

Is Increased Mortality from Alzheimer's Disease in Sweden a Reflection of Better Diagnostics?

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Abstract: Mortality data were retrieved from the Swedish death registry for the years 1970-2006. This report presents updated information on mortality from Alzheimer's disease (AD) through the year 2006, as well as a statistical model of AD mortality with predictive value. This model was developed based on a mortality risk function acting after a specific time point, either step-wise on the whole population or on an increasing part of it. Data collected in recent years indicate that mortality is increasing continuously amongst the oldest patients, while younger age-groups show more stable mortality rates. After fitting the statistical model to age-standardized mortality data it also gave age-specific rates that fit well with reported data without further adjustments in model parameters. The data and the corresponding model for AD mortality suggest that the ability of the body to protect itself from AD-related neurological damage has in general become increasingly impaired since about 1985. This impairment has mainly affected people 65 years of age and older since 1985; the model predicts that in 2020, the age-standardized mortality in Sweden will be 13/100,000 person-years. The author concludes that the increasing mortality is real and not only a result of increasing use of the death classification code for AD.

Keywords: Alzheimer's disease, mortality, mobile phone, blood-brain barrier.

INTRODUCTION

The reported mortality due to Alzheimer's disease (AD) in Sweden has increased markedly in the last thirty years. Before 1980, mortality was around 0.2/100,000 person-years. However, age-standardized mortality (ASR Se 1970) increased to 0.6/100,000 person-years in 1982 and has increased continuously since 1987. In 2006, reported mortality was greater than 9/100,000 person-years. It is unclear whether increased mortality reflects a real increase in the rate of deaths due to AD, or whether it is an artifact due to improved diagnostics. The increase in deaths in the early 1980s led to the definition of a specific death code, 290.1, that was added to the ICD-9 code list in 1987. In 1997, the updated ICD-10 list included a code that was specific for deaths associated with AD.

In Sweden, many people develop AD symptoms each year (prevalence 83,000 and incidence 23,000 in 2003), but relatively few people are hospitalized (around 1500 per year since 1997) or have AD listed as the cause of death on their death certificates (547 in 1998, and 1540 in 2006). It may be that the risk of death from AD depends on the body's ability to protect itself from accelerating brain damage caused by the disease. If this protective ability is suddenly reduced, the risk of serious and lethal consequences increases. Thus, in a 'natural' environment, a patient with AD has a baseline mortality risk that is minimized by the body's ability to protect the brain, but alterations in the physiological or external environment could shift the balance so that the risk of death

would not only become much greater, but would also continue to increase over time. For example, if the protective blood-brain barrier (BBB) was damaged in patients with AD symptoms, the AD symptoms might worsen. In fact, exposure to radiation from mobile phones or closely located base stations can reduce the protective properties of the BBB, as can very low radiation levels [1]. In this study, the author assumed that patients with AD are very sensitive to environmental changes that affect their brain protection system.

A detailed analysis of AD death rates in Sweden through the year 2002 was published previously [2]; data through the year 2006 are now available for analysis. The author wished to develop a mathematical model that could estimate both age-standardized and age-specific future mortality rates and simulate mortality trends. The author previously developed a model that predicted the incidence of melanoma in Swedish, Norwegian, and American populations [3]. Based on the success of this model, a similar approach to model AD mortality was used. The validity of a mathematical model based on this assumption was tested after adjusting model parameters to fit age-standardized data by checking whether age-specific data was in agreement with the reported data.

METHODS

Data on reported mortality due to AD were retrieved from the National Board of Health and Welfare in Sweden [4]. Age-specific data on patients' hospital visits due to AD were collected from this source for the years 1998 to 2006. During this time period, the number of hospital visits per age group was fairly constant over time so that it was appropriate to use an average number for the whole time period. These data were used to assign an AD risk number from a total of 100,000 points for each age-group per year. Thus, the oldest age groups were assigned the highest risk numbers.

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It was assumed that AD-associated damage occurring in a given year could result in death according to a statistical life distribution, that is, a log-normal distribution characterized by two parameters: 1) dispersion (in time decades) and 2) median time, transformed into the time it takes for the percentage of deaths to be 0.1%. The probability of death for an individual in a specific year of life based on their risk number could then be calculated over time. The total probability over time for one birth cohort was then calculated by adding the probabilities from all of the five-year periods. The probabilities of death for all birth cohorts were calculated in a similar way to determine age-standardized mortality over calendar time. Based on the sudden increase of reported AD mortality from the mid-1980s, we used 1985 as the starting year at which the statistical function for increased mortality was applied. The model also allowed for a gradual increase in added mortality to reflect environmental changes over time.

The two parameters used in the probability function were then varied to achieve the best fit between calculated and reported age-standardized mortality. To check the validity of this calculation, we compared the calculated age-specific mortality (without any further variation of the parameters) with the reported data. We used the model to investigate two hypotheses: first, that increased mortality from AD is due to a sudden change in reporting of AD-related deaths 1987; and second, that increased mortality is due to gradual changes in the environment since 1985.

Definitions

Mortality was defined as the number of deaths attributed to AD per 100,000 persons per year. Age-standardized mortality was based on statistics for the Swedish population in 1970. Age-specific mortality is given for five-year age groups. The basic statistical function used to determine mortality was a log-normal life distribution with two defining parameters: dispersion, defined here in time decades, and median time, transformed into the time to 0.1% death instead of time to 50% death.

Mortality due to Alzheimer’s disease was given a separate ICD-9 code in 1987, namely code 290.1. In 1997, ICD-10 was issued, which used code G30 for deaths due to Alzheimer’s disease.

RESULTS

Fig. (1) shows the reported age-standardized mortality from AD in Sweden. Data from the Swedish patient registry provided information on the number of patients visiting hospitals per year and per 100,000 people within an age group (Fig. 2). The data from Fig. (2) was used to define a risk number per 100,000 people for each five-year age group (Table 1). For the past 10 years, the number of hospital visits due to Alzheimer’s disease has been quite stable over time (Fig. 3). Fig. (4) shows the increasing use of mobile phones in Sweden expressed as the total usage time per year relative to usage time in the year 2006.

The model assumed that the probability of dying from AD could be described by probability functions from the year 1985 onward. The two parameters mentioned earlier

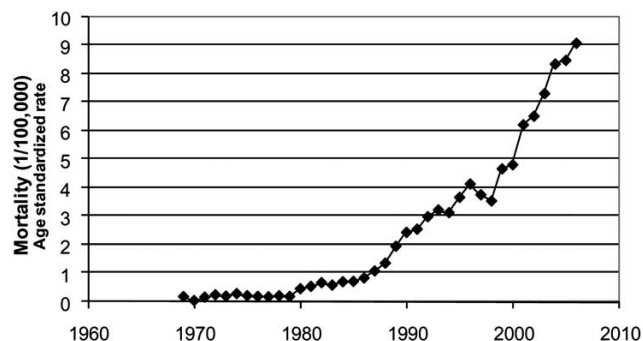


Fig. (1). Age-standardized mortality due to Alzheimer’s disease (Sweden 1970-2006).

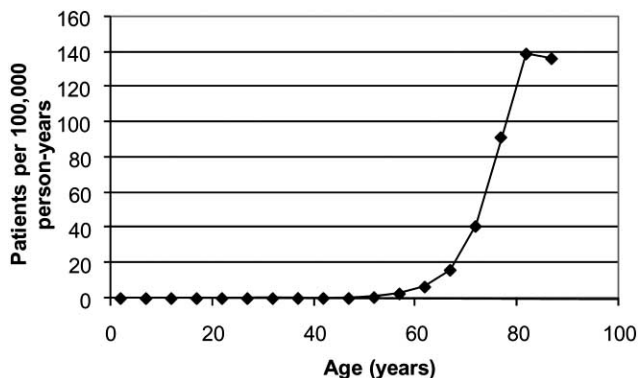


Fig. (2). Alzheimer’s disease patients per year and per 100,000 by age group for the years 1998 to 2007.

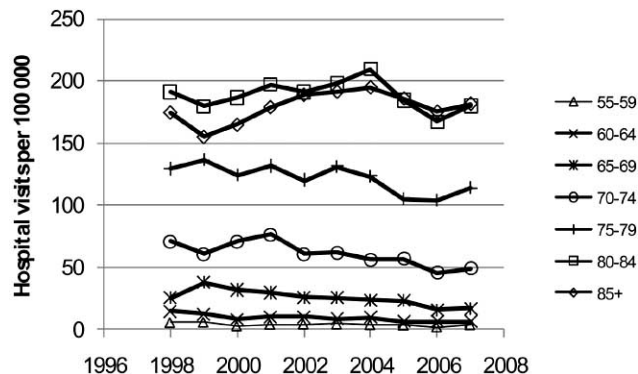


Fig. (3). Hospital visits per year for 100,000 by each age group in Sweden from 1998 to 2007.

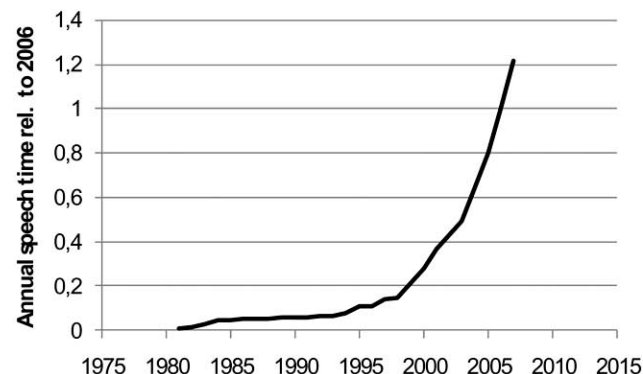


Fig. (4). Total speech time/year via mobile phones relative to year 2006 in Sweden.

Table 1. Derivation of a Risk Number Per Five-Year Age Group and per 100,000 Persons

Age group	Hospital visits per 100,000 persons ^A	% of total visits ^B	Risk number of 100,000 persons per age group and year ^C
0-4	0.042	0.0	7
5-9	0	0.0	0
10-14	0	0.0	0
15-19	0	0.0	0
20-24	0	0.0	0
25-29	0	0.0	0
30-34	0.03	0.0	5
35-39	0.03	0.0	5
40-44	0.017	0.0	3
45-49	0.101	0.0	17
50-54	0.876	0.15	148
55-59	3.984	0.7	674
60-64	9.398	1.6	1,590
65-69	25.643	4.3	4,339
70-74	60.973	10.3	10,317
75-79	122.038	20.6	20,649
80-84	189.019	32.0	31,983
85+	179.497	30.4	30,372

^AThe number of hospital visits for patients with AD per age group and per 100,000 persons. The total number of visits by these 1.8 million people was 591 per year (1998-2006).

^BThe relative distribution of visits per age group (equal to A as a percentage of 591).

^CThe relative risk number for AD is calculated from B*100,000 people born each year within the age group.

(i.e. dispersion and median time) were varied to obtain the best fit with the reported age-standardized data to test for the two scenarios, i.e. that increased AD-associated mortality was due to either the 1987 definition of a specific code for death due to AD or that it was due to changes in the environment, and specifically due to the increasing use of mobile phones (Figs. 4, 5, and 6). Because the calculated age-standardized mortality was based on a calculation of age-specific mortality for many birth cohorts, age-specific data were already available for plotting for the two scenarios (Figs. 7 and 8). The definition of the risk numbers turned out not to be critical: if these numbers were doubled, the parameters changed accordingly, and still fit both the reported data and the age-specific data.

The parameters associated with the best fit with the reported age-standardized mortality are reported in Table 2.

DISCUSSION

For the past two decades, mortality from AD has been increasing in many parts of the world. The Swedish National Board of Health and Welfare attributes this increase to improved diagnostics and changing demographics. Historically, deaths due to AD were mainly registered before the age of 60-65 years, while today deaths due to AD are also registered at older ages.

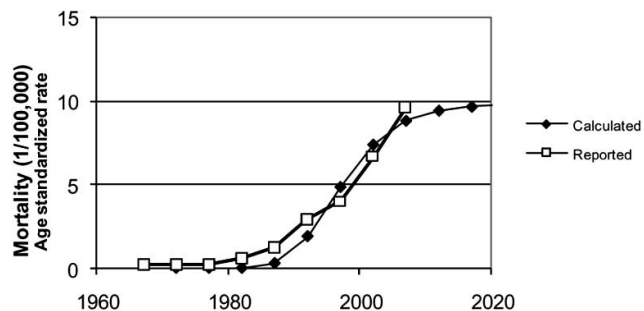


Fig. (5). Reported and calculated age-standardized mortality after a step-wise change in 1985.

The number of hospital visits due to AD over the past 10 years has been fairly stable, suggesting that the causal factors for AD have also been unchanged. However, the mortality rate associated with this disease has seemed to accelerate since 1987. There are two possible explanations for this observation. First, deaths due to AD may reflect increased use of the AD-specific ICD code since 1987. Second, this increase may indicate changes in the environment since 1985 that make patients with AD symptoms more likely to die from the disease. This environmental change could either be

a sweeping change, such as the sudden roll-out of mobile phone base stations to provide mobile service coverage throughout Sweden, or it could be a more gradual change, such as the increased use of mobile phone handsets by the elderly. Huss *et al.* recently reported that mortality from AD was higher in populations living close to power lines [5].

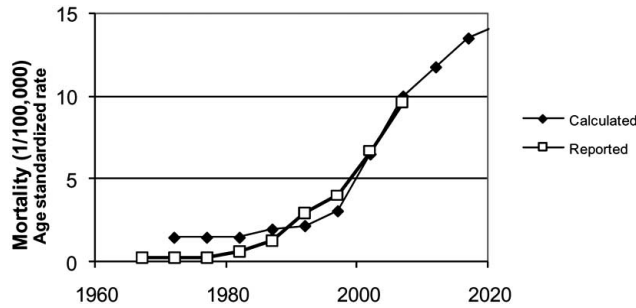


Fig. (6). Reported and calculated age-standardized mortality after a ramp change (based on data from 1985 onward) [Fig. (4)].

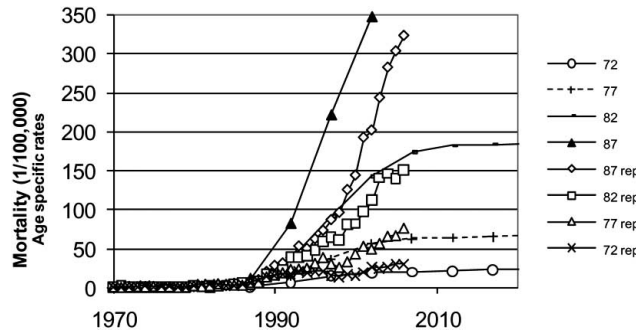


Fig. (7). Calculated age-specific mortality based on parameters that provided the best fit to age-standardized mortality in Fig. (5). Reported data (rep) for 87-, 82-, 77-, and 72- year-olds are also shown.

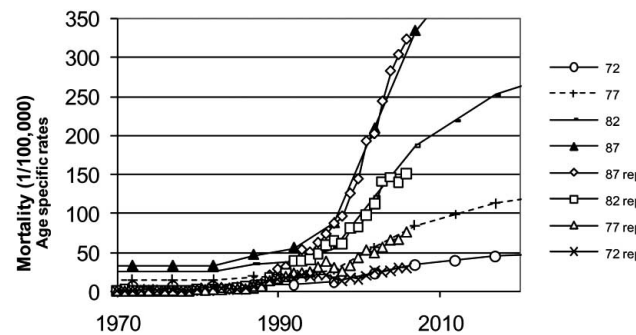


Fig. (8). Calculated age-specific mortality based on the parameters that provided the best fit to age-standardized mortality in Fig. (6). Reported data (rep) for 87-, 82-, 77-, and 72- year-olds are also shown.

In the present study, the calculations of mortality over time were based on an arbitrary number (100,000) called the risk number that was distributed among all years of life according to the distribution of AD-related hospital visits (Fig. 2). This risk number (100,000) can be related to the number of people affected by the pathogenesis or progression of AD over a lifetime per 100,000 people. Most often, the damage is hardly noticed; other times, the damage can lead to hospitalization, and less frequently, to death.

Table 2. The Parameters Used to Fit Age-Standardized Mortality due to Alzheimer’s Disease to the Reported Data Based on the Annual Risk Numbers from Table 1

Dispersion (time decades)		Time to 0.1% deaths (in years)	
Single step model	Ramp model	Single step model	Ramp model
0.22	0.78	10.87	3.56

The data shown in Fig. (5) were calculated assuming a sudden administrative change was instituted as a step function from 1987 onward; this change was the new code for Alzheimer deaths that was introduced in 1987 (ICD 9), and several years may have passed before it was systematically and consistently used on death certificates. This scenario did not fit the reported age-specific data, especially not for the oldest age groups (Fig. 7). Similarly, the age-specific data did not match a model in which an administrative change was gradually introduced (as a linear ramp) starting in either 1985 or in 1995.

Environmental changes in Sweden over a period of years could also explain the observed increase in AD-associated mortality. One such change was the roll-out of the mobile phone system, i.e. base stations and handsets. Fig. (4) shows mobile phone usage per annum relative to usage in 2006 in Sweden.

To test the influence of using a non-linear ramp instead of a step function, we used data from Fig. (4) to define the ramp-up of the new environment. Fig. (6) shows the calculated and reported age-standardized rates at optimum fit. It is interesting that the model predicts a higher-than-reported mortality before 1985. This is most likely because prior to 1985, there was no specific death code defined for AD; thus, reported deaths were likely lower than actual deaths. Fig. (8) shows that calculated age-specific data using this model was a very good fit when we used the parameters that were determined by the best fit for reported age-standardized rates (Fig. 6).

Hallberg and Johansson [2] reported previously that the death rate of AD is increasing most in sparsely populated areas of Sweden, and that this increase can be associated with the higher-than-average output power from mobile phones in these more remote areas. This raises the possibility that the use of mobile phones, rather than general exposure to base station radiation (which would be lower in sparsely populated areas) could be contributing to the increasing death rate. From a medical point of view, it is likely that a damaged BBB would result in exposure of the brain to increased albumin levels as well as to increased levels of other possibly toxic substances. This might accelerate the pathogenesis of AD and increase the mortality rate.

CONCLUSIONS

This study indicates that patients with AD seem to have a greater risk of dying from their disease today than they did prior to 1985. After 1987, this increased risk can be explained in part by improved diagnostics; however, environmental changes in the mid-1980s (which accelerated after

1995) seem to account for much of the increased risk. Other diseases, including melanoma, lung cancer, prostate cancer, and breast cancer, have shown similar sudden trend breaks, possibly due to environmental changes that impair the body's immune system and cell repair capabilities [6]. While health care providers often dismiss these trends as entirely due to improved diagnostics, better doctors, and better instruments, they should also investigate the potential contribution of environmental factors, such as the sudden increase in cellular phone use, to these alterations in disease trends.

CONFLICT OF INTEREST STATEMENT

The author reports no conflicts of interest related to this work.

ABBREVIATIONS

AD = Alzheimer's disease

BBB = Blood-brain barrier

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