American Journal of Epidemiology
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Vol. 188, No. 2
DOI: 10.1093/aje/kwy234
Advance Access publication:
October 9, 2018

Original Contribution

Life Expectancy With and Without Dementia: A Population-Based Study of Dementia Burden and Preventive Potential

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Initially submitted April 25, 2018; accepted for publication October 5, 2018.

Reliable population estimates of life expectancy with dementia are required for shaping health-care policy. From the Dutch, population-based Rotterdam Study, 10,348 persons were followed during 1990-2015 for dementia and death. We created multistate lifetables, and assessed the effect of postponing disease onset. During 120,673 person-years, 1,666 persons developed dementia, and 6,150 died. Overall life expectancy of women ranged from 18.0 years (95% confidence interval (CI): 17.8, 18.2) at age 65 to 2.3 years (95% CI: 2.2, 2.3) at age 95. Of total life expectancy at age 65, 5.7% (1.0 year (95% CI: 1.0, 1.1)) was lived with dementia, increasing with age to 42.1% (1.0 year, 95% CI: 0.9, 1.0) at age 95. For men, life expectancy ranged from 15.6 years (95% CI: 15.4, 15.9) at age 65 to 1.8 years (95% CI: 1.7, 1.8) at age 95, of which 3.7% (95% CI: 0.6 year, 0.5, 0.6) and 35.3% (95% CI: 0.6 year, 0.5, 0.7), respectively, was lived with dementia. Postponing dementia onset by 1–3 years resulted in 25%–57% reductions in years lived with dementia. Survival after diagnosis ranged from 6.7 years (95% CI: 5.3, 8.1) before age 70, to 2.6 years (95% CI: 2.3, 2.9) after age 90. The burden of dementia on individuals and society in terms of healthy life-years lost is large but could potentially be mitigated by preventive interventions at the population level.

dementia; life expectancy; prevention; prognosis

Abbreviations: APOE, apolipoprotein E; CI, confidence interval.

At present, 48 million people worldwide live with dementia, and due to rapidly aging populations this number is expected to rise to 131 million by 2050 (1). Because effective preventive and curative interventions are lacking, the already enormous burden on patients, their caregivers, and health-care systems will increase further, and monetary costs of dementia could reach $1 trillion as soon as 2018 (1). This foresight has led to a widespread call to render dementia a public health priority (2), yet standards of care for patients often remain below par (3, 4), and public health intervention lags behind a timely facilitation of improvement (5). To better allow health-care policy to adapt to these challenges, understanding the disease burden in terms of years lived with disability and healthy life years lost is paramount (6).

Various studies have assessed the prognosis of dementia in the general population in terms of survival after diagnosis (7–10). Although invaluable for informing clinicians, patients, and their relatives, the application of these data to public health interventions requires understanding in light of population structure, underlying dementia risks, and life expectancy without dementia. Few studies, however, provide the comprehensive life-course data required to fulfill this objective, with careful ascertainment of dementia and mortality over prolonged follow-up in the community. Consequently, life expectancy without and with dementia has been less well studied than prognosis after disease onset. The few published studies date back to the 1970s and 1980s (11–13), were modeled using only prevalence data of dementia (13, 14) or follow-up data limited to 3 years (12), or rely in part on simulations rather than empirical data for calculation of life expectancy (15). Moreover, these estimates may vary by population characteristics that influence dementia risk and survival, such as sex, educational attainment, and the apolipoprotein E (APOE) genotype, as the most important common genetic risk factor for dementia. As improvements in education are put forward in preventive strategies against dementia, and various clinical trials against Alzheimer disease

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now focus on high-risk *APOE*-ε4 carriers, insight in the effect of these characteristics in the population is important to tailor these interventions and map changes in the burden of disease.

We therefore aimed to investigate life expectancy, segregated by years lived with and without dementia and stratified by sex, APOE genotype, and education, using multistate life tables with data from the longstanding, population-based Rotterdam Study.

METHODS

Study population

This study is embedded within the Rotterdam Study, a large population-based cohort study in the Netherlands, details of which have been described previously (16). Briefly, the original study population in 1990 consisted of 7,983 participants aged ≥55 years from the Ommoord area, a suburb of Rotterdam. In 2000, the cohort was expanded with 3,011 persons who had reached age 55 years or had moved into the study area. Participants undergo extensive follow-up examinations at a dedicated research center every 4 years. The current study includes all 10,520 participants who underwent sufficient cognitive screening to determine dementia status at study entry.

Ethics, consent, and permissions

The Rotterdam Study has been approved by the medical ethics committee according to the Population Study Act Rotterdam Study, executed by the Ministry of Health, Welfare and Sports of the Netherlands. Written informed consent was obtained from all participants.

Assessment of mortality

Information on vital status was obtained through automated linkage of general practitioner files with the study database as well as a bimonthly check of municipal records (16). Follow-up for mortality until January 1, 2015, was virtually complete.

Dementia screening and surveillance

Participants were screened for dementia at baseline and subsequent home interviews with the Mini-Mental State Examination and the Geriatric Mental State Schedule organic level (17). Those with a Mini-Mental State Examination score <26 or Geriatric Mental State Schedule score >0 underwent further investigation and informant interview at the research center, including the Cambridge Examination for Mental Disorders of the Elderly (18–20). In addition, the entire cohort was continuously under surveillance for dementia through electronic linkage of the study center with medical records from general practitioners and the regional institute for outpatient mental health care. Within the Dutch health-care system, the general practitioner functions as a "gatekeeper" to specialist care, to which all health-care providers report back about any investigation, diagnosis, or treatment. With this linkage, the entire cohort is thus continuously monitored for detection of new cases or possible clinical signs of cognitive decline between center visits. Roughly 1 in 5 diagnoses of dementia in our study were adjudicated during in-person examination at the study center. Of the remainder that were captured through continuous surveillance, we had information from detailed cognitive assessment available in about 90%, whereas the other 10% were diagnosed based solely on information from the general practitioner, nursing home account, and/or occasionally hospital admission without further detailed assessment. A consensus panel headed by a consultant neurologist established the final diagnosis according to standard criteria for dementia (DSM-III-R). Follow-up for dementia until January 1, 2015, was virtually complete (97.8% of potential person-years). Within this period, participants were censored at date of dementia diagnosis, death, loss to follow-up, or January 1, 2015, whichever came first.

Other measurements

Educational attainment was ascertained at study entry by interview and classified as primary education only, further education (i.e., lower or intermediate vocational, or general secondary education), and higher education (i.e., higher vocational or university education). We assessed marital status, history of smoking (i.e., current, former, or never smoker), and use of antihypertensive or lipid-lowering medication at baseline by interview. Systolic and diastolic blood pressures were measured with a random-zero sphygmomanometer; the mean of 2 readings was used for analysis. Blood samples were obtained at baseline to determine serum total cholesterol, high-density lipoprotein cholesterol, and glucose. Type 2 diabetes was defined as the use of blood glucose-lowering medication at baseline, a fasting serum glucose level ≥7.0 mmol/L (126 mg/dL), or a nonfasting serum glucose level ≥11.1 mmol/L (200 mg/dL). Body mass index was computed from measurements of height and weight (weight (kg)/height $(m)^2$). Information on the prevalence of cancer, chronic obstructive pulmonary disease, and cardiovascular disease (i.e., stroke, myocardial infarction, heart failure, and atrial fibrillation) was obtained by interview and inspection of medical records. APOE genotype was determined by polymerase chain reaction on coded DNA samples in the original cohort, and by biallelic Taqman assays (TaqMan Gene Expression Assays; Thermo Fisher Scientific, Waltham, Massachusetts) (rs7412 and rs429358) for the expansion cohort. In 258 participants with missing APOE status from this blood sampling, genotype was determined by genetic imputation (610 K BeadChip and 660 K BeadChip; Illumina Inc., San Diego, California; imputation with Haplotype Reference Consortium (HRC) reference panel (v1.0) with Minimac3). Overall, APOE genotype was determined in 91.4% of participants and classified as *APOE*-ε4 carrier (≥1 ε4 allele) or noncarrier.

Statistical analysis

Participants were included in the analysis from the moment they reached age 65 years. Of 10,520 eligible participants, 144 (1.4%) died prior to age 65, and 28 (0.3%) were lost to follow-up for dementia prior to reaching this age, leaving 10,348 participants for the analyses. For participants with delayed entry (i.e., aged <65 years at study entry) covariate data of the closest study visit were used. Missing data for covariates were imputed using the mean of 5-fold multiple imputations (applicable to missing data for education (3.4%), APOE genotype (8.5%), marital status (3.8%), body mass index (12.1%), total cholesterol (8.4%), high-density lipoprotein cholesterol (8.8%), use

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of statins (0.6%), systolic and diastolic blood pressure (7.6%), use of blood pressure–lowering medication (0.8%), smoking (4.6%), and type 2 diabetes (12.1%)). For the stratified analyses, imputed data for education and APOE were not included.

We created multistate lifetables to calculate life expectancy, defining 3 health states: nondemented, demented, and deceased (21–24). Unidirectional transition between these states was possible from nondemented to demented, from nondemented to deceased, and from demented to deceased. We obtained the age-specific transition rates for each transition. Dementia prevalence was then determined per 10-year age groups (i.e., 65–74; 75–84; 85–94; ≥95). Next, we determined hazard ratios for incident dementia and death using Poisson regression with the Gompertz distribution (most suitable to model exponential increases with age), comparing 1) women with men, 2) individuals who had further and higher education with those who had primary education only, and 3) carriers of 1 or 2 *APOE*-ε4 alleles with noncarriers. To disentangle effects of education and APOE status from those of potential confounders, this model adjusted for age, birth year (to address potential cohort effects), educational attainment (except for the education-stratified models), APOE genotype (except for the APOE-stratified models), marital status, smoking, total cholesterol, high-density lipoprotein cholesterol, use of lipid-lowering medication, systolic and diastolic blood pressure, use of blood pressure–lowering medication, body mass index, type 2 diabetes, and prevalent cancer, chronic obstructive pulmonary disease, or cardiovascular disease. Hence, the hazard ratios used for calculation of life expectancy were adjusted for these confounders to provide valid estimates of life expectancy across the stratified population. We stratified analyses by sex and additionally determined differences in life expectancy with and without dementia across 3 levels of educational attainment and separately for *APOE*-ε4 carriers and noncarriers. We then constructed the multistate lifetables using the overall transition rates, dementia prevalence, and adjusted hazard ratios. Sex-specific lifetables started at age 65 years and closed at age 100 years. In addition, we calculated the percentage of remaining life years lived with dementia by dividing years lived with dementia by the life expectancy at each year of life. We used Monte Carlo simulation (parametric bootstrapping) with 10,000 runs to calculate the confidence intervals of (differences in) life-expectancy estimates with @RISK software (Palisade Corporation, New York, New York). We repeated the sex-stratified analyses for hypothetical scenarios in which the onset of dementia was delayed by 1, 2, and 3 years, respectively, while keeping mortality constant, and we determined the reduction in years lived with dementia compared with the empirical data.

Finally, proceeding to prognosis of individual patients with dementia, we determined survival after dementia diagnosis in all individuals who were diagnosed with dementia during follow-up until January 1, 2013, using the Kaplan-Meier estimator. For these individuals, additional mortality data were ascertained until June 2017, and 1,397/1,526 (91.5%) participants with dementia had died within this follow-up period. We calculated the percentage of expected life years lost due to diagnosis of dementia by dividing the expected survival after diagnosis by the expected life expectancy in the overall population at ages 65–69 years and 85–89 years.

Analyses were performed using IBM SPSS Statistics, version 21.0 (IBM Corp, Armonk, New York); Microsoft Excel 2010 (Microsoft Corp, Redmond, Washington); and Stata, version 14.1 (StataCorp LLC, College Station, Texas).

RESULTS

Table 1 shows the baseline characteristics of the study population. The median age at baseline was 67.3 years (range, 65–106 years), and 59.6% of the participants were women. Baseline characteristics according to educational attainment and APOE genotype are presented in Web Table 1.

Risk of dementia and death

Of all 10,348 participants, 521 (5.0%) were diagnosed with dementia at baseline. During 120,673 person-years of follow-up (mean = 11.7 years), 1,666 (17.0%) participants developed dementia, and 6,150 (59.4%) died. Women were at higher risk of dementia than men (hazard ratio = 1.19, 95% confidence interval (CI): 1.05, 1.36), while they were at lower risk of death (without dementia, hazard ratio = 0.68, 95% CI: 0.64, 0.73; with dementia, hazard ratio = 0.76, 95% CI: 0.66, 0.87). Table 2 shows the sex-stratified associations of educational attainment and APOE genotype with risk of dementia and mortality. Higher educational attainment was associated with a lower risk of dementia and death among nondemented individuals, and relative risk estimates for dementia thereby exceeded those of mortality (Table 2). The presence of 1 or 2 *APOE*-ε4 alleles was associated with an increased risk of dementia as well as a more modest increase in risk of death in individuals without but not with dementia (Table 2).

Life expectancy and years lived without and with dementia

Life expectancy of women ranged from 18.0 years (95% CI: 17.8, 18.2) at age 65 to 2.3 years (95% CI: 2.2, 2.3) at age 95. Of total life expectancy at age 65, 5.7%, which corresponds to 1.0 year (95% CI: 1.0, 1.1), was lived with dementia, increasing with age to 42.1% (1.0 year, 95% CI: 0.9, 1.0) of life expectancy at age 95 (Figure 1). For men, overall life expectancy ranged from 15.6 years (95% CI: 15.4, 15.9) at age 65 to 1.8 years (95% CI: 1.7, 1.8) at age 95, of which 3.7% (0.6 year, 95% CI: 0.5, 0.6) and 35.3% (0.6 year, 95% CI: 0.5, 0.7), respectively, were lived with dementia (Figure 1). Absolute numbers are presented in Web Table 2.

In 3 different scenarios for preventive interventions against dementia, delaying the onset of dementia in the population by 1, 2, or 3 years resulted in reductions in the number of observed incident cases from 1,666 to 1,417, 1,154, and 886, respectively. The number of life years lived with dementia thereby decreased by 25% in the 1-year scenario, 46% in the 2-year scenario, and 57% in the 3-year scenario, broadly similar for women and men (Figure 2).

Effect of educational attainment and APOE genotype

Overall life expectancy differed across levels of educational attainment (Figure 3). Highly educated 65-year-olds were

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Table 1. Population Characteristics of the 10,348 Participants, Rotterdam Study, the Netherlands, 1990–2015

Characteristic	Mean (SD)	No.	%
Age at study entry, years[a]		67.3 (65–106)	
Age at dementia diagnosis, years	83.4 (6.6)		
Women		6,172	59.6
Educational attainment			
Primary education		2,118	21.2
Further education		6,814	68.1
Higher education		1,068	10.7
APOE genotype			
ε4 noncarriers		6,819	72.0
ε4 carriers		2,652	28.0
Marital status			
Living with partner		6,487	65.2
Unmarried, widower, or living apart		3,468	34.8
Smoking status			
Never smoker		3,563	36.1
Former smoker		4,381	44.4
Current smoker		1,925	19.5
Systolic blood pressure, mm Hg	143 (22)		
Diastolic blood pressure, mm Hg	76 (12)		
Antihypertensive medication		3,670	35.7
Body mass index[b]	26.8 (4.0)		
Type 2 diabetes		1,002	11.0
Serum total cholesterol, mmol/L	6.3 (1.2)		
Serum high-density lipoprotein cholesterol, mmol/L	1.4 (0.4)		
Lipid-lowering medication		862	8.4
History of cardiovascular disease		1,564	15.1
History of cancer		410	4.0
History of chronic obstructive pulmonary disease		515	5.0

Abbreviation: APOE, apolipoprotein E.
[a] Values are expressed as median (interquartile range).
[b] Body mass index calculated as weight (kg)/height $(m)^2$.

expected to live on average a year and a half longer than those of similar age with primary education only (for women, 1.6 years, 95% CI: 0.6, 2.5; and for men, 1.2 years, 95% CI: 0.4, 2.1 years). Due to reductions in both mortality and dementia risk with higher education, educational attainment did not materially affect the number of years lived with dementia (for highly educated women, −0.3 years (95% CI: −0.7;0.1), and for men, 0.0 years (95% CI: −0.3;0.3)). However, because individuals with only primary education lived shorter lives on average, the share of remaining life expectancy lived with dementia was substantially greater than among those with further or higher education, in particular for women (Figure 3). For ease of comparison, absolute numbers are presented in Web Table 3.

APOE-ε4 carriership was associated with, on average, 2.4 healthy life years (95% CI: 2.1, 2.8) lost in women and 1.7 years (95% CI: 1.2, 2.1) lost in men. This effect was due to a reduction in overall life expectancy at age 65 of 1.3 years (95% CI: 1.0, 1.7) in women and 1.1 years (95% CI: 0.7, 1.6) in men, along with an increased number of years lived with dementia (at age 65 in women, 1.1 years, 95% CI: 0.9, 1.3; and for men, 0.5 years, 95% CI: 0.4, 0.7). This resulted in a percentage share of remaining life expectancy lived with dementia of 71.3% at age 95 in female carriers compared with 38.8% at the same age in noncarriers (Figure 4). In men, these percentages were slightly lower at 64.4% and 31.9%, respectively (Figure 4). Absolute numbers are shown in Web Table 4.

Prognosis after dementia diagnosis

Median survival after diagnosis of dementia was 3.7 years (95% CI: 3.5, 3.9) but varied with sex and, in particular, with age at diagnosis (Table 3). In women, median survival ranged from 7.7 years when diagnosed before age 70 to 2.6 years

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Table 2. Associations of Educational Attainment and Apolipoprotein E ε4 Genotype With Risk of Dementia and Death According to Sex, Rotterdam Study, the Netherlands, 1990–2015

Variable	Risk of Dementia				Mortality Among Nondemented				Mortality Among Demented			
	Women		Men		Women		Men		Women		Men	
	HR[a]	95% CI	HR[a]	95% CI	HR[a]	95% CI	HR[a]	95% CI	HR[a]	95% CI	HR[a]	95% CI
Educational attainment												
Primary	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Further	0.86	0.76, 0.99	0.82	0.65, 1.04	0.94	0.87, 1.02	0.95	0.85, 1.06	0.97	0.86, 1.11	1.13	0.91, 1.40
Higher	0.67	0.48, 0.94	0.78	0.56, 1.07	0.79	0.65, 0.95	0.85	0.73, 0.99	1.03	0.72, 1.47	0.85	0.62, 1.16
APOE genotype												
ε4 noncarriers	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
ε4 carriers	2.25	1.99, 2.55	2.20	1.84, 2.64	1.15	1.05, 1.24	1.12	1.02, 1.23	0.98	0.87, 1.11	1.00	0.84, 1.21

Abbreviations: APOE, apolipoprotein E; CI, confidence interval; HR, hazard ratio.

[a] Model adjusted for age at study entry, year of birth, educational attainment (if applicable), APOE genotype (if applicable), marital status, body mass index, total cholesterol, high-density lipoprotein cholesterol, use of lipid-lowering medication, systolic and diastolic blood pressure, use of blood pressure–lowering medication, smoking, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, and cancer.

with diagnosis after the age of 90. Among men, these numbers were 5.3 years and 2.4 years, respectively. A diagnosis of dementia was thus associated with a reduction in median life expectancy of close to 60% (53% for women and 63% for men) when diagnosed between 65 and 69 years and of about 20% (24% for women and 21% for men) when diagnosed at ages 85–89 years. Prognosis was not affected by educational attainment or *APOE*-ε4 carrier status (data not shown).

DISCUSSION

In this large population-based study we found that, of the overall life expectancy at age 65 years, on average 5% is spent with dementia, increasing to about 40% of remaining life expectancy at age 95, varying by sex, educational attainment, and APOE genotype. This burden of disease in the population is highly amenable to preventive interventions that could postpone dementia onset by 1–3 years.

The added value of this study is the combination of the observed role of sex, educational attainment, and APOE genotype in dementia incidence and mortality, evaluated in a well-defined population observed for a substantial period of time and translated into population measures important to clinicians, patients, and policy makers in tackling the growing dementia epidemic. We found overall life expectancy and years lived with dementia similar to previous reports from France and Australia that were modeled using prevalence data (13, 14). Results from other studies have been more diverse. A US study of the Kaiser Permanente Medical Care Program in the 1970s and 1980s found life expectancies with dementia at age 65 years similar to ours, but at higher ages overall life expectancy was longer and there was less time lived with dementia (11), possibly owing to a healthier population or the lower sensitivity of registry-based dementia diagnoses (24). Differences in outcome assessment (e.g., intervals between assessment) may further contribute to variation in estimates, in particular with very high incidence rates in the oldest old. Another US study among community-dwelling individuals with in-person screening for dementia, reported higher, partly modeled, estimated years lived with dementia, along with longer overall life expectancy (15). Both have been reported to be lower in Japan (12). Differences in genetic make-up between populations and, for example, access to education may explain some of the discrepancies. Calendar time at which the studies were performed also differed, along with methodological variation in use of prevalent versus incident data, simulations rather than direct observation, and a generally limited incorporation of comorbidity into the life-year estimates (11–15). What emerges from these studies jointly is a relatively low, on average, absolute number of remaining years lived with dementia, which nevertheless accounts for large shares of healthy life years lost for individual elderly patients, accompanied by an overwhelming burden on caregivers (25), as well as health-care expenditures that are substantially larger than those for other diseases (26).

Importantly, a large share of the years lived with dementia in the population is amenable to preventive interventions at the population level. We show that interventions that succeed in postponing dementia onset by 1–3 years could result in 24%–60%

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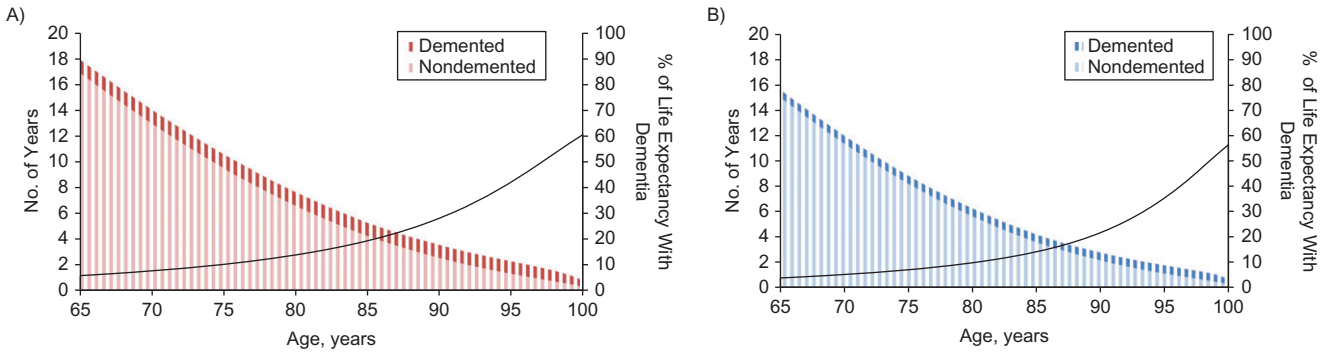

Figure 1. Total life expectancy with and without dementia, Rotterdam Study, the Netherlands, 1990–2015. The life expectancy per year from the age of 65 years, for women (A) and men (B). Bars represent the total number of years lived (left *y*-axis), segregated by years without dementia (light color) and with dementia (dark color). The solid line reflects the percentage of remaining life-years lived with dementia (right *y*-axis).

reductions in life years spent with dementia, which is in line with previously modeled reductions in the prevalence of Alzheimer disease in the United States (27). These percentages may be somewhat attenuated when interventions simultaneously benefit overall life expectancy, but they nevertheless illustrate that, at a population level, relatively minor gains in dementia prevention might yield large benefits in public health, supporting the view that primary prevention has the largest effect on reduction of dementia occurrence and disability (6). Moreover, given the estimated yearly care costs for dementia of nearly a trillion US dollars (28), equating to around $50,000 per patient per year in the United States (29), such interventions would likely turn out to be cost-effective (30). Given recently reported increases in life years spent with disability, much of which is likely attributable to cognitive impairment (31), such preventive interventions promoting healthy aging are paramount.

Higher educational attainment in our study related to lower shares of total life expectancy lived with dementia, in line with findings for individuals with at least a college education in the United States (15). Although this may be attributable in part to, for instance, lifestyle differences, it fits well with the concept of cognitive reserve, reflecting the idea that higher educational attainment is able to mitigate the impact of brain pathology on clinical symptoms (32). However, this would also imply increased mortality after diagnosis of dementia in highly educated individuals, for which we, similar to a systematic review in 2009 (33), found no evidence in the present study. In any case, universal access to education and resolving associated lifestyle differences might warrant consideration in public health debate about dementia prevention. We additionally determined the effect of the APOE genotype on life expectancy with and without disease, which had not, to our knowledge, yet been studied. Our findings indicate an especially large burden of disease in ε4 carriers, both in terms of the absolute number of years and the share of total life-years lived with dementia. Although this may support the focused search for Alzheimer therapies in this group of individuals (34), it should not delay preventive or curative efforts that are generalizable and thus beneficial to the larger community.

Extensive data are available on prognosis after diagnosis of dementia, mostly from unselected populations (35). Results, however, are rather heterogeneous (7, 10, 35), with reported

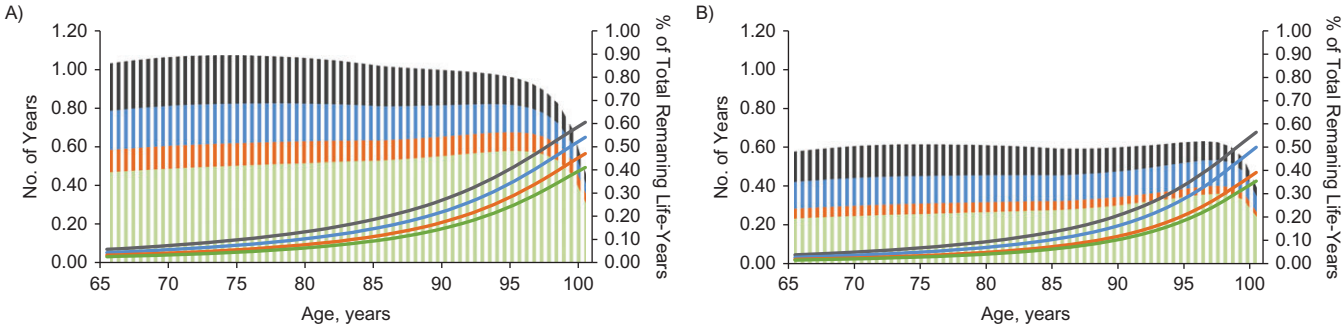

Figure 2. The effect of preventive intervention against dementia, which would delay its onset by 1, 2, and 3 years respectively, on life-years lived with dementia in the population, using data from the Rotterdam Study, the Netherlands, 1990–2015. Depicted are the expected life-years lived with dementia, in absolute numbers and as a share of the total remaining life expectancy, from age 65 years to 100 years for women (A) and men (B). Bars represent the total number of years lived with dementia (left *y*-axis), comparing the factual data (corresponding to Figure 1) with hypothetical scenarios in which the onset of dementia is delayed by 1, 2, and 3 years, respectively. Stacks are cumulative (i.e., the factual scenario is the sum of the black, blue, orange, and green stacks). For the same scenarios, the solid lines reflect the percentage of total remaining life-years that is expected to be lived with dementia (right *y*-axis).

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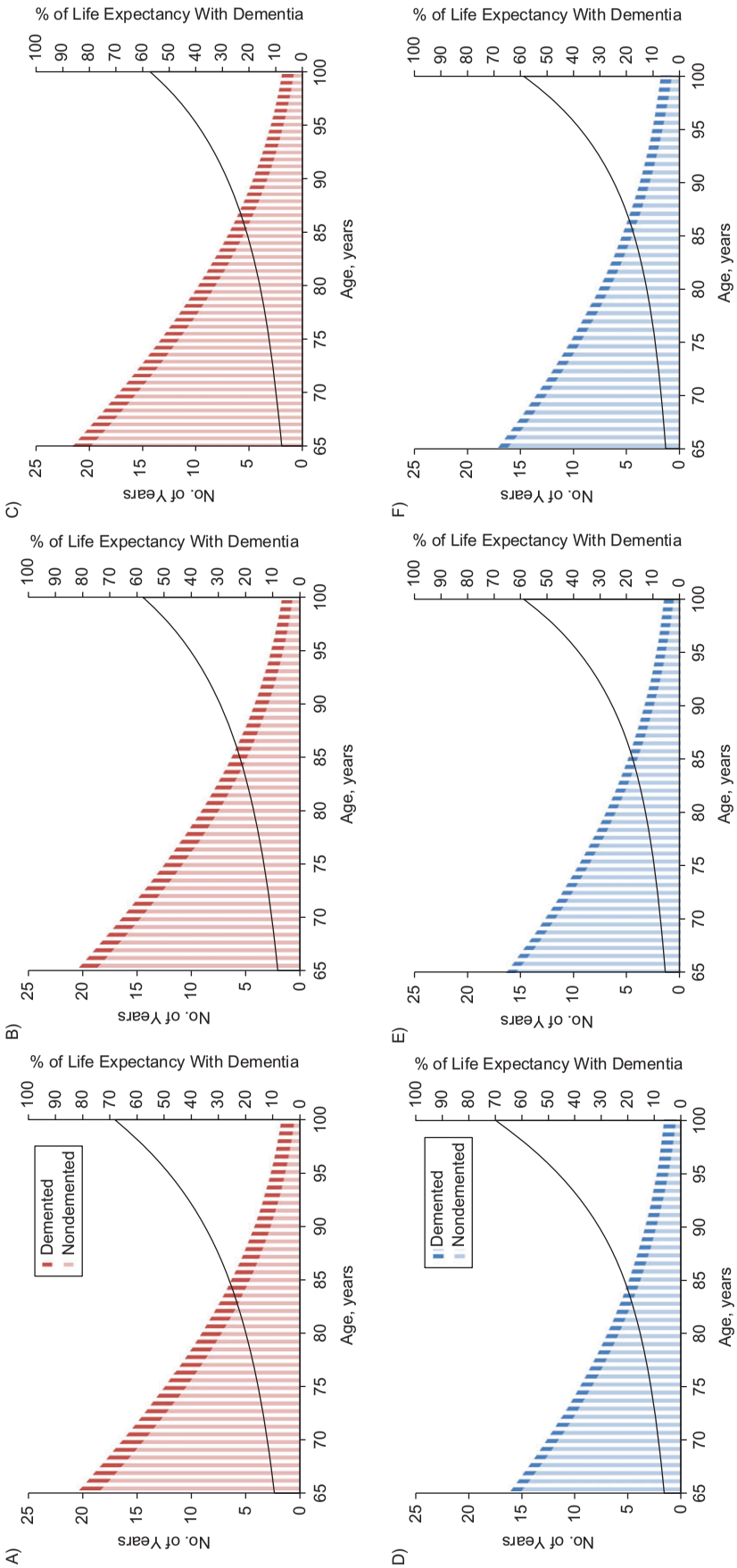

Figure 3. Life expectancy with and without dementia, stratified by educational attainment, Rotterdam Study, the Netherlands, 1990–2015. The life expectancy per year from the age of 65 years, for women (A–C) and men (D–F), stratified from left to right by educational attainment: A and D) primary school only; B and E) further education; C and F) higher education). Bars represent the total number of years lived (left *y*-axis), segregated by years without dementia (light color) and with dementia (dark color). The solid line reflects the percentage of remaining life-years lived with dementia (right *y*-axis).

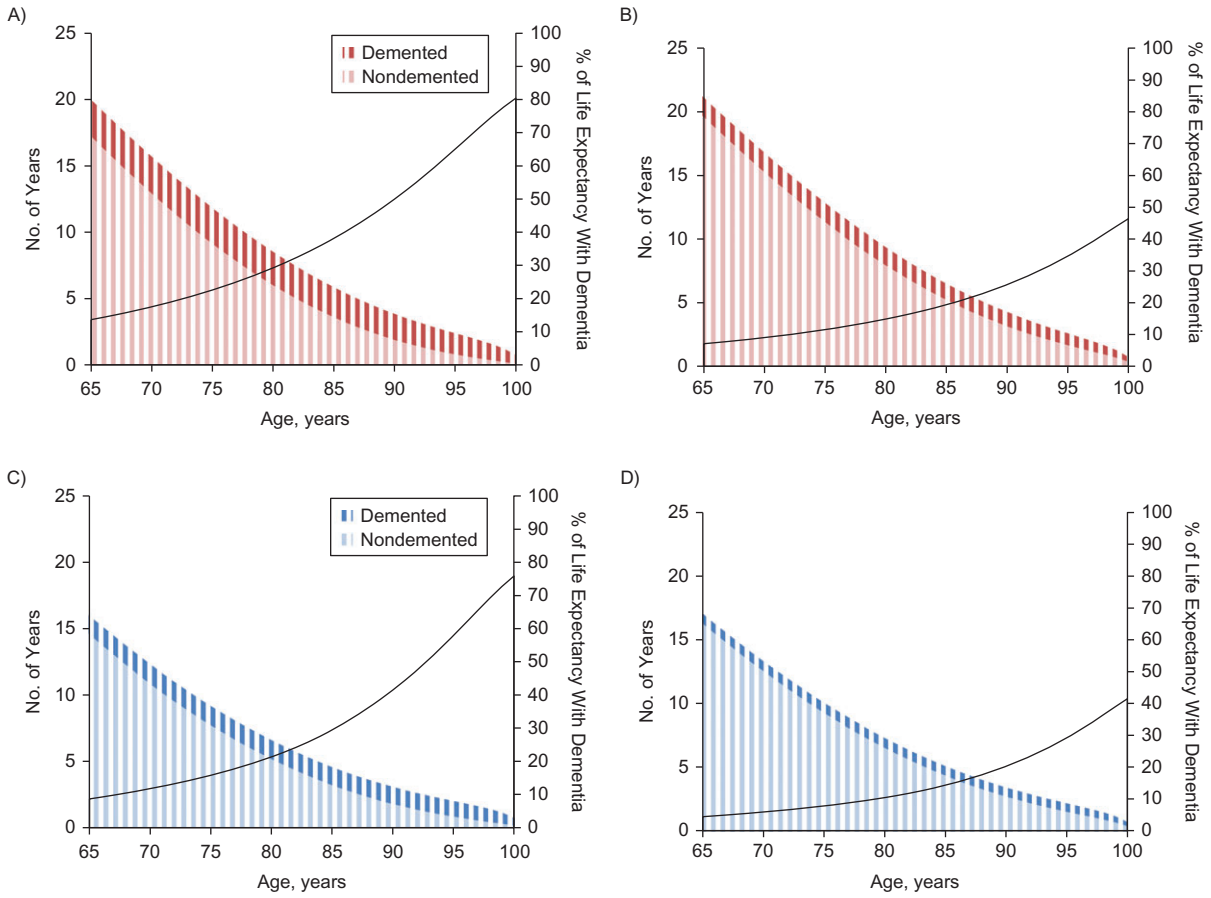

Figure 4. Life expectancy with and without dementia, stratified by APOE genotype, Rotterdam Study, the Netherlands, 1990–2015. The life expectancy per year from age 65 years, for female ε4 carriers (A) and noncarriers (B) and male ε4 carriers (C) and noncarriers (D). Bars represent the total number of years lived (left *y*-axis), segregated by years without dementia (light color) and with dementia (dark color). The solid line reflects the percentage of remaining life-years lived with dementia (right *y*-axis).

survival times ranging considerably from 1.8 to 7.2 years. This heterogeneity is largely attributable to age and sex composition of the study populations and further caused by (vascular) comorbidity at time of diagnosis (36), as well as methodological differences in dementia ascertainment, inclusion of prevalent versus incident cases, severity at time of diagnosis, follow-up time, and general life expectancy in the source population. Following postulated recommendations to overcome several

Table 3. Prognosis After Diagnosis of Dementia, Stratified by Age and Sex, Rotterdam Study, the Netherlands, 1990–2015

Age	Men				Women			
	No. Deceased	No. With Dementia	Median Survival, years	95% CI	No. Deceased	No. With Dementia	Median Survival, years	95% CI
Age at diagnosis, years								
65–70	17	19	5.3	2.6, 7.9	22	24	7.7	6.1, 9.3
70–74	42	45	4.2	2.2, 6.2	64	78	5.4	3.3, 7.5
75–79	115	126	3.5	2.9, 4.0	158	182	5.5	4.5, 6.4
80–84	129	136	3.3	2.6, 3.9	244	277	4.1	3.5, 4.7
85–89	100	103	2.8	2.4, 3.3	291	309	3.4	3.1, 3.7
≥90	34	38	2.4	1.5, 3.3	181	189	2.6	2.3, 3.0
Overall	437	467	3.3	3.0, 3.5	960	1,059	3.9	3.7, 4.2

Abbreviation: CI, confidence interval.

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methodological limitations (35), we affirm that prognosis needs to be seen in particular in light of age at diagnosis, and likely also sex, as a reflection of underlying survival differences in the population.

Strengths of the current study including its large, structured, population-based design with long-term follow-up and meticulous case-finding strategies for dementia, which limited attrition to 2.2%. Certain potential limitations should also be considered. First, the embeddedness of the Rotterdam Study in the Dutch health-care system, with uniform access to care, and the predominantly white ethnicity of the study population may limit generalizability. Standards of care and overall life expectancy in the Netherlands rank average when compared with other industrialized countries (37), making our findings applicable to most of present-day dementia-related public health policy, notwithstanding the need for additional data from ethnically diverse populations and low- to middle-income countries. Second, the study population consisted of individuals recruited during 2 consecutive recruitment waves of the Rotterdam Study, 10 years apart, and although we adjusted for year of birth in the analyses, certain cohort effects may persist. In particular, several studies have suggested a decline in the age-specific incidence of dementia over the past decades, potentially leading to an overestimation of the remaining lifetime spent with dementia. Third, the effects of education and APOE genotype might vary with age, which was not accounted for in our analysis due to sample size restrictions. Fourth, we did not have information about institutionalization of participants in our study, which could provide additional perspective for public health policy, as well as for informal care provision and informing physicians and their patients.

In conclusion, the estimates presented here provide reliable and current information to facilitate public health policies on dementia care in the face of the growing burden of disease. Moreover, they highlight the potential of preventive strategies at the population level to limit this burden in years to come.

ACKNOWLEDGMENTS

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This work was supported by the Erasmus Medical Center and Erasmus University Rotterdam; the Netherlands Organization for Scientific Research; The Netherlands Organization for Health Research and Development,; the Research Institute for Diseases in the Elderly,; the Netherlands Genomics Initiative; the Ministry of Education, Culture and Science; the Ministry of Health, Welfare and Sports; the European Commission (DG XII); and the Municipality of Rotterdam. Further support was obtained from the Netherlands Consortium for Healthy Ageing and the Dutch Heart Foundation (grant 2012T008). This research was further supported by funding from the European Union Seventh Framework Program (FP7/2007e2013, grant 601055), VPH-Dare@IT (FP7-ICT-2011-9e601055); and funding from the European Union's Horizon 2020 research and innovation program (grant 667375 (Co-STREAM) and 678543 (European Research Council-funded project: ORACLE)).

We thank the study participants, general practitioners, and pharmacists of the Ommoord district for their dedication and commitment to the Rotterdam Study. We thank all staff at the Rotterdam Study research center, who have facilitated assessment of participants throughout the years, and Frank J. A. van Rooij as data manager. We also thank acknowledge Arjola Bano for kind support in part of the analyses.

Conflict of interest: none declared.

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