over time were measured using analyses of covariance. Model 1: adjusted for baseline domain scores. Model 2: adjusted for baseline domain scores, age, sex.

<sup>a</sup>Model 2 additionally adjusted for study center.

# Key Considerations

- **What is the cognitive status of the subjects?**
  - Cognitively normal?
  - Mild cognitive impairment?
  - Dementia?
- **What are the cognitive outcomes?**
  - Improve cognitive function?
  - Slow or prevent cognitive decline?
- **What cognitive function tests are used?**
  - MMSE (global)?
  - Subdomains?
- **What is the B vitamin/homocysteine status of the subjects?**
  - Is homocysteine elevated?
- **How long is the intervention?**
  - Months?
  - Years?

# Challenge and Opportunity

## Challenge

- Applying what we've learned from population-based studies to inform personalized medicine and personalized nutrition.

## Opportunity

- To design and implement smarter intervention trials with nutritional supplements to determine if age-related cognitive decline can be slowed or prevented.