A Modest Proposal for a Longitudinal Study of Dementia Prevention (with apologies to Jonathan Swift, 1729)

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Accepted 13 August 2012

Abstract. Many studies have documented the role of risk and protective factors for late life dementing illnesses, particularly Alzheimer’s disease. A “Systematic Review” from the US Agency for Healthcare Research and Quality and the National Institute on Aging concluded that because the overall quality of evidence was low, recommendations for public health could not be made. In order to gain evidence for the efficacy of lifestyle interventions, we propose a “Modest Proposal” to study 10,000 subjects over 40 years randomly assigned to groups of low or high saturated fat in the diet, head injury, and high or low levels of mental activity, physical activity, or inactivity as well as smoking or non-smoking. This proposed study cannot be accomplished. The “Modest Proposal” illustrates that the absence of definitive evidence should not restrict physicians from making reasonable recommendations based on the evidence that is available.

Keywords: Alzheimer’s disease, dementia, epidemiology, prevention, risk factors

It has been widely proposed that dementia risk may be lowered through control of modifiable risk factors such as low levels of cognitive and physical activity, hypertension, obesity, high fat diet, head injury, diabetes mellitus, low dietary intake of fish, fruit and vegetables, antioxidants, B vitamins, and smoking [1, 2]. Yet, in a “Systematic Review” supported by the US Agency for Healthcare Research and Quality and the National Institute on Aging, Plassman and colleagues concluded, “few potentially beneficial factors were identified from the evidence on risk or protective factors associated with cognitive decline, but the overall quality of the evidence was low.” The absence of randomized clinical trials was pointed out by the authors of the “Systematic Review” as a basis for this conclusion. Therefore the authors concluded, “The current literature does not provide adequate evidence to make recommendations for interventions” [3, 4].

We agree that definitive evidence for the effectiveness of dementia prevention methods is lacking, and concur that large-scale population-based randomized clinical trials of these complex issues are critically needed. The NIH Conference Statement identified potential leads for dementia prevention, which they recommended should be pursued with “potentially novel approaches and increasingly rigorous scientific methods” [3]. We agree that current evidence to document the influence of lifestyle factors on cognitive impairment in late life are limited, and offer a “modest proposal” to obtain the needed evidence for the effectiveness of these interventions.

We propose a 40-year longitudinal single-blind study of these risk factors in 10,000 healthy volunteers, aged 20–30. Two thousand subjects each will be randomly assigned to groups of either high or low
levels of intake of saturated fat, physical activity, cognitive activity, head injury or smoking (Fig. 1). The long period of observation is necessary because of the prolonged pre-clinical course of Alzheimer’s disease (AD). The large number of subjects is required to allow for adequate statistical analysis considering the many covariates (age, gender, ethnicity, education, dropouts, and others). The importance of the results justifies the long period of observation and considerable expense.

But can such a study be done? It is time to realize that the ultimate study of the interactions of interest in regard to lifestyle and cognitive health in aging cannot be done. Yet the absence of definitive evidence should not restrict physicians from making reasonable recommendations based on the evidence that is available. For example, in an observational study, Johnson and associates studied the effects of blood pressure control on women with a 4.5 years follow up and concluded that “Hypertension and high blood pressure at baseline were not independently associated with MCI or probable dementia over time in older, cognitively intact, postmenopausal women…” [5]. This result does not inform as to whether a lifetime of blood pressure control will have a beneficial effect on cognitive outcomes in late life. There is ample evidence that midlife hypertension is associated with the risk of late life dementia [6]. Furthermore, a study of 8,534 Swedish twins found that obesity in midlife is a risk factor for dementia [7]. There is evidence to suggest that being overweight in late life is not as much a risk factor for dementia as in midlife, because weight loss may occur with dementia onset [6]. While a randomized controlled trial of the effects of weight reduction over four decades of midlife cannot be performed, in the absence of conclusive evidence, it is clearly reasonable to advise avoidance of obesity in midlife as a dementia prevention method.

There are currently three dementia prevention trials underway in Europe. The “Prevention of Dementia by Intensive Vascular Care” study (ISRCTN29711771) examines the influence of control of vascular risk factors on the incidence of dementia or the burden of functional disability in the aged, with 3,700 subjects studied over 8 years. The “Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability” (NCT01041989) evaluates the effects of 2 years of interventions on cognitive impairment, dementia, and disability in 1,200 subjects. The “Omega-3 Fatty Acids and/or Multi-domain Intervention in the Prevention of Age-related Cognitive Decline” (NCT000672685) project examines the influence of isolated supplementation with omega-3 fatty acids on cognitive decline in 1,680 aged subjects, studied over nearly 6 years. We should keep in mind that even an eight-year study of these interventions will not tell us if early life interventions are effective. While the aforementioned European studies are an important step in the evaluation of potential interventions for dementia prevention [8], we do not need to wait for
Institutes of Health (AG017173).

ACKNOWLEDGMENTS

lower dementia risk. That because there are no randomized controlled trials of a satire, in order to emphasize the fallacy of assuming evidence will not be forthcoming. Calculations of the population attributable risk of AD risk factors have led to the estimate that a 10–25% reduction in the main AD risk factors could potentially prevent as many as 1.1 to 3 million AD cases worldwide [1].

As the Gideons of the public health measure has not received sufficient emphasis. We cannot and must not wait until definitive proof on the value of such recommendations—such evidence will not be forthcoming. Calculations of the population attributable risk of AD risk factors have led to the estimate that a 10–25% reduction in the main AD risk factors could potentially prevent as many as 1.1 to 3 million AD cases worldwide [1]. It is already well known that obesity, smoking, diabetes, hypertension, head injury, and low levels of education and mental and physical activity have negative effects on both systemic and brain health [13]. This message should be widely promoted, and there is every reason to promote healthy behaviors while continuing efforts to obtain further data.

At 1729 Jonathan Swift published anonymously “A Modest Proposal for Preventing the Children of Poor People in Ireland Being a Burden on Their Parents or Country, and for Making Them Beneficial to the Publick” [14]. He proposed that poverty in Ireland could be improved through the use of children for food. Our “Modest Proposal” is similarly intended as a satire, in order to emphasize the fallacy of assuming that because there are no randomized controlled trials we cannot make reasonable recommendations to lower dementia risk.

ACKNOWLEDGMENTS

This work was supported in part by the National Institutes of Health (AG017173).

REFERENCES

[14] Swift, Jonathan (1729) A modest proposal for preventing the children of poor people of Ireland from being a burden to their parents or country, and for making them beneficial to the public. Published anonymously in Ireland.