

Dementia in western Europe: epidemiological evidence and implications for policy making



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Dementia is receiving increasing attention from governments and politicians. Epidemiological research based on western European populations done 20 years ago provided key initial evidence for dementia policy making, but these estimates are now out of date because of changes in life expectancy, living conditions, and health profiles. To assess whether dementia occurrence has changed during the past 20–30 years, investigators of five different studies done in western Europe (Sweden [Stockholm and Gothenburg], the Netherlands [Rotterdam], the UK [England], and Spain [Zaragoza]) have compared dementia occurrence using consistent research methods between two timepoints in well-defined geographical areas. Findings from four of the five studies showed non-significant changes in overall dementia occurrence. The only significant reduction in overall prevalence was found in the study done in the UK, powered and designed explicitly from its outset to detect change across generations (decrease in prevalence of 22%; $p=0.003$). Findings from the study done in Zaragoza (Spain) showed a significant reduction in dementia prevalence in men (43%; $p=0.0002$). The studies estimating incidence done in Stockholm and Rotterdam reported non-significant reductions. Such reductions could be the outcomes from earlier population-level investments such as improved education and living conditions, and better prevention and treatment of vascular and chronic conditions. This evidence suggests that attention to optimum health early in life might benefit cognitive health late in life. Policy planning and future research should be balanced across primary (policies reducing risk and increasing cognitive reserve), secondary (early detection and screening), and tertiary (once dementia is present) prevention. Each has their place, but upstream primary prevention has the largest effect on reduction of later dementia occurrence and disability.

Introduction

Dementia has only recently received focused attention worldwide similar to other major public health priorities, such as HIV/AIDS.^{1,2} Societies comprise an increasing proportion of elderly people who, because of age alone, are at an increasing risk of dementia.³ Governments and politicians have become aware of the effect of dementia on individuals, families, and societies, and are worried about the likely increase in the number of people with dementia.² Although policies are usually assumed to be based on robust scientific evidence, epidemiological studies that measure who has, who will get, and who escapes dementia in populations, and whether these change over time, are surprisingly rare.⁴ Estimations can be based on health service use or death certificates, as for many other disorders such as cardiovascular diseases and cancer, but this approach is not helpful for dementia because these sources register a changing proportion of people who meet dementia diagnostic criteria in the community.⁵ Population studies are often based on single sites within countries, rarely whole geographical regions.⁶ Estimation of occurrence from population-based epidemiological studies is crucial for planning and costing of health services and economic burdens, and therefore robust, relevant, and up-to-date estimates are needed to support the creation of useful dementia policies. These policies need to be sensitive to many individual and contextual factors, such as gender, culture, and socioeconomic, meaning that policies should differ between countries and with time.

Despite the trauma of two world wars, high-income countries in Europe have relatively stable social environments, wealthy living conditions, and advanced care

systems, meaning that life expectancy is increasing, populations are ageing, and concern about dementia is increasing. The first epidemiological investigations of dementia in western Europe were started in the 1980s and had a discernible effect on policy 10 years later.⁷ These studies are still affecting policy development nowadays and continue to provide an estimate of the size and distribution of dementia within European countries and across Europe, and are used at both national and local levels (eg, the UK's NHS primary care targets^{8,9}). Projections of the findings from these old studies support the idea of a continuing so-called dementia epidemic.

Although robust information about dementia was provided from these previous studies, policy makers need to now take into account societal changes and their potential effect on population health. Each generation of elderly people will have had different positive and negative effects on their health during their lives.¹⁰ Established risk (eg, vascular diseases) and protective (eg, education) factors for dementia have changed hugely during successive generations.^{11–13} Because of

Lancet Neurol 2015

Published Online
August 21, 2015
[http://dx.doi.org/10.1016/S1474-4422\(15\)00092-7](http://dx.doi.org/10.1016/S1474-4422(15)00092-7)

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Panel 1: Aims of this Policy View

- To synthesise epidemiological evidence from population-based studies that have compared dementia occurrence over time in Europe using the same methods.
- To suggest implications for dementia policy based on evidence from epidemiological research.
- To provide recommendations to policy makers for assessment of scientific evidence for dementia epidemiology.

these changes in life expectancy and risk profiles, we would expect to see emerging variation in occurrence of dementia over time and between different countries.

Policy making needs to incorporate up-to-date information based on evidence from up-to-date epidemiological studies in western Europe, which will take into account any such changes in dementia occurrence in representative populations. In addition to estimating the changing epidemiology of dementia and contributing to the body of knowledge on the changing nature and definition of this syndrome, these findings have

implications for health policy and inform the debate on the direction of research funding. Policy makers from outside of western European countries could use evidence from these countries as a reference for their own dementia policy planning.

In this Policy View, we present evidence from the only European studies that have analysed changes in dementia occurrence. The aims of this Policy View are listed in panel 1. Explanations of key epidemiological terms and concepts are provided in panel 2.

Panel 2: Epidemiological terms and measures

Cohort

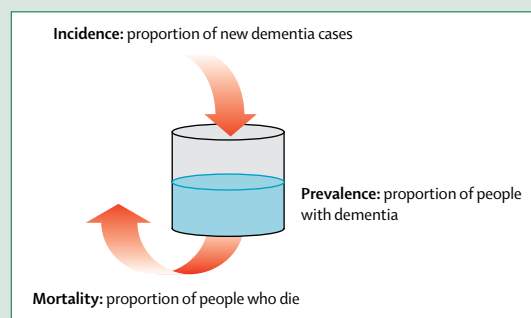
A cohort is a defined group of people.¹⁴ This group is measured for risk and protective factors at baseline and then followed up by researchers, who regularly collect health data of the cohort over time. A population-based cohort is a representative sample of the entire target population.

Prevalence, incidence, and mortality

If we assume that occurrence of new cases (incidence) is comparable to a water stream into a container, and the stream leaking out represents those who die (mortality), the water level would be the prevalence. The flow rate of the water streams (incidence and mortality) therefore affects the water level (prevalence) at different timepoints.

Present policies are based on findings from prevalence studies (water level) because incidence (the flow rate) of non-communicable diseases is quite difficult to measure except through cohort studies, which might be or might not be population-based (ie, in a representative sample). Incidence and mortality are difficult to measure because estimations need to be based on the same study population over time. Not all the population-based cohort studies have sufficient resources and funding to complete the follow-up surveys.

If diagnostic criteria for dementia are made more restrictive, the water will seem to flow into the container at a slower rate and prevalence will seem to decrease, not because dementia is actually less common, but because its formal criteria have changed. If diagnostic criteria are made more inclusive, the converse will occur, with prevalence seeming to increase.



How to assess and interpret epidemiological evidence

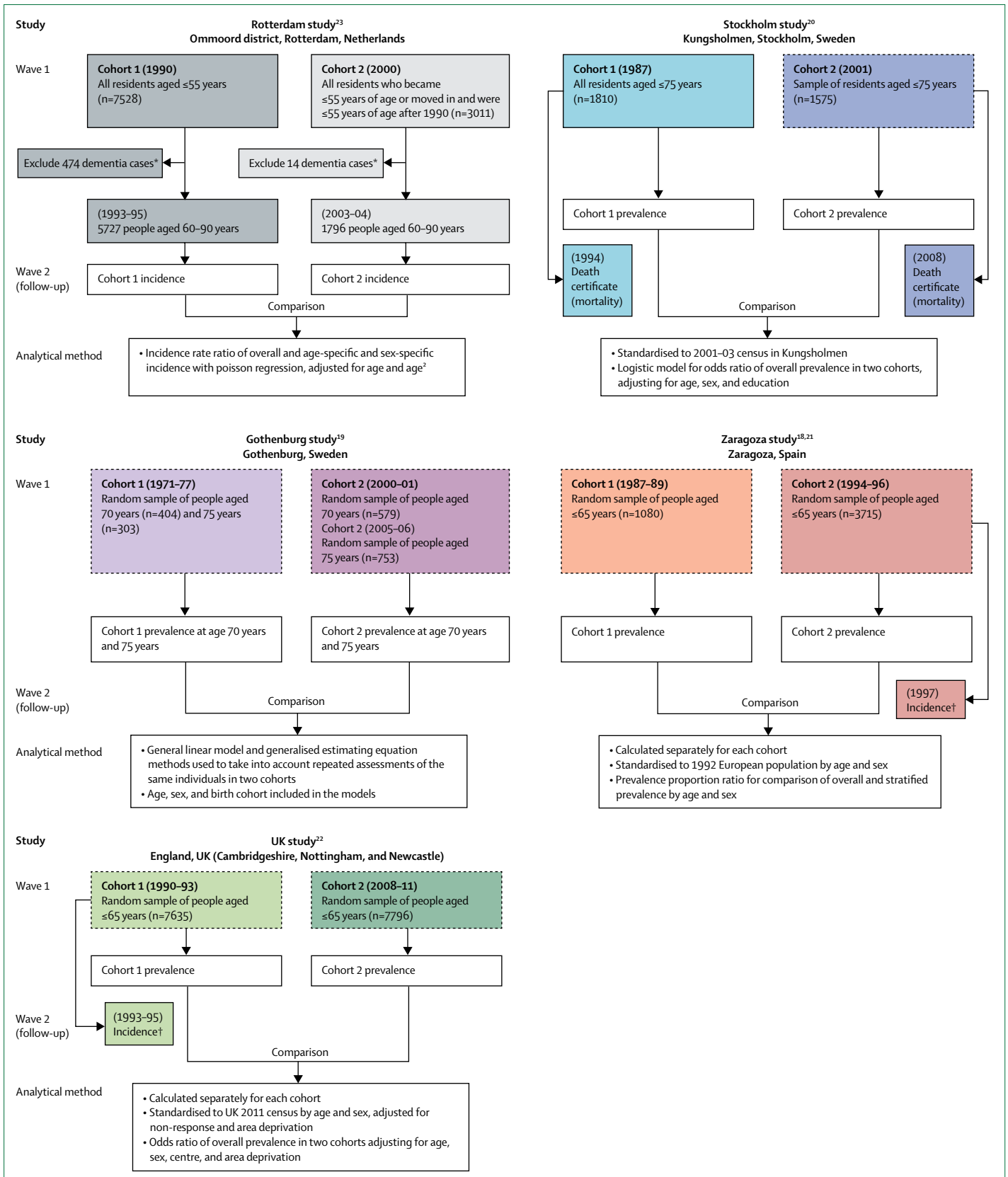
Although epidemiologists have been working for decades with population-based cohorts to establish the extent of dementia in populations, such research is, as all research is, only strictly relevant to a certain population over a certain time period. Policy makers need to interpret the evidence for dementia occurrence, bearing in mind possible variations with time and place, and generalisability to their own society.

Interpretation of scientific findings can vary depending on different perspectives and contexts. An illustration of the difficulty inherent in interpretation of new findings in relation to old findings, or comparisons across geography, is the comparative analysis of two systematic reviews of Chinese prevalence studies of dementia.^{15,16} In one systematic review,¹⁵ the conclusion is that dementia prevalence is increasing in China. In the other, the increase in prevalence is attenuated compared with unadjusted estimates and does not reach significance when variation in methods is taken into account, showing that introduction of new and more inclusive diagnostic criteria seems to have been instrumental in the noted increase in dementia case identification. Such results provide a cautionary note about interpretation of potential changes in dementia occurrence. Prevalence reported from any studies that are based on present diagnostic practices and contact with health services are likely to be affected by increased attention to and awareness of dementia, and shifting diagnostic boundaries. This increase in awareness and diagnosis will counter the actual effect of reduction in occurrence through increased detection of so-called mild cases that were previously not recognised as meeting dementia criteria.

Inconsistent methods, enormous political interest, and stakeholder and public awareness could influence interpretation of scientific evidence for dementia. Catastrophic estimates of dementia in future ageing societies serve present political and charity campaigns, and encourage investment into pharmaceutical and health-care industries,

Figure 1: Designs of the five western European studies

Dashed boxes show random samples of people in the study areas. *Because the Rotterdam study compared changes in incidence over time, people with dementia at baseline were removed from wave 1. †Incidence estimates available, but changes over time have not yet been published.



maintained by sustained attention of social and general media. Scientific evidence needs to match this excitement to continue to secure research funding and resources. Evidence-based policy does not only require consultation of the evidence, but also assessment of the relevance of the evidence, taking the quality of the research and potential effects of social context into account.

In addition to considering the source of the evidence, policy makers have to assess the quality of the evidence and its relevance to diverse settings. Whether the estimate from western Europe is generalisable to different countries and time periods needs to be ascertained. Until the past decade, very little evidence existed of systematic variation in prevalence or incidence of dementia between high-income countries, where life expectancy is high. By contrast, substantial variation is reported in low-income and middle-income countries, where life expectancy is

still lower than the median age of dementia incidence in high-income countries (about 83 years of age).¹⁷ For example, high estimated dementia prevalence has been reported in Latin America,⁶ a population that also has a high vascular risk profile. Differences in economic development, population structure, and societal and cultural contexts could limit application of scientific evidence, which is mainly from high-income countries. Policy makers need to assess the relevance of the scientific evidence to different contexts in different countries over different time periods.

The relevance of the study design

Five western European studies have reported a valid comparison of prevalence^{18–22} and incidence²³ between two comparable cohorts. These studies were carried out in Sweden (the Stockholm study [first cohort: the Kungsholmen Project; second cohort: Swedish National Study on Aging and Care in Kungsholmen]²⁰ and the Gothenburg study [the H70 study]),¹⁹ the Netherlands (the Rotterdam study),²³ the UK (the UK study [the Cognitive Function and Ageing Studies]),²² and Spain (the Zaragoza study [the Zaragoza Dementia Depression Project]).^{18,21} In eastern and central Europe, this kind of comparison has not been possible because no population-based cohort studies have been done.⁴ The age of the study populations was 70 years and older in the Swedish studies^{19,20} and 55 years²³ or 65 years^{18,21,22} and older in the other studies. The first cohorts were studied between 1976 and 1989, with the second cohorts studied between 1994 and 2008. The time separation of the comparisons ranged from 7 years (the Zaragoza study)^{18,21} to 30 years (the Gothenburg study).¹⁹

A detailed analysis of study design and population sampling is needed to interpret results, particularly if they are to be applied nationally and compared internationally. Figure 1 is a schematic representation of the designs and population sampling of these five studies, and the methods used in these studies are summarised in the appendix. Three studies^{18,19,21,22} were direct comparisons of two cohorts, with new sampling of the population independent of the previous cohort. The Rotterdam cohort²³ did not do new independent sampling, but incomers and the so-called newly old were periodically included.²³ The study based in Stockholm was originally a dedicated local study, but the most recent study was based on a local subsample from a national study.²⁰ Response rates decreased in three of the studies,^{18,19,21,22} with varying ability to assess the effect of such changes on the findings. The other two studies^{20,23} had stable response rates. Although analytical methods were different across studies, each attempted to keep the diagnostic methods as stable as possible between the two timepoints, recognising that changes over time in approaches to diagnosis are likely to affect estimated prevalence and incidence, but only one²² used a fixed algorithm method (a standardised psychiatric interview, the Geriatric Mental State Examination, and its diagnostic algorithm).

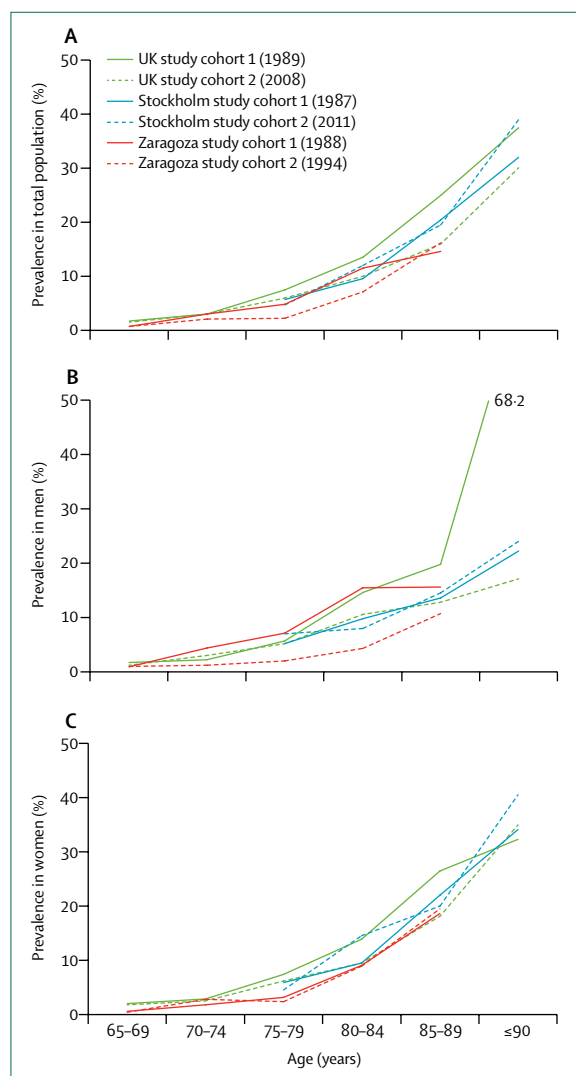


Figure 2: Change of dementia prevalence with age in (A) the whole study population, (B) men, and (C) women

See Online for appendix

Dementia prevalence changes over time

Findings from the first cohorts in each study showed similar prevalence estimates of dementia across different countries, with prevalence consistently doubling every 5 years.⁷ The two studies of populations of people aged 65 years and older (in the UK²² and Zaragoza^{18,21}) with independent sampling over time reported decreased dementia prevalence between cohorts—in Zaragoza,^{18,21} the reduction in men reached significance, although the reduction in overall prevalence did not and, in the UK,²² overall prevalence significantly decreased (appendix). Stable prevalence of dementia over time was reported in both Swedish studies.^{19,20} Changes in age-specific and gender-specific estimates of prevalence for the three studies that directly compared cohorts^{18,21,22} are shown in figure 2. The Gothenburg study¹⁹ is not included because its analyses only focused on populations of particular ages and the Rotterdam study²³ is not included because it investigated changes in incidence. The estimates of high prevalence in men in the oldest age group of the UK study 1 cohort were obtained because of the small sample size, resulting in the unstable high estimate with a wide confidence interval. Figure 3 shows prevalence change over time for both sexes in four of the five studies.^{19–22} The findings shown in figure 3 suggest decreases in prevalence in men and stability in women in the studies from mainland Europe.^{18–21} Findings from the UK-based study²² showed decreased prevalence in both sexes.

The Rotterdam study²³ is the only study that reports incidence data. A reduction in incidence during a 10 year period, although not significant, was detected. The Stockholm study²⁰ inferred changes in incidence during a 20 year period by integrating prevalence and mortality, also suggesting a reduction. The Stockholm study²⁰ and the Rotterdam study²³ examined mortality, and both reported a decrease for the whole population. Only the Stockholm study²⁰ compared changes in mortality of people with dementia, and findings showed a decrease between 1987 and 2001. Detailed findings are provided in the appendix.

Thus, despite differences in how the studies were done, no evidence from any of these studies suggests a significant increase in prevalence over time when diagnostic methods and age structure are stabilised. Findings from four of the five studies showed non-significant changes in overall dementia occurrence (appendix). The only significant reduction in overall prevalence was found in the UK study, powered and designed explicitly from its outset to detect change across generations (22%; $p=0.003$). Findings from the Zaragoza study showed a significant reduction in men's prevalence (43%; $p=0.0002$; calculated post-hoc with the method suggested by Altman and Bland²⁴). Findings from the Stockholm²⁰ and Rotterdam²³ studies suggest reduced incidence, one using indirect methods.²⁰ The indirect comparison of incidence was inferred using prevalence and mortality.

The strengths of the studies that we have selected for this Policy View are that they are population-based and attempt to retain similar study methods over time. Use of consistent study methods suggests an actual reduction in prevalence and incidence across time and generations, as opposed to an increase seeming to occur because of use of more inclusive diagnostic criteria. These studies provide, by far, the most compelling evidence from a Europe region on estimated population changes affecting prevalence and potentially incidence of and mortality from dementia.

A potential limitation of these western European studies is low response rates in recent cohorts, particularly in the UK²² and Spain.^{18,21} The UK study²² is the only study to provide detailed sensitivity analyses to address the potential effect of dropouts. Response rates in the

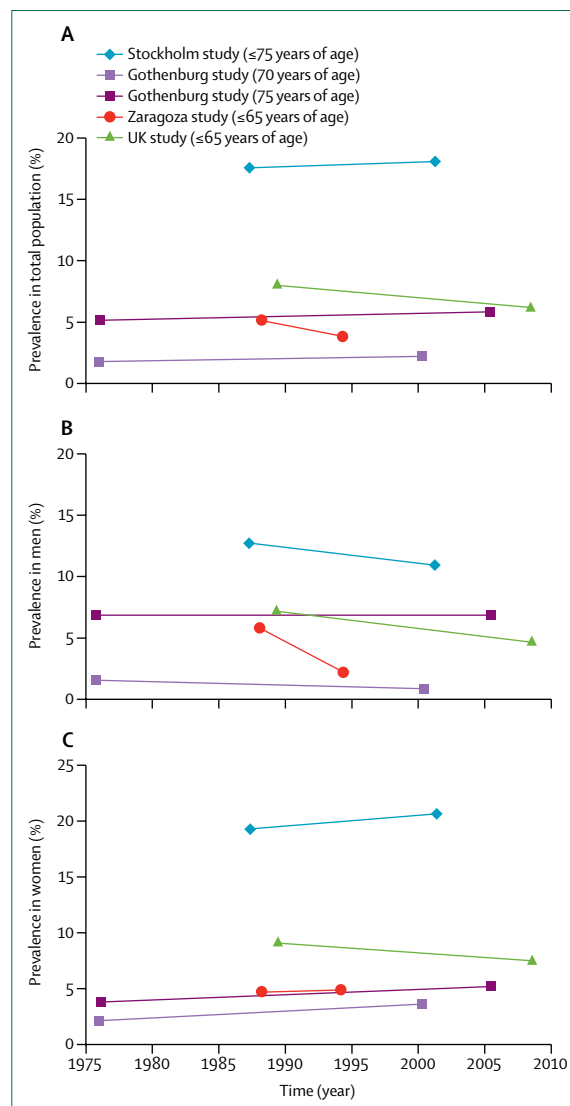


Figure 3: Change of dementia prevalence over time in (A) the total population, (B) men, and (C) women

Rotterdam²³ and Sweden^{19,20} studies have been steady between cohorts, although the profiles of people who refused to take part could have changed. Another factor that could have affected estimated prevalence and incidence is the likelihood of dementia being mentioned in medical records if these records are used to supplement incomplete information. Medical records data were used in some studies (the Rotterdam,²³ Gothenburg,¹⁹ and Zaragoza^{18,21} studies), which could be expected to increase estimates because this method will be subject to increased inclusiveness of broader diagnostic criteria and increased likelihood of contact with health services across time. Although each study used consistent methods between the cohorts within the studies, study designs and research methods were different among studies, so meta-analysis is not possible.

Reasons for prevalence change over time

One reason for this decrease in dementia prevalence over time could be societal changes and their effects on the

health of different generations (figure 4). Life expectancy at birth in the four countries is related to the effect of wars (World War 1 and 2, and the Spanish Civil War), famine (Dutch famine of 1944), and infectious diseases (1918 influenza). These historical events seem likely to have had a profound effect on living conditions, growth and development, physical and mental health in early life, and cognition late in life across different generations.⁹ In the two Swedish studies,^{19,20} people in the first cohorts born before 1915 could have had poorer education, worse living conditions, and a higher threat of influenza in their early life than those in the second cohorts had. In Spain,^{18,21} although only a 7 year difference existed between the two cohorts, the Civil War and continual famines during and after the Civil War could have had substantial effects on the nutrition and primary or secondary education of the cohorts.²⁵ People in the two Dutch cohorts²³ who experienced the 1944 famine at different life stages and survived war periods have been reported to have different health profiles late in life between cohorts.²⁶ Those in the

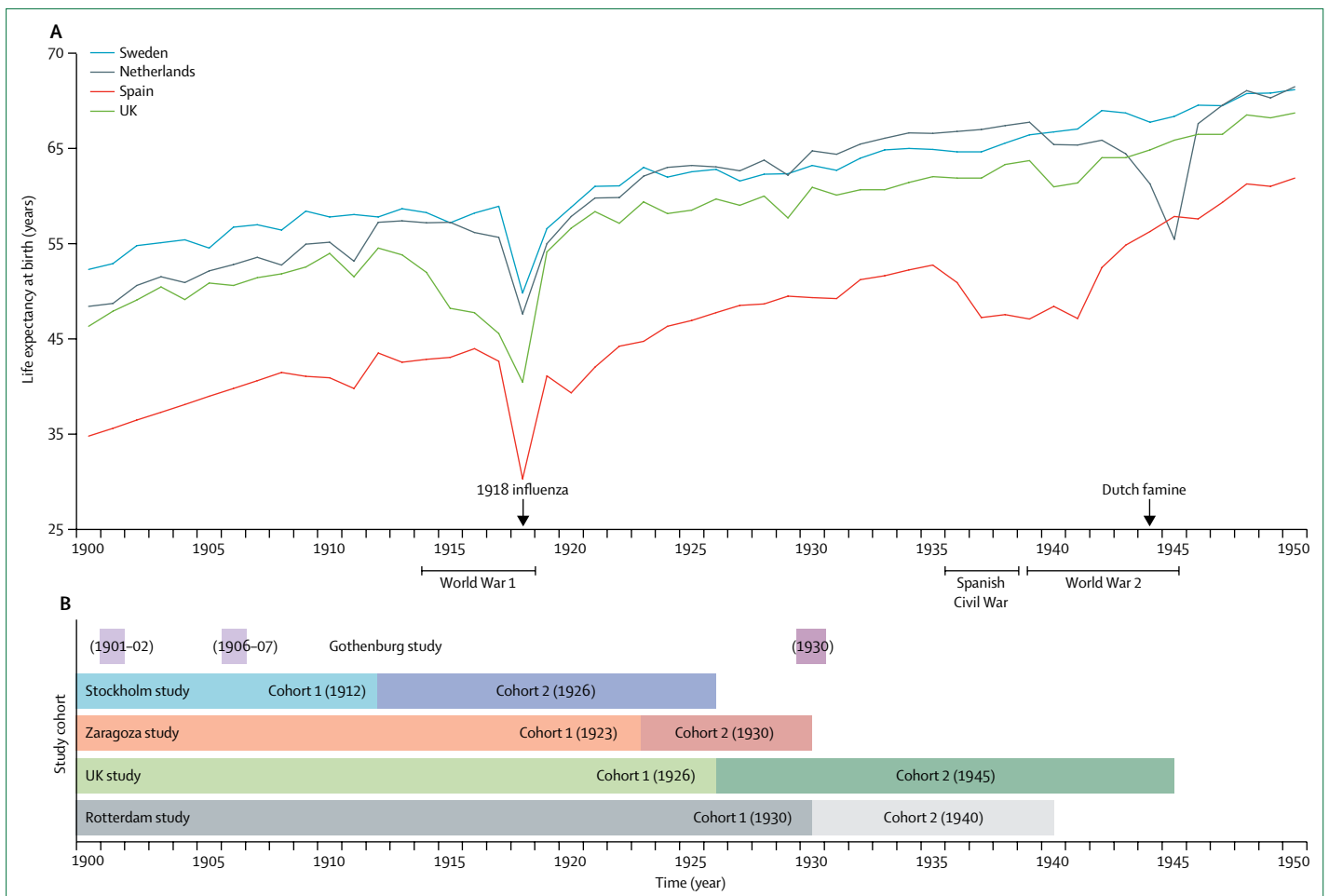


Figure 4: Life expectancy of different generations (A) Life expectancy at birth from 1900 to 1950, showing relevant historical events. (B) Birth years of the study cohorts. The most recent birth years are shown in each cohort. The Gothenburg study included cohorts born in 1901–02, 1906–07, and 1930.

second cohort in the UK study²² can be deemed a so-called post-war generation, with better survival, education, cognitive and physical development in early age, and health status throughout their life than those in the first cohort.

Adverse environments in early years will affect survival and might be different according to sex and deprivation. We found a greater reduction in dementia prevalence in men than in women. Since the 19th century, women in western Europe started to have longer life expectancy than did men, but this sex difference has decreased since the 1980s.²⁷ Although improvement of living conditions, education, and health care might reduce dementia occurrence in generations born more recently, societal changes might have more complex effects on women's behaviour and life experiences than on men's. Changes in behaviour and lifestyle, such as smoking, drinking, and employment, have been suggested to have a substantial effect on premature mortality and occurrence of non-communicable diseases in women.^{28,29} Some of these factors are known to increase the risk of dementia and might affect the trends of dementia prevalence over time. People with better education, socioeconomic status, and health conditions are usually more resilient and have a higher probability of survival to older ages.^{30,31} Research into the effect of change in behaviour, such as that related to smoking or risk factors for vascular diseases, was very much focused on men in the 20th century.

In addition to demographic and lifestyle factors, findings from observational studies³² have consistently shown the strong relation between vascular risk factors and cognitive decline and dementia. Incidence and mortality of major cardiovascular diseases have decreased in high-income countries since the 1980s.³³ Prevention and treatment of vascular diseases and chronic conditions might play an important part in the reduced or stable occurrence of dementia during the past 20–30 years. Decreasing morbidity with shortening periods of physical and cognitive infirmity might be occurring, and our data concur with this assertion.³⁴ Investigators studied changes in physical and cognitive functions in Danish people aged 90 years or older between two cohorts with a 10 year difference. The young generation had better cognitive and physical functions than did the old generation in this very old age group.

Implications for policy

In this Policy View, we provide a positive and encouraging message in terms of a possible decrease in dementia occurrence (panel 3). This decrease underlines the potential long-term benefits of national policies related to education, social determinants of health affecting inequalities, and health behaviours for future generations. Cognitive and brain health late in life are rooted in physical and mental health from early in life, so every stage of life matters. Policies aimed at whole populations, such as prevention policies, health promotion, and

health-care provision, through all stages of life, are likely to be important.³⁵ This evidence from the western European studies reinforces the potential of preventive strategies throughout life to reduce dementia risk rather than the overemphasis on pharmaceutical interventions in late life; policy makers need to bear this potential in mind when drafting their present plans for investment.

Panel 3: Overview of and take-home messages from this Policy View

Dementia

A clinical syndrome characterised by altered cognitive function (decreased cognitive function, such as decreased memory, altered language, and executive function).

Risk factors for dementia

Demographic factors:

- Old age
- Being a woman
- Low education
- Low social class

Comorbidity of chronic disorders:

- Diabetes
- Vascular disease
- Stroke
- Hypertension
- Depression

Lifestyle factors:

- Smoking
- Reduced physical activity

Prevalence change over time

- The number of people with dementia in some western European countries is stabilising, despite population ageing.
- Health in early and middle life stages might be affecting this emerging pattern.

Strengths and limitations

- The epidemiological studies that we have covered in this Policy View used the same study methods between two timepoints to compare changes in dementia occurrence over time.
- Meta-analysis of the heterogeneous data from these studies cannot be done. Response rates vary across countries and are generally lower in more recent cohorts, with the limitation, particularly in the UK and Spain studies, of decreased response rates.

Policy implications

- All policies aiming to prevent dementia need to take health factors in early life into account. Policy planning should be balanced across primary (policies reducing risk and increasing cognitive reserve), secondary (early detection and screening), and tertiary (once dementia is present) prevention.
- Primary prevention has the largest effect on reduction of later dementia occurrence and disability.
- Policy makers need to carefully assess evidence provided to them for dementia, taking into account changes in diagnostic procedure, time, geographical location, and relevance for present and future populations.
- Population-based epidemiological research with use of consistent methods across different locations, time periods, and cultures provides robust evidence for policy making and dementia care planning, and a comprehensive understanding of health in old age.

Search strategy and selection criteria

We searched PubMed and Web of Knowledge using the search terms (“dementia” OR “Alzheimer’s disease”) AND (“time” OR “trends”) for reports published between Jan 1, 2000, and Feb 28, 2015. We used two inclusion criteria to select publications: they had to report on population studies with contemporary findings in European populations and had to have potential for comparison with earlier prevalence or incidence data. We extracted information about study design, methods, and results. For the identified recent studies, we used earlier publications reporting first cohort results for more detailed information. We identified six studies done over two time periods, including two based on specific age groups. We identified one of these as relevant and included it. We excluded the other one because the study populations of the two time periods were not sampled independently and only had a 5 year gap for comparison. We therefore analysed five studies for this Policy View.

Although life expectancy at birth continues to show substantial variation between social environments across countries, previous research shows that combined prevalence estimates in western Europe are reasonably consistent across countries.⁷ Trends in prevalence and incidence of dementia are likely to be modulated by a complex combination of societal changes affecting survival, lifestyle factors, and health profiles across life stages.

The European studies synthesised here present a rather different picture to the so-called dementia epidemic reported in some systematic reviews and meta-analyses,^{3,15} and suggest that the number of people with dementia in European countries is stabilising, despite population ageing. However, dementia care will remain a lasting challenge for many years. In particular, the oldest old (eg, 85 years and older) is the fastest growing age group in the population, with about 40% currently estimated to be affected with dementia, and many more with cognitive decline and frailty.^{36,37} The case for balanced investment in research across primary (policies reducing risk and increasing cognitive reserve), secondary (early detection and screening), and tertiary (once dementia is present) prevention has never been stronger. In a health policy study of dementia, the Organisation for Economic Co-operation and Development³⁸ mentioned that health systems across member countries allocate less than 3% of their health system spending to dementia prevention. Dementia research still emphasises biomarkers, biochemical mechanisms, treatments, and cure. In the UK, the research impact report from the Alzheimer’s Society³⁹ shows that 5% of research funding between 1990 and 2012 was dedicated to studies of risk factors and preventive strategies, with 11% invested in those of dementia diagnosis and 20% in those of care and support, whereas nearly 65% was invested in research on causes, cure, and treatment development.

Scientific evidence needs to be assessed for its strengths and weaknesses, bearing in mind the population that it comes from to provide greatest value for investments made. The strength of these western European studies—including stable study methods over time, appropriate and representative population sampling, good response rates, and repeated, fresh sampling on a regular basis—need to be sustained and developed further. The advance of epidemiological research could inform not only policy and practice, but also our understanding of health in old age.

Contributors

CB developed the original idea and designed the approach. Y-TW searched the literature, collected data, and reviewed the studies. Y-TW, CB, LF, FEM, AL, MMBB, and IS wrote the report.

Declaration of interests

We declare no competing interests.

References

- 1 WHO. Dementia: a public health priority. Geneva, World Health Organization, 2012.
- 2 UK Government Department of Health. Global action against dementia. April 10, 2014. <https://www.gov.uk/government/publications/g8-dementia-summit-global-action-against-dementia/g8-dementia-summit-global-action-against-dementia-11-december-2013> (accessed June 8, 2015).
- 3 Alzheimer’s Disease International. Policy brief for heads of government: the global impact of dementia 2013–2050. Illinois: Alzheimer’s Disease International, 2013.
- 4 Breeze E, Hart NJ, Aarsland D, Moody C, Brayne C. Cohort studies have a role to play in dementia research. *Alzheimers Dement* 2014; **10** (suppl 4): p189.
- 5 Brayne C, Davis D. Making Alzheimer’s and dementia research fit for populations. *Lancet* 2012; **380**: 1441–43.
- 6 Llibre Rodriguez JJ, Ferri CP, Acosta D, et al. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey. *Lancet* 2008; **372**: 464–74.
- 7 Hofman A, Rocca WA, Brayne C, et al. The prevalence of dementia in Europe: a collaborative study of 1980–1990 findings. Eurodem Prevalence Research Group. *Int J Epidemiol* 1991; **20**: 736–48.
- 8 Alzheimer’s Society. Dementia UK. London: Alzheimer’s Society, 2007.
- 9 Alzheimer’s Society. Dementia UK: update. London: Alzheimer’s Society, 2014.
- 10 Whalley LJ, Dick FD, McNeill G. A life-course approach to the aetiology of late-onset dementias. *Lancet Neurol* 2006; **5**: 87–96.
- 11 Larson EB, Yaffe K, Langa KM. New insights into the dementia epidemic. *N Engl J Med* 2013; **369**: 2275–77.
- 12 Di Cesare M, Khang YH, Asaria P, et al. Inequalities in non-communicable diseases and effective responses. *Lancet* 2013; **381**: 585–97.
- 13 GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; **385**: 117–71.
- 14 Webb P, Bain C. Essential epidemiology: an introduction for students and health professionals. Cambridge: Cambridge University Press, 2011.
- 15 Chan KY, Wang W, Wu JJ, et al. Epidemiology of Alzheimer’s disease and other forms of dementia in China, 1990–2010: a systematic review and analysis. *Lancet* 2013; **381**: 2016–23.
- 16 Wu YT, Lee HY, Norton S, et al. Period, birth cohort and prevalence of dementia in mainland China, Hong Kong and Taiwan: a meta-analysis. *Int J Geriatr Psychiatry* 2014; **29**: 1212–20.
- 17 Xie J, Brayne C, Matthews FE, for the Medical Research Council Cognitive Function and Ageing Study collaborators. Survival times in people with dementia: analysis from population based cohort study with 14 year follow-up. *BMJ* 2008; **336**: 258–62.

- 18 Lobo A, Saz P, Marcos G, D a JL, De-la-C amara C. The prevalence of dementia and depression in the elderly community in a southern European population: the Zaragoza study. *Arch Gen Psychiatry* 1995; **52**: 497–506.
- 19 Wiberg P, Waern M, Billstedt E, Ostling S, Skoog I. Secular trends in the prevalence of dementia and depression in Swedish septuagenarians 1976–2006. *Psychol Med* 2013; **43**: 2627–34.
- 20 Qiu C, Strauss E, B ackman L, Winblad B, Fratiglioni L. Twenty-year changes in dementia occurrence suggest decreasing incidence in central Stockholm, Sweden. *Neurology* 2013; **80**: 1888–94.
- 21 Lobo A, Saz P, Marcos G, et al. Prevalence of dementia in a southern European population in two different time periods: the ZARADEMP Project. *Acta Psychiatr Scand* 2007; **116**: 299–307.
- 22 Matthews FE, Arthur A, Barnes LE, et al. 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* 2013; **382**: 1405–12.
- 23 Schrijvers EM, Verhaaren BF, Koudstaal PJ, Hofman A, Ikram MA, Breteler MM. Is dementia incidence declining? Trends in dementia incidence since 1990 in the Rotterdam study. *Neurology* 2012; **78**: 1456–63.
- 24 Altman DG, Bland JM. How to obtain the p value from a confidence interval. *BMJ* 2011; **343**: d2304.
- 25 Mira E. Psychiatric experience in the Spanish War. *BMJ* 1939; **1**: 1217–20.
- 26 Roseboom T, de Rooij S, Painter R. The Dutch famine and its long-term consequences for adult health. *Early Hum Dev* 2006; **82**: 485–91.
- 27 Barford A. Life expectancy: women now on top everywhere. *BMJ* 2006; **332**: 808.
- 28 Thun MJ, Carter BD, Feskanich D, et al. 50-year trends in smoking-related mortality in the United States. *N Engl J Med* 2013; **368**: 351–64.
- 29 Perls T, Fretts R. Why women live longer than men. June, 1998. https://www.cmu.edu/CSR/case_studies/women_live_longer.html (accessed June 8, 2015).
- 30 Lynch JW, Smith GD, Kaplan GA, House JS. Income inequality and mortality: importance to health of individual income, psychosocial environment, or material conditions. *BMJ* 2000; **320**: 1200–04.
- 31 Idler EL, Benyamini Y. Self-rated health and mortality: a review of twenty-seven community studies. *J Health Soc Behav* 1997; **38**: 21–37.
- 32 Taylor B, Rehm J, Murray CJ, et al. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. *PLoS Med* 2009; **6**: e1000058.
- 33 Ergin A, Muntner P, Sherwin R, He J. Secular trends in cardiovascular disease mortality, incidence, and case fatality rates in adults in the United States. *Am J Med* 2004; **117**: 219–27.
- 34 Christensen K, Thinggaard M, Oksuzyan A, et al. Physical and cognitive functioning of people older than 90 years: a comparison of two Danish cohorts born 10 years apart. *Lancet* 2013; **382**: 1507–13.
- 35 Beaglehole R, Bonita R. Public health at the crossroads: achievements and prospects. Cambridge: Cambridge University Press, 2006.
- 36 Corrada MM, Brookmeyer R, Berlau D, Paganini-Hill A, Kawas CH. Prevalence of dementia after age 90: results from the 90+ study. *Neurology* 2008; **71**: 337–43.
- 37 Lucca U, Tettamanti M, Logroscino G, et al. Prevalence of dementia in the oldest old: the Monzino 80-plus population based study. *Alzheimers Dement* 2015; **11**: 258–70.e3.
- 38 Organisation for Economic Co-operation and Development. Addressing dementia: the OECD response. Paris: Organisation for Economic Co-operation and Development, 2015.
- 39 Alzheimer’s Society. Cause, cure, care and prevention: impact of Alzheimer’s Society’s dementia research programme 1990–2012. London: Alzheimer’s Society, 2012.