



What the recent NIH Expert Panel on Alzheimer’s Prevention Means – and Doesn’t Mean

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In late April 2010, an independent expert panel organized by the NIH released a thoughtful report on the state of the science for prevention of Alzheimer’s Disease and cognitive decline* (insert reference, see bottom of article). The report summarizes the panel’s review of the scientific literature by saying:

“Firm conclusions cannot be drawn about the association of modifiable risk factors with cognitive decline or Alzheimer’s disease.”

Which was basically reported as “nothing can prevent Alzheimer’s Disease.”

Which is very true. And also very different from what most readers may assume it means.

First of all, we need to understand that the goal of the independent panel and review was to make recommendations to policy makers affecting an entire population of people, which obviously requires the use of the strongest filters possible to evaluate the evidence. The purpose of the review was NOT to inform individuals, caregivers, health professionals – were that the case, the filters would have been less rigorous (at least regarding non-invasive, side effect-free options) since what would help people most is guidance to reduce their probability to develop Alzheimer’s symptoms and manifest cognitive decline – not just the absolute certainty of being able to “prevent” disease altogether.

Second, as professionals in aging we need to dig a bit deeper into what the report actually said. After their extensive and rigorous scientific review, the panel did share very interesting findings on what, from the individual and community perspective at least, it makes a lot of sense TO DO and NOT TO DO. Again, not to prevent AD with certainty, but at least to proactively reduce the probability of doing so.

The panel reviewed the literature (25 systematic reviews, 250 primary research studies, 6907 citations) with 2 different aims in mind: 1) what prevents Alzheimer’s Disease; 2) what prevents cognitive decline.

The factors showing an association for both AD and cognitive decline were just a few:

(Table 1)

Increased risk:	Decreased risk:
Diabetes APOE e4 Smoking Depression	Mediterranean diet (limited data) Cognitive engagement Physical activities

In other words, what we do still matters. We can lower risks by reducing risk factors such as diabetes, smoking and depression, and by increasing protective factors such as cognitive engagement (including games, puzzles, and cognitive training) and physical activities (and Mediterranean diet, perhaps).

Taking into account all the myths and misinformation that many people believe – isn't this a great start?

Now, in the spirit of cognitive engagement, let's dig even deeper. (In the spirit of physical activity, consider reading what follows in the treadmill).

The panel used standardized criteria prepared by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group (www.gradeworkinggroup.org) to summarize the level of evidence for a wide variety of factors and interventions as Low, Moderate, or High. As the panel explains, "The approach considers the body of evidence for each outcome, assigning an initial rating of low quality to observational studies and high quality to Randomized Clinical Trials (RCTs). These initial ratings may be modified by the following factors: detailed study design, consistency, strength of association, dose-response effect, directness, precision, and if all plausible confounding would reduce a demonstrated effect."

These are the factors whose direction of association had High degree of evidence (meaning we can be confident about causality, beyond mere association):

(Table 2)

For Alzheimer's Disease			For cognitive decline		
Increased risk	Decreased risk	No association	Increased risk	Decreased risk	No association
		Ginkgo biloba		Cognitive training	Vitamin C, Vitamin E, beta-carotene

					supplements, Conjugated equine estrogen, HMG-CoA reductase inhibitors (statins)
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In other words, based on the evidence with highest level of quality alone, it would make sense to

- 1) Engage in more cognitive training (not just games or puzzles, but structured, targeted training)
- 2) Only do things like Ginkgo biloba, Vitamin C, Vitamin E, beta-carotene supplements, Conjugated equine estrogen, HMG-CoA reductase inhibitors (statins) for reasons unrelated to Alzheimer’s disease or cognitive decline. They don’t seem to either help or harm

What happens if we include factors with both High and Moderate levels of evidence?

(Table 3)

For Alzheimer’s Disease			For cognitive decline		
Increased risk	Decreased risk	No association	Increased risk	Decreased risk	No association
		Ginkgo biloba Vitamin E , Cholinesterase inhibitors*		Cognitive training	Vitamin C, Vitamin E, beta-carotene supplements, Conjugated equine estrogen, HMG-CoA reductase inhibitors (statins), Aspirin,, Dehydroepiandrosterone, Cholinesterase inhibitors, Multivitamin supplement, Vitamins B6, B12 and folic acid supplements

Based on that data, it would then make sense to:

- 1) Engage in more cognitive training
- 2) Be aware of that longer list of things that don't seem to either help or harm

If we included the lower level evidence, we would get to the Increased Risk and Decreased Risk factors included in Table 1, which notably would then include Physical Activities as a protective factor.

And this is where things may become most confusing. You may wonder, does this mean that all recent news on the brain benefits of aerobic exercise are somehow unscientific? No, it doesn't mean that.

In fact, what is does is to illustrate perhaps the most important take-away from this whole exercise, panel and report: a) preventing Alzheimer's Disease/ cognitive decline is a different outcome from b) improving Cognitive Fitness which, I would argue, is what most people care about, and what we will discuss in the next article.

*Reference: Williams JW, Plassman BL, Burke J, Holsinger T, Benjamin S. Preventing Alzheimer's Disease and Cognitive Decline. Evidence Report/Technology Assessment No. 193. (Prepared by the Duke Evidence-based Practice Center under Contract No. HHS 290-2007-10066-I.) AHRQ Publication No. 10-E005. Rockville, MD: Agency for Healthcare Research and Quality. April 2010. Available online: <http://www.ahrq.gov/clinic/tp/alzcoftp.htm>