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# Projections of Alzheimer's Disease in the United States and the Public Health Impact of Delaying Disease Onset

## A B S T R A C T

*Objectives.* The goal of this study was to project the future prevalence and incidence of Alzheimer's disease in the United States and the potential impact of interventions to delay disease onset.

*Methods.* The numbers of individuals in the United States with Alzheimer's disease and the numbers of newly diagnosed cases that can be expected over the next 50 years were estimated from a model that used age-specific incidence rates summarized from several epidemiological studies, US mortality rates, and US Bureau of the Census projections.

*Results.* In 1997, the prevalence of Alzheimer's disease in the United States was 2.32 million (range: 1.09 to 4.58 million); of these individuals, 68% were female. It is projected that the prevalence will nearly quadruple in the next 50 years, by which time approximately 1 in 45 Americans will be afflicted with the disease. Currently, the annual number of new incident cases is 360 000. If interventions could delay onset of the disease by 2 years, after 50 years there would be nearly 2 million fewer cases than projected; if onset could be delayed by 1 year, there would be nearly 800 000 fewer prevalent cases.

*Conclusions.* As the US population ages, Alzheimer's disease will become an enormous public health problem. Interventions that could delay disease onset even modestly would have a major public health impact. (*Am J Public Health.* 1998;88:1337–1342)

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There has been growing concern and recognition that as the United States population ages, Alzheimer's disease will place an enormous burden on the country's health care system. The Food and Drug Administration has approved 2 drugs for Alzheimer's disease, but the efficacy of these drugs in terms of significantly delaying the progression of cognitive decline in patients with moderate to severe disease appears marginal. At the same time, a number of tantalizing clues have emerged about the etiology and pathogenesis of Alzheimer's disease. The apolipoprotein E-4 allele on chromosome 19 is associated with a higher risk for late-onset Alzheimer's disease.[1] Several putative factors have recently been suggested that may delay the onset of Alzheimer's disease, including the use of anti-inflammatory drugs, particularly nonsteroidals,[2–6] and estrogen replacement therapy in women.[7–12] While confirmation of these preliminary findings must await larger epidemiological studies and randomized prevention trials, they nevertheless suggest avenues for future prevention programs that may have a significant public health impact.

Estimates of the future incidence and prevalence of Alzheimer's disease are important for projecting future institutional and home health care needs and the economic burden of this disease. Nevertheless, there are uncertainties in estimates of the numbers of individuals living with Alzheimer's disease. This uncertainty arises because of methodological differences among the limited number of epidemiological studies that have directly measured incidence and prevalence rates in community-based populations and because of the difficulty in establishing a precise age of onset of a disease that follows a gradually progressive, insidious course. The objectives of this article are to estimate the future incidence and prevalence of Alzheimer's disease and to quantify the potential impact on these estimates of interventions that could delay the onset of disease.

## Methods

### Age-Specific Incidence Rates of Alzheimer's Disease

Projections of the numbers of individuals living with Alzheimer's disease (i.e., prevalence) depend crucially on age-specific incidence rates. In reviewing studies reporting such rates, we initially considered only studies of US populations because of concerns regarding cross-cultural differences[13–15]; however, as discussed later, our results are very consistent with those of a number of international studies, particularly of European populations.[16] Four studies of US populations that reported age-specific incidence rates were identified; these studies were conducted in Framingham, Mass[17]; East Boston, Mass[18]; Rochester, Minn[19]; and Baltimore, Md.[20] Each of these studies used established criteria for dementia[21] and Alzheimer's disease.[22] Figure 1 shows age-specific incidence rates plotted at the midpoints of age intervals or the mean ages in the interval if they could be determined. The variation in incidence rates among the 4 studies is due not only to sampling variation but, as discussed later, also to differences in methodology (e.g., methods of case ascertainment).

Regression methods were used to obtain smooth age-specific incidence curves for each of the 4 studies (see Table 1, foot-

note). In order to obtain a summary estimate of incidence, the mean of the 4 smoothed age-specific incidence curves was calculated at each year of age. The resulting curve, shown in Figure 1 on a log scale, is given by the following equation for the incidence rate at age $t$:

(1)   Incidence (% per year) = $.084e^{0.142(t-60)}$.

According to equation 1, incidence rates grow exponentially, and the doubling time of this curve (i.e., the time necessary for incidence rates to double) was 4.9 years. The age-specific incidence rate rises from about 0.17% per year at 65 years of age to 0.71%, 1.0%, and 2.92% per year, respectively, at 75, 77, and 85 years of age. Incidence rates based on equation 1 were used to develop population projections of Alzheimer's disease in the United States. To establish a plausible range, we also performed calculations using the range of incidence rates (minimum and maximum) from each of the studies; these rates are shown in Table 1.

There are conflicting reports as to whether Alzheimer's disease incidence rates continue to rise at the oldest ages, eventually plateau, or even decline.[23,24] The data in Figure 1 suggest that Alzheimer's disease incidence continues to rise at least through the ninth decade of life. There is very limited information in any of the studies about age-specific incidence beyond about 95 years of age, and any estimates beyond age 95 would be based almost exclusively on model extrapolation. When model 1 is extrapolated, it predicts very high incidence rates at the oldest ages. We performed 2 sets of calculations using 2 different assumptions, one in which the incidence rose indefinitely according to equation 1 and another in which the incidence rose according to equation 1 until age 95 and then remained constant thereafter. It was conjectured that our projections would not be sensitive to assumptions about incidence after age 95 because of the small population size of this age group. This was confirmed by a sensitivity analysis showing that our prevalence estimates using either assumption were within 2% of each other.

### Projecting Alzheimer's Disease Incidence and Prevalence

Age-specific prevalence rates are the proportions of living individuals at each age who have Alzheimer's disease. These rates were calculated from a formula (see equation 2) that required input of age-specific incidence rates of Alzheimer's disease (Table 1) and mortality rates among individuals with and without the disease. US mortality rates,
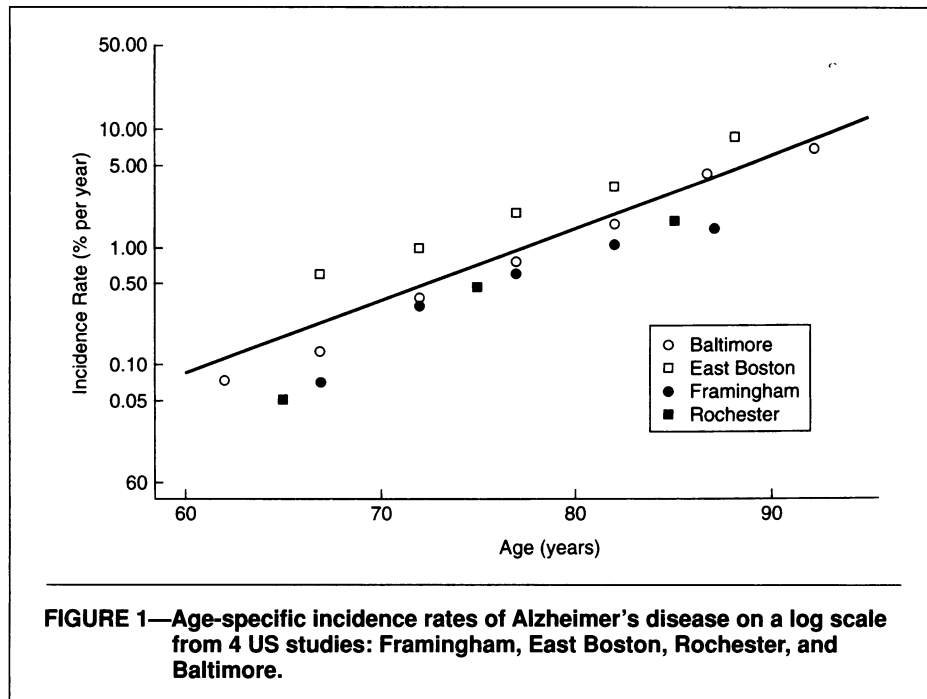


FIGURE 1—Age-specific incidence rates of Alzheimer's disease on a log scale from 4 US studies: Framingham, East Boston, Rochester, and Baltimore.

by age, sex, and calendar year, were obtained from national vital statistics.[25–31] The higher mortality among Alzheimer's disease patients was accounted for by multiplying US rates by 1.44.[32] The proportions of living individuals at age $t$ in year $y$ who have the disease (age-specific prevalence rates) can be estimated from $P_{t,y}(D)/[P_{t,y}(D) + P_{t,y}(\overline{D})]$, where $P_{t,y}(D)$ and $P_{t,y}(\overline{D})$ are, respectively, the probabilities that a person born in year $y - t$ is alive at age $t$ with disease and without disease. These probabilities are approximately given by

$$P_{t,y}(D) = \sum_{i=1}^{t} \{ r_{i,y-t+i} \prod_{1 \leq j < i} (1 - r_{j,y-t+j})(1 - d_{j,y-t+j})$$
$$\times \prod_{k \geq i}^{t} (1 - \lambda d_{k,y-t+k}) \}$$

and

(2)   $P_{t,y}(\overline{D}) = \prod_{j=1}^{t} (1 - r_{j,y-t+j})(1 - d_{j,y-t+j})$,

where $r_{j,y}$ and $d_{j,y}$ are, respectively, the age-specific disease incidence and US mortality rates at age $j$ in year $y$ and $\lambda$ is the relative risk of death for Alzheimer's disease patients relative to individuals of the same age and sex without the disease ($\lambda = 1.44$). US mortality rates in future years were predicted from trends in mortality rates for the past 15 years from a regression model of log $d_{j,y}$ on log $y$ for each age $j$. US mortality rates are typically provided in 5-year age intervals, and so regression models were used to estimate rates by individual years of age.

To project the numbers of individuals living with Alzheimer's disease (the

Alzheimer's disease prevalence), we multiplied the age-specific prevalence rates by the size of the population in terms of age and sex, using middle series US Census projections.[33,34] Similarly, we obtained the projected annual numbers of newly diagnosed Alzheimer's disease cases (incidence) by multiplying the age-specific incidence rates by the projected sizes of the at-risk (without Alzheimer's disease) US population. The projections refer to late-onset (after 60 years of age) disease.

The potential effects of interventions to delay the onset of Alzheimer's disease were evaluated. A range of values for the efficacy of a prevention program were considered, including 5%, 10%, 25%, and 50% reductions in age-specific incidence rates, corresponding to relative risks of intervention of 0.95, 0.90, 0.75, and 0.5. Age-specific disease incidence rates after interventions were obtained by multiplying the mean (estimated) incidence rates in Table 1 by the relative risk of intervention. The intervention was assumed to begin in 1998. These relative risks of 0.95, 0.90, 0.75, and 0.5 correspond, respectively, to delays in the mean age of Alzheimer's disease diagnosis of approximately 0.5, 1.0, 2.0, and 5.0 years in the absence of competing causes of death. This correspondence is based on mathematical relationships between age-specific incidence $I(t)$ (equation 1) and mean age of diagnosis. The mean age of diagnosis is the area under the curve $S(x)$, where $S(x) = \exp(-\int_0^x I(t)dt)$.

The public health burden of Alzheimer's disease depends not only on the overall prevalence of disease but also on prevalence by severity of disease. The types of resources

## TABLE 1—Estimate, Minimum, and Maximum Age-Specific Incidence Rates of Alzheimer's Disease From 4 Studies

| Age, y | Rate, %/y | | |
| --- | --- | --- | --- |
| | Estimate | Minimum | Maximum |
| 60 | 0.08 | 0.02 | 0.24 |
| 65 | 0.17 | 0.05 | 0.44 |
| 70 | 0.35 | 0.13 | 0.82 |
| 75 | 0.71 | 0.33 | 1.53 |
| 80 | 1.44 | 0.71 | 2.86 |
| 85 | 2.92 | 1.48 | 5.33 |
| 90 | 5.95 | 3.06 | 9.95 |
| 95 | 12.10 | 6.36 | 18.57 |

*Note.* A smoothed age-specific incidence curve was obtained for each of the 4 studies from the data presented in Figure 1. For the Boston, Framingham, and Rochester studies, a polynomial regression model was fit to the log of the incidence rates in each age interval plotted at the interval midpoint (or mean age, if it could be determined). The Baltimore study was analyzed by fitting a logistic regression model to the yearly age-specific conditional probabilities of Alzheimer's disease using follow-up data from 1985 through 1996. In each study, the linear age term was significant, but quadratic terms were not and thus were omitted. The estimate is the average of the smoothed age-specific incidence curves from the 4 studies (given to an excellent approximation in equation 1). The minimum and maximum are the extremes for the 4 smoothed age-specific incidence curves.



*Note.* Estimates and ranges are based on the mean, minimum, and maximum age-specific incidence rates shown in Table 1.

**FIGURE 2—Numbers of individuals in the United States with Alzheimer's disease, by age: 1997.**

used to care for a patient (e.g., adult day care or nursing homes) depend on the patient's stage of disease. It is not yet possible to accurately predict the course of Alzheimer's disease; because it is a progressive disease, however, individuals who have been living with it for longer periods generally require a higher level of care. A recent study[35] developed an algorithm for predicting time to nursing home care showing that the median time to the point at which a patient needed nursing home care depended on a number of predictors but that, in general, this period was less than about 6 years. We calculated the numbers of Alzheimer's patients who have been living with the disease for different periods of time and the impact of delaying disease onset on these numbers. To obtain these estimates, we modified the methods and formulas described earlier to calculate prevalence as follows. We used a formula for the proportion of living individuals at age $t$ in year $y$ who have been living with the disease for at least $z$ years. This proportion can be estimated by $x/[P_{t,y}(D) + P_{t,y}(\bar{D})]$, where the numerator $x$ is given by the same formula as $P_{t,y}(D)$ in equation 2 with the modification that the upper limit of the summation ($t$ in equation 2) is replaced by $t - z$.
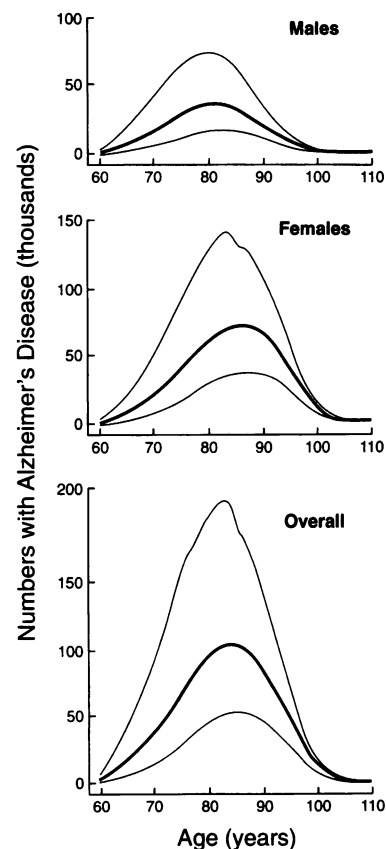
## Results

In 1997, the prevalence of Alzheimer's disease in the United States was 2.32 million (range: 1.09 to 4.58 million). Of these 2.32 million persons, approximately 68% were female and 32% were male. The higher numbers of women reflect the higher proportion of women at older ages in the US population owing to their lower mortality rates. The percentages of persons living with Alzheimer's disease among 75-, 80-, 85-, and 90-year-olds are 4.3%, 8.5%, 16.0%, and 28.5%, respectively. Figure 2 shows the US prevalence in 1997 (numbers of persons with Alzheimer's disease) by age and sex. The curves rise steeply in the seventh and eighth decades of life and then fall off in the ninth decade (even though the age-specific incidence rates continue to rise) (Figure 1, Table 1). Approximately 43% of persons with Alzheimer's disease are between the ages of 75 and 85 years. It is estimated that there are approximately 360 000 new (incident) cases of Alzheimer's disease each year (range: 200 000 to 600 000).

Projections of the future prevalence of Alzheimer's disease are shown in Figure 3. Within the next 50 years, the prevalence could be expected to rise by a factor of 3.7, to 8.64 million (range: 4.37 to 15.4 million). The annual number of new (incident) cases could be expected to rise more than 3-fold, from 360 000 cases in 1997 to 1.14 million new cases in 2047.

The potential effects of interventions to delay the onset of Alzheimer's disease were evaluated. Table 2 shows projected prevalence rates after 10, 30, and 50 years following an intervention assumed as initiated in 1998. An intervention that could delay the mean onset of Alzheimer's disease by approximately 5 years, corresponding to a 50% reduction in risk, would reduce the expected prevalence by 1.15 million after 10 years (2007) and 4.04 million after 50 years (2047). A 2-year delay in disease onset would reduce the expected prevalence by 1.94 mil-
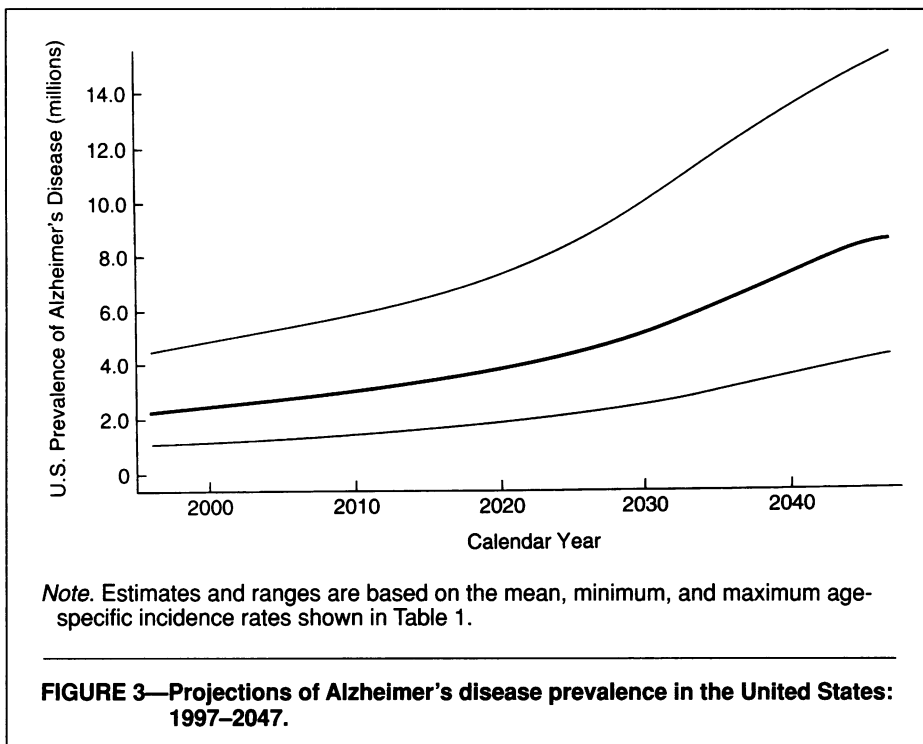
lion after 50 years. Perhaps more striking is that delays even as short as 6 months or 1 year can also have huge public health implications. If onset could be delayed, on average, 1 year, there would be nearly 210 000 and 770 000 fewer persons afflicted with Alzheimer's disease than projected 10 and 50 years after initiation of the intervention, respectively. If onset could be delayed, on average, only 6 months, there would be nearly 100 000 and 380 000 fewer persons afflicted with Alzheimer's disease than projected after 10 and 50 years, respectively.

Individuals living with the disease for longer periods are likely to require considerably more health services than newly diagnosed individuals. The numbers of individuals in 1997 who had been living with Alzheimer's disease for at least 3, 6, and 9 years were 1.41 million, 840 000, and 490 000, respectively. Table 3 shows projections and intervention effects on the numbers of individuals living with the disease for at least 6 years; for exam-

Note. Estimates and ranges are based on the mean, minimum, and maximum age-specific incidence rates shown in Table 1.

**FIGURE 3—Projections of Alzheimer's disease prevalence in the United States: 1997–2047.**

ple, if onset could be delayed 2 years, there would be nearly 890 000 fewer such cases 50 years after initiation of the intervention.

The economic costs of Alzheimer's disease include both direct costs, such as nursing home care, acute care, and paid home care, and indirect costs, including unpaid home care provided by family and friends.[36] Some analyses have estimated the total costs associated with an Alzheimer's disease patient at about $47 000 per year in 1990 dollars.[37] To obtain this estimate, the costs associated with unpaid home care were estimated by multiplying hours spent by unpaid caregivers by imputed hourly wages. An average 1-year delay in disease onset would result in an annual savings of nearly $10 billion at 10 years after initiation of the intervention ($47 000 × 210 000 fewer prevalent cases). Even a modest 6-month delay would correspond to an annual savings of perhaps $4.7 billion at 10 years after initiation of the intervention and nearly $18 billion annually after 50 years. Caveats associated with these

estimates are that they were based on annual costs of $47 000 (including imputed estimates of unpaid care) and were derived from a single study conducted in the San Francisco Bay area that may not have accurately reflected costs in other parts of the country.

## Discussion

These analyses suggest that the number of Americans with Alzheimer's disease in 1997 was 2.32 million (range: 1.09–4.58 million) and that this number will nearly quadruple in the next 50 years, at which time 1 in 45 Americans will be living with the disease. The growth in the prevalence of Alzheimer's disease results from the aging of the US population. In 1997, the percentages of Americans more than 65, 75, and 85 years of age were 13%, 6%, and 1.4%, respectively. By the year 2047, the corresponding percentages of such individuals will increase to approximately 20%, 11%,

and 4%.[34] The majority of individuals with Alzheimer's disease will continue to be female, and a significant proportion of these women will not have a spouse to depend on for caregiving, in part because of the higher male death rates.

There is clearly uncertainty in estimates of the current and future prevalence of Alzheimer's disease. The main source of this uncertainty is the age-specific incidence rate of disease that arises from different methods and criteria used for diagnosing and ascertaining cases. With an insidious disease such as Alzheimer's, the exact age at which an individual passes the threshold for a diagnosis is difficult to determine, and the criteria used to define these thresholds vary among investigators. The ranges we have described for prevalence rates reflect these uncertainties. Our prevalence estimate of nearly 2.32 million is somewhat lower than an estimate of 4 million reported in the literature,[38–40] although the latter still falls within our range of 1.09 to 4.58 million. This higher estimate was based on a prevalence survey conducted in a single community in East Boston that found correspondingly higher age-specific incidence rates.[18] The East Boston study included "mild" and "moderate" cases; when such cases are excluded, the study's age-specific incidence rates are more consistent with those of other investigations. Thus, the upper ends of our ranges may better reflect the prevalence of the combined total of both mild and moderate cases of disease. While one might question whether the Boston figures represent an overestimate, it is also plausible that incidence rates from other studies might represent underestimates. The Framingham study used a criterion of moderate or severe, removed cases of early dementia from the at-risk population at the start of follow-up,[17] and used the Mini-Mental State Examination to initially screen the population. All of these factors could explain the lower incidence rates found in that study.

The Rochester study included only Alzheimer's disease cases that came to medical attention.[19] The Baltimore study was composed of highly educated individuals, and thus the incidence rates described in that investigation may not be representative of the general US population.[20] Furthermore, none of the published US studies adequately represent African American or Hispanic populations. Nevertheless, the worldwide literature, including numerous European studies, is consistent with the ranges of incidence rates shown in Table 1. Indeed, a recent review of international studies of Alzheimer's disease incidence rates[16] that included populations in Sweden (Lundby[41] and Gothenberg[42]), France,[43] the United

**TABLE 2—Potential Effects on Prevalence of Interventions to Delay Onset of Alzheimer's Disease**

| Relative Risk of Intervention | Mean Delay, y | Alzheimer's Disease Prevalence (Millions) | | |
|---|---|---|---|---|
| | | 2007 | 2027 | 2047 |
| 1.00 | 0 | 2.89 | 4.74 | 8.64 |
| 0.95 | 0.5 | 2.79 | 4.52 | 8.26 |
| 0.90 | 1.0 | 2.68 | 4.31 | 7.87 |
| 0.75 | 2.0 | 2.32 | 3.64 | 6.70 |
| 0.50 | 5.0 | 1.74 | 2.49 | 4.60 |

**TABLE 3—Prevalence Projections of Numbers of Individuals With Alzheimer's Disease Living With the Disease for at Least 6 Years**

| Relative Risk of Intervention | No. (Millions) | | | |
|---|---|---|---|---|
| | 1997 | 2007 | 2027 | 2047 |
| 1.00 | 0.84 | 1.07 | 1.80 | 3.53 |
| 0.95 | 0.84 | 1.04 | 1.71 | 3.34 |
| 0.90 | 0.84 | 1.01 | 1.62 | 3.17 |
| 0.75 | 0.84 | 0.92 | 1.34 | 2.64 |
| 0.50 | 0.84 | 0.78 | 0.89 | 1.76 |

Kingdom,[44] and Japan[45] showed incidence rates in excellent agreement with those predicted by equation 1, and these rates all fell within the ranges given in Table 1. This range of incidence rates establishes the plausible range for the current prevalence of Alzheimer's disease of between 1.09 and 4.58 million.

The absolute prevalence of Alzheimer's disease is sensitive to assumptions about age-specific incidence rates, but proportional growth is relatively insensitive. The prevalence of Alzheimer's disease will grow by a factor of nearly 4 over the next 50 years for the range of incidence rates shown in Table 1 (the mean, minimum, or maximum series of incidence rates) in the absence of an effective intervention to delay disease onset.

There are additional sources of uncertainty. Some studies have reported higher Alzheimer's disease incidence rates in women than in men,[24] while others have not reported differences between the sexes.[16,17] Some studies have suggested a lower incidence among highly educated individuals,[46] but that finding was not confirmed in several other studies.[16,47,48] As additional epidemiological data accumulate concerning the validity of these and other risk factors, it will be possible to incorporate their effects into future population forecasts.

In spite of these uncertainties, it is reassuring that the age-specific prevalence rates deduced from our model assumptions (disease incidence and mortality rates) are compatible with reported prevalence rates directly observed in a number of community-based surveys.[49–50]

To date, the success of interventions designed to stabilize progression in patients with mild to moderately severe disease has been modest.[51] Statistical analyses support the conclusion that Alzheimer's disease will become an enormous public health problem in the next 50 years and that modest delays in onset can have a significant impact in terms of reducing the burdens and costs associated with this debilitating disease. Epidemiological studies have suggested some candidate approaches for delaying the onset of disease[52]; antioxidant therapy is one such

approach.[53] Some studies have suggested that estrogen replacement therapy in women may offer protection against Alzheimer's disease and may reduce incidence rates by as much as 50%. Similar levels of protection have been reported with the use of nonsteroidal anti-inflammatory drugs.[54]

However, these findings have not been supported by all studies in the literature,[55,56] and they must be viewed cautiously because of the potential biases inherent in epidemiological studies of elderly populations. For example, exposure histories among elderly people are susceptible to differential recall biases; patients who are in the earliest stages of dementia but do not yet meet the criteria for a diagnosis may recall exposures differently than nondemented individuals. Randomized prevention trials are the most reliable study designs to control these biases and to control the subtle effects of confounding variables. However, such studies would need to be large, perhaps involving tens of thousands of individuals in order to detect modest delays in disease onset and to account for the appreciable mortality and loss to follow-up typical in elderly populations. Accordingly, the resources needed to conduct such trials are large, but these costs are small in comparison with the long-term economic and social costs of delaying disability even modestly in an increasingly aging population. ☐

## Acknowledgments

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