

Faculty Scholarship

---

11-3-2015

## **A Tale of Two Reports: What Recent Publications from the Alzheimer's Association and Institute of Medicine Say About the State of the Field**

Peter J. Whitehouse

Case Western Reserve University, [peter.whitehouse@case.edu](mailto:peter.whitehouse@case.edu)

Follow this and additional works at: <https://commons.case.edu/facultyworks>

---

### **Recommended Citation**

Whitehouse, Peter J., "A Tale of Two Reports: What Recent Publications from the Alzheimer's Association and Institute of Medicine Say About the State of the Field" (2015). *Faculty Scholarship*. 76.

<https://commons.case.edu/facultyworks/76>

This Editorial is brought to you for free and open access by Scholarly Commons @ Case Western Reserve University. It has been accepted for inclusion in Faculty Scholarship by an authorized administrator of Scholarly Commons @ Case Western Reserve University. For more information, please contact [digitalcommons@case.edu](mailto:digitalcommons@case.edu).

**A tale of two reports: What recent publications from the Alzheimer's Association and  
Institute of Medicine say about the state of the field**

**Peter J Whitehouse MD-PhD (corresponding)**

[peter.whitehouse@case.edu](mailto:peter.whitehouse@case.edu)

**2895 Carlton Road**

**Shaker H, OH 44122**

**Daniel R. George**

**dgeorge2844@gmail.com**

Scientific reports hold a mirror up to a culture, reflecting the beliefs, values, assumptions, practices, technologies, and political-economic interests that shape discourse around particular diseases in particular cultural moments.<sup>1</sup> Indeed, despite their authoritative patina, such reports are “living documents” that invite critical analysis about where discourse in a particular field has been and where it is going. In this spirit, two recent reports from the Alzheimer’s Association ([\*Changing the Trajectory of Alzheimer’s Disease: How a Treatment by 2025 Saves Lives and Dollars\*](#)) and the Institute of Medicine in the United States ([\*Cognitive aging: Progress in Understanding and Opportunities for Action\*](#)) are worthy of attention from those endeavoring to understand and contextualize the science and politics of brain health, aging, and dementia.

### ***Changing the Trajectory of Alzheimer’s Disease – the Alzheimer Association report<sup>2</sup>***

The Alzheimer’s Association’s report, published in winter 2015, begins with a reasonable assertion that the world is aging and that age-related cognitive problems deserve serious attention. Specifically, the report projects that by 2050, 13.5 million Americans will have Alzheimer’s, with half of these cases being severe, at an estimated overall cost of care exceeding \$1 trillion. However, recent epidemiological studies, which the Alzheimer’s Association tends to ignore, in fact suggest that the incidence of dementia is going down in such developed countries as Sweden<sup>3</sup>, the Netherlands<sup>4</sup>, the United Kingdom<sup>5</sup>, etc. The reasons for this trend are unclear, but it is plausible that social policy and public health measures that have improved diet, created better educational and exercise opportunities, and contributed to the amelioration of certain risk factors for cognitive impairment, such as smoking, may be

playing a role.<sup>6,7</sup> However, regardless of these apparent successes it is still reasonable to point out that there will be a growing number of people who require help as they age because their cognitive functions are affected. Slowed reaction time, short-term memory loss, and executive dysfunctions do occur in many, if not all of us, to one degree or another as we age.

Consistent with their advocacy through the National Alzheimer's Advisory Panel and through other policy efforts, the Alzheimer's Association uses the phenomenon of population aging as a backdrop to more directly ask for an additional \$2 billion a year for medical research to find a more effective drug. In various places, they refer to this as a quest for a "cure", a "preventative", or a "disease-modifying" drug. In their envisioned scenario, with enhanced investment, this drug could be available by 2025 and the number of people with memory loss would fall from 13.5 million to 7.8 million by 2050, a decline of about 42 percent. From 2026-2035, costs would decline by about \$935 billion, with Medicare costs declining by \$345 billion and Medicaid costs by \$190 billion.

At the World Health Organization's Global Dementia Summit in Geneva, Switzerland in March 2015 Richard Hodes, the Director of the National Institute on Aging, referred to this as an "aspirational" goal, but, frankly, there are very few experts in the field who think that this is even remotely achievable. Even if one were to extrapolate the recently reported (but not peer-reviewed) data on Biogen's amyloid agent,<sup>8</sup> one cannot imagine that the effect size of this drug, even if it were to be replicated in larger studies, could accomplish what the Alzheimer's Association is expressing we need to have in the way of a curative or preventive drug. Because this powerful pill is rather illusory (and many believe unrealistic) on *any* timeframe let alone in 10 more years, this concept is sometimes referred to as the discovery of a "magic bullet". Such

a promise is rhetorically effective in gaining public attention and advocating for increased public and private research investment; yet we have elsewhere questioned whether this strategy – more in the vein of science-fiction than science – verges on the promotion of false hope.<sup>9</sup>

The *Changing the Trajectory of Alzheimer's Disease* report was prepared with the assistance of the Lewin Group who conducted pharmacoeconomic modeling to approximate cost-benefit outlays for society. Various scenarios (delayed onset and slowed progression) were created, but essentially the hypothetical drug was hypothesized to prevent people from advancing as rapidly through the stages of dementia. Because people in the more severe stages may require greater resources, the model predicts saving hundreds of billions of dollars, or even trillions if one extrapolates beyond 2035. So, in essence, the report is telling a story about an imaginary drug creating imaginary effects that essentially rescue our healthcare system from bankruptcy – not to mention recouping any increased research investment within three years, or so it is claimed.

However, the report is more than just an exercise in imagining drug effects but also a case study in irresponsible financial modeling. Our colleague Anders Wimo, a researcher from the Karolinska Institute in Sweden who has organized several conferences with one of us (PJW) over the years on pharmacoeconomics of dementia drugs, has reported<sup>10,11</sup> that the two major factors that affect cost savings are assumptions about the cost of the drug and about the effects of the drug on mortality. The first is obvious and the second is as well, if we think, for instance, that an effective drug for people with dementia might keep them out of nursing homes. But would such a powerful drug affect mortality? Nursing homes have been shown to accelerate death<sup>12,13</sup>, for example. Patients who live longer consume more health care resources on average, which creates a net increase in societal cost. For instance, with regard to

the theoretical transition from severe dementia to moderate dementia, if a person taking an effective drug were to live longer and still eventually become severely demented to consume resources at that stage of their illness, then they may cost more, not less, money if treated with the drug. It is, of course, quite complex to figure out how a drug might affect length of life, and equally difficult to model the implications. If a drug were wonderful enough to cure memory impairment and not to delay death then that drug might be ideal in an economic sense.

The most obvious factor that affects projected cost savings is the cost of the drug itself. Much attention has been paid to cancer drugs that can cost hundreds of thousands of dollars a year. With regard to the potential costs associated with the hoped-for Alzheimer's drug, we have solicited the opinion of many ostensibly knowledgeable people who are familiar with the *Changing the Trajectory* report – including Harry Johns, CEO of the Alzheimer's Association. When one of us (PJW) met Harry in Geneva at the aforementioned WHO meeting, we discussed which drug costs the Alzheimer's Association modeled with the Lewin Group. Obviously, it is difficult to know what the cost of a hypothetical magic bullet would be. In fact, the best answer is probably that the drug companies will charge whatever they think people will pay just before an outrage-driven campaign uprising occurs against the power of the pharmaceutical industry over our health and political systems. If one is not sure of the cost to the drug, then an appropriate maneuver is to conduct a so-called sensitivity analysis. Using this method, one examines a range of drug prices and reports the cost savings/increases associated with each. That gives the reader of any report that uses this responsible approach an idea under different assumptions what the effects of the drug price on overall costs might be.

However, in their report the Alzheimer's Association did not use this technique; rather the Association chose to model the cost of the drug as *zero*. In other words, this magic drug is particularly magical because it is free. Furthermore, they also assume everyone has access to the drug (this is an easier assumption to make if the drug is free) and that it elicits the same magical effects equally, in everyone, always. No wonder these sorts of projections can extrapolate cost savings into our healthcare system. No wonder they also claim that we can recoup our investments in research to develop this pill in three short years. Critical minds must take these assumptions and claims into deep consideration when deducing whether the report is in fact a responsible document, or not.<sup>14</sup>

***Cognitive Aging: Progress in Understanding and Opportunities for Action – The Institute of Medicine report***<sup>15</sup>

Published in April 2015, the Institute of Medicine's report was authored by a star-studded, although perhaps somewhat medically biased, group of panel members led by Dr. Dan Blazer of Duke University. Rather incredulously, this group accepted the daunting mission to consider cognitive aging as "separate" or "distinct" from Alzheimer's disease and other dementias. Obviously, the relationships between cognitive aging and Alzheimer's disease are contentious, but many believe that the biological changes that occur with aging overlap with those we attribute to disease.<sup>16</sup> Based on this bold conceptual leap, the authors then imagine that the difference between a neurodegenerative disease and cognitive aging is whether neuronal loss occurs or not. The word "neurodegeneration" in fact implies cell dysfunction and then loss. In these conditions, such as Parkinson's disease or ALS, cells develop microscopically visible disruptions in their cell contents, then shrink, and finally disappear. The report authors review

human and animal studies, concluding that cognitive aging can be separated from disease-related aging by virtue of the former being free of cell loss. This allows them to justify looking at cognitive aging in the absence of disease.

The science behind this assertion is not clear, as many of the papers quoted in the report demonstrate. Neuronal loss has been reported in various brain structures as a function of aging. The selection of cases is critically important because there is no good way of knowing with certainty who has cognitive aging free of disease and who has it with disease. For example, it is well-known that amyloid plaques are found in people who do not have a clinically apparent dementia.<sup>17</sup> Neuronal dysfunction measured by intracellular inclusions, synaptic dysfunction and cell shrinkage occur in both aging and disease. In fact, one can ask whether it is logical that before cells die in a so-called “neurodegenerative disease” they necessarily demonstrate dysfunction and morphological signs like cell shrinkage. In other words, everybody talks about a continuum of severity starting with ‘normal’ in neurodegenerative disease, so how can one separate out the neuronal dysfunction that precedes neuronal loss from that which does not lead ultimately to cell death? According to members of the panel who spoke to us in private conversation, this topic consumed a lot of time and created dissension in the group – perhaps the most contentious issue being: “what is cognitive aging and how is it different than disease?”. Our own belief, shared by many, is that this distinction cannot be made so clearly. The main implication of considering Alzheimer’s on a continuum with aging is that cures become more difficult to imagine while interventionist approaches, such as brain health and public health measures, become more relevant to everyone who is aging.



However, despite the controversial premise, the authors end up in a positive place by recommending later in the report that cognitive aging can be addressed by a variety of brain health interventions that have been well-described elsewhere including: diet, exercise, mental activity, community engagement, and generally taking good care of your health across the lifespan. This advice, along with the recent publication of the *Blackfriars Consensus on promoting brain health*<sup>18</sup> (the product of a meeting between high-level scientists, public health practitioners, policy makers, lay representatives and others that took place at the UK Health Forum on 30 January 2014 and makes an evidence-based argument for “integrated prevention approaches”) should motivate increased attention in the public health space around cognitive aging. Indeed, there are clear and actionable socio-environmental risk factors, including physical inactivity, tobacco, alcohol use and substance abuse, traumatic brain injury, low education, poor workplace health, reduced social networks, access to healthcare and support resources, poor diet, diabetes, high blood pressure, obesity, and high cholesterol that deserve our immediate societal attention. One of us (PJW) is currently working with the American Public Health Association as a member of their Governing Council to try to develop such a reasonable policy. Generally, the Institute of Medicine report captures the field’s current shift away from exclusively molecular approaches and towards prevention-oriented paradigms. Furthermore, it is commendable that the Institute of Medicine chose to use the term ‘cognitive aging’ rather than the more biologically-oriented ‘brain aging’, and focused on cognitive interventions rather than brain interventions. Ultimately, it is not neural tissue that we want to keep healthy for its own sake but rather for its actual function (i.e. our thinking and emotional abilities).

So where's the problem? Maybe the ends do justify the means, and we all need to be out there taking better care of our brains. But here's one problem: in Geneva, Harry Johns presented a talk on risk reduction and claimed that the evidence is better that we can prevent cognitive decline without disease rather than cognitive decline with disease. In other words, by using public health interventions we can reduce the rate of normal brain aging but not necessarily Alzheimer's. The evidence for this assertion is not so clear, as Harry realized when asked whether we should develop prevention programs for people who already have memory problems. He seemed to agree that we should, but his position sets up the scenario that justifies drug development over greater emphasis on public health measures for those who already have cognitive challenges. It would seem important that we not segment the world into people with Alzheimer's and the rest of us, and regard the former as irredeemably afflicted. This is another reason why a conceptualization of cognitive aging occurring across a continuum – rather than in binary categories (i.e. “normal aging” and “disease”) – may offer more humanizing potential.

However, the end of the report is most revealing of our current semantic confusion as it reinforces the challenges we have with labels. Having considered people who do not have disease, the authors report that such non-demented individuals can have trouble driving and with financial management. Older drivers can have difficulties reacting in emergency situations because of cognitive changes, and can have trouble with getting lost. Financial abuse of the elderly is widely known and it can involve either outright crooks and charlatans or the somewhat more legitimate variety that live on Wall Street taking advantage of people's retirement planning. So non-diseased elders can be impaired in making financial decisions.

Well, but wait a minute – aren't those challenges with automobiles and financing impairments of 'activities of daily living'? Yes, of course they are. The authors are considering so-called instrumental activities of daily living rather than more basic ones, such as feeding and toileting. So at the end of the report, the authors basically conclude that people who have cognitive aging without disease end up being at risk for impairments in activities of daily living. Put differently, disease-free people become demented. Of course, the authors end up in this awkward position because of their initial, and internally debated assumption that you can clearly separate cognitive aging from disease-related aging.

## **Conclusions**

Ultimately, the two reports serve as a fascinating cross-section of where the Alzheimer's field currently sits in 2015. From a Responsible Innovation framework <sup>19</sup> we believe the report by the Alzheimer's Association could be labeled as irresponsible in its attempts to demonstrate that investment in biological research to find disease-modifying or curative drugs will save hundreds of billions of dollars in our healthcare system. In contrast, the Institute of Medicine's report represents a more balanced and collaborative effort to justify an investment in public health related to cognitive health across the lifespan. Although the latter reports ends up in the right place – that is, advocating for actions that we can all make as individuals and communities to keep our minds fit as we age – its struggle with terminology demonstrates once again the danger of medical labels as applied to all of us, but particularly elders with cognitive challenges.

## References

- 
- <sup>1</sup> Young A (1995) *The Harmony of Illusions: Inventing Post-Traumatic Stress Disorder*. Princeton: Princeton University Press.
- <sup>2</sup> The full report can be accessed at: [http://www.alz.org/documents\\_custom/trajectory.pdf](http://www.alz.org/documents_custom/trajectory.pdf)
- <sup>3</sup> C Qiu, E von Strauss, L Bäckman, B Winblad, L Fratiglioni (2012) Twenty-year changes in dementia occurrence suggest decreasing incidence in central Stockholm, Sweden. *Neurology*, **80**, 1888–1894.
- <sup>4</sup> EM Schrijvers, BF Verhaaren, PJ Koudstaal, A Hofman, MA Ikram, MM Breteler (2012) Is dementia incidence declining? Trends in dementia incidence since 1990 in the Rotterdam Study. *Neurology* **78**, 1456–1463
- <sup>5</sup> Matthews FE, Arthur A, Barnes LE, et al. (2013) A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II. *Lancet* **382**(9902), 1405-1412.
- <sup>6</sup> Banerjee S (2013) Good news on dementia prevalence—we can make a difference. *Lancet* DOI: [http://dx.doi.org/10.1016/50140-6736\(13\)61579-2](http://dx.doi.org/10.1016/50140-6736(13)61579-2)
- <sup>7</sup> D'Alton S, Hunter S, Whitehouse PJ, Brayne C, George DR (2014) Adapting to dementia in society: a challenge for our lifetimes and a charge for public health. *J Alzheimer's Dis* **42**, 1151-1163.
- <sup>8</sup> Herper M. (2015). Biogen Drug Could Inspire New Hope For Alzheimer's Treatments. *Forbes* 3/20/15. Accessed July 20, 2015.  
<http://www.forbes.com/sites/matthewherper/2015/03/20/biogen-drug-could-inspire-new-hope-for-alzheimers-treatments/>
- <sup>9</sup> Whitehouse PJ, George DR (2008) *The Myth of Alzheimer's: What You Aren't Being Told About Today's Most Dreaded Diagnosis*. New York: St. Martin's Press.
- <sup>10</sup> Wimo A, Jonsson L, Bond J, Prince M, Winblad B (2013) The worldwide economic impact of dementia 2010. *Alzheimer's Dement* **9**, 1–11.
- <sup>11</sup> Wimo A, Ballard C, Brayne C, et al. (2014) Health economic evaluation of treatments for Alzheimer's disease: impact of new diagnostic criteria. *J Intern Med* **275**; 304–316.
- <sup>12</sup> [van Dijk PT](#), [van de Sande HJ](#), [Dippel DW](#), [Habbema JD](#) (1992) The nature of excess mortality in nursing home patients with dementia. *J Gerontol* **47**(2), M28-34.
- <sup>13</sup> Rothera IC, Jones R, Harwood R, Avery AJ, Waite J (2002) Survival in a cohort of social services placements in nursing and residential homes: factors associated with life expectancy and mortality. *Pub Health* **116**(3):160-5.
- <sup>14</sup> Gleckman H. How Much Money Would An Alzheimer's Treatment Really Save? *Forbes*. 2/11/2015.  
<http://www.forbes.com/sites/howardgleckman/2015/02/11/how-much-money-would-an-alzheimers-treatment-really-save/>. Accessed July 20, 2015.
- <sup>15</sup> The full report is available at:  
[http://iom.nationalacademies.org/~media/Files/Report%20Files/2015/Cognitive\\_aging/Cognitive%20Aging%20report%20brief.pdf](http://iom.nationalacademies.org/~media/Files/Report%20Files/2015/Cognitive_aging/Cognitive%20Aging%20report%20brief.pdf)
- <sup>16</sup> Brayne C, Calloway P. 1988. Normal ageing, impaired cognitive function, and senile dementia of the Alzheimer's type: A continuum? *Lancet* **331**(8597), 1265–1267.
- <sup>17</sup> Snowdon DA. Kemper SJ. Mortimer JA. Greiner LH. Wekstein DR. Markesbery WR (1996) Linguistic ability in early life and cognitive function and Alzheimer's disease in late life. Findings from the Nun study. *JAMA* **275**, 528-532.
- <sup>18</sup> Report available at:  
[http://nhfshare.heartforum.org.uk/RMAssets/Reports/Blackfriars%20consensus%20%20\\_V18.pdf](http://nhfshare.heartforum.org.uk/RMAssets/Reports/Blackfriars%20consensus%20%20_V18.pdf)
- <sup>19</sup> Stilgoe J, Owen R, Macnaghten (2013) Developing a framework for Responsible Innovation. *Research Policy* **42**; 1568-1580.