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Dementia occurrence in Europe: epidemiological evidence and implications for current policy making

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Summary

Dementia impact has received increasing attention of governments and politicians across the globe in recent years. Epidemiological research based Western European populations twenty years ago provided key evidence for dementia policy making, but these estimates are now out of date given dramatic changes in life expectancy, living conditions and health profiles across different generations. To test whether dementia occurrence has changed over the last decades, five studies in Western Europe have now compared the dementia occurrence across time using consistent research methods. These five studies report stable or reduced dementia occurrence of up to 25% over the last decades and suggest stabilising numbers of people with dementia in Western Europe despite population ageing. This may be the result of better education, living conditions, prevention and treatments of vascular risk and chronic conditions and indicate a potential "lifecourse approach" that promoting health in earlier life stages may benefit cognitive and brain health in later life across successive generations. Policy planning and future search must be balanced across primary, secondary and tertiary prevention. Each has their place but primary prevention has the largest modelled potential impact on dementia and disability in societal terms.

Background

Dementia has only relatively recently received focused attention in global societies as compared with other major public health priorities.[1,2] Societies around the world face an increasing proportion of older people who by reason of age alone are at increasing risk of dementia, a declining proportion of people in the workforce as well as unfavourable economic circumstances.[3] Governments and politicians have become aware of the impact of dementia on individuals, families and societies and are worried about the likely increase in numbers of people with dementia.[2] Policy makers have started to request evidence and already are promoting relevant policies around the globe using the available evidence for justification. Although these 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 this changes over time are surprisingly rare.[4] The estimations can be based on health service contact or death certification as used in many other conditions to assess population impact but this is not helpful for dementia.[5] Where studies based on populations do exist they are often single sites within countries, rarely whole geographical regions.[6] Studies conducted in different sites to test for differences within countries are also rare. Estimation of occurrence from true population-based epidemiological studies is critical for exercises such as costing, and therefore robust, relevant, up to date estimates should be required when creating dementia policies. These also need to be sensitive to many relevant

individual and contextual factors, such as gender, culture and socioeconomics creating

potential variation across time and geography.

Despite the trauma of two world wars, compared to the rest of the world, high income

countries in Europe have had relatively stable social environments, wealthy living conditions

and advanced health science, with the consequence of extended life expectancy, population

ageing and increasing concerns about dementia. The first epidemiological investigations of

dementia in Western Europe were initiated thirty or so years ago and took at least a decade to

have discernible policy impact.[7] These primary fieldwork studies are still influencing policy

development today and continue to provide a statement of the size and distribution of

dementia within countries and across Europe, going on to be used at national and local levels

e.g. England's NHS primary care targets.[8,9]

Although robust information on dementia has been provided through this investment in earlier

decades, it is important for policy makers to remember societal changes and their potential

impact on population health. Each generation of older people will have experienced different

positive and adverse influences on health across their lives.[10] Established risk and protective

factors for dementia such as education and vascular diseases have been subject to huge

changes over successive generations. [11-13] Given these changes in life expectancy and risk

profiles in the whole populations, we would expect to see emerging variation in the occurrence of dementia across populations over time and geography. Policy making needs to incorporate up to date information based on evidence from up to date epidemiological studies in Western Europe, which will reflect any such changes in dementia occurrence in representative populations. In additional to the estimation of changing epidemiology of dementia and implications for health policy, these findings may also inform the debate on the direction of research funding and science on the changing nature and definition of dementia syndrome across time and in different contexts. Evidence from Western European populations can be a demonstrator of changes in dementia occurrence over time. Policy makers from outside of Western European countries may use this information as a reference for their dementia policy planning.

Here we conduct an in depth presentation of the only European studies that can currently test for changes in dementia occurrence (Box 1). Epidemiological terms can be confusing and the key concepts and measures are provided in Box 2 to assist non-epidemiological readers.

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Box 1 The aims of this review

- To synthesise the epidemiological evidence from population-based studies which compared dementia occurrence over time in Europe using the same methodologies.
- To suggest implications for dementia policy based on the evidence from current epidemiological research
- To provide suggestions for policy makers on assessing the scientific evidence on dementia

Box 2 Epidemiological terms and measures

A cohort indicates a group of people in a specific time and space.[14] In epidemiological studies, this defined group is measured often for risk and protective factors at baseline and then is followed by researchers and their health data regularly collected over time. A population-based cohort is a representative sample or the entire of the target population (For example, the UK older population including those living in care settings). It is possible to measure prevalence at baseline and track incidence and mortality in the follow-up investigation.

The relationship of three basic measures: prevalence, incidence and mortality, is illustrated as below. Prevalence is as a result of incidence and mortality (i.e. new cases occurring and death). Dementia is not reversible and therefore recovery does not feature in this explanation. If we assume that the occurrence of new cases (incidence) is a water stream into a container and a water stream leaking out is those who die (mortality), the water level would be the prevalence. The flow rate of water streams will affect the water level observed at different time points. Current research and evidence is based on the findings from prevalence studies (observed water level) since it is relatively difficult to measure incidence (the flow rate) of non-communicable diseases except through cohort studies, which may be or may not be population-based (representative sample).

Incidence: proportion of new dementia cases in a defined population over a time period
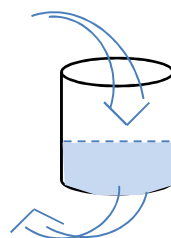
Prevalence: proportion of people with dementia in a defined population

Mortality: proportion of people who died in a defined population over a time period (which will differ between people with and without dementia)

Changes in diagnostic criteria: if diagnostic criteria for dementia are made more restrictive, the water will flow at a slower rate and prevalence will decrease, not because dementia is less common but because its formal criteria have changed. If they are made more inclusive the converse will occur with increasing prevalence.

Data sources and analysis

A literature search was conducted to identify all European population-based prevalence and incidence studies using the search terms "dementia" or "Alzheimer's disease" and "time" or "trends" in PubMed and Web of Knowledge up to February 2015. Two inclusion criteria were used to select papers: (1) reporting on true population studies with contemporary findings published after 2000 in European populations; (2) the potential for comparison with earlier prevalence or incidence data. Information was extracted from each study on study design, methodological features and details of results. For the identified recent studies, earlier papers reporting first cohort results were used to supply more detailed information.[15-22] Six studies were identified with two time periods, including two based on specific age groups.[23,24] One of these was identified as relevant and included.[24] The other one was excluded as the study populations of the two time periods were not sampled independently and only had a five-year gap for comparison.[23]

Five European studies reported a valid comparison of prevalence and/or incidence between two comparable cohorts.[24-28] These were carried out in Western Europe[1]: Sweden (Stockholm study- the Kungsholmen Project and the Swedish National study on Aging and Care in Kungsholmen (SNAC-K) and Gothenburg study), Netherlands (the Rotterdam study), UK (the Cognitive Function and Ageing Studies (CFAS)) and Spain (the Zaragoza study,

ZARADEMP Project). In Eastern and Central Europe, this kind of comparison was not possible.[4] The age of study populations was 70 years and over in the Swedish studies and 55 or 65 and over in the other studies. The first cohorts were examined between late 1970s and early 1990s and the second cohorts between mid-1990s and late 2000s. The time separation for the comparisons ranged from 7 years (the Zaragoza study) to 30 years (the Gothenburg study). The first cohort studies found similar prevalence estimates by five-year age groups across different countries with consistent demonstration of the prevalence doubling every five years.[6]

A detailed analysis of study design and population sampling is required to know how to interpret results, particularly if they are to be applied nationally and compared internationally. Figure 1 presents a schematic representation of the designs and population sampling of these studies, Table 1 summarises the methodological features of these studies. Only three were direct comparisons of cohorts with new sampling of the population, independently of the previous cohort.[24,27,28] The Rotterdam cohort did not have new independent sampling but added incomers and the "newly" old periodically.[25] The study based in Stockholm was originally a dedicated local study, the most recent study was based on a local subsample from a national study.[25] Response rates declined in three of the studies with varying ability to assess the impact of such changes on the findings.[24,27,28] The Stockholm and Rotterdam

studies had stable response rates.[25,26] Although analytical methods were different across

studies, each study attempted to keep the diagnostic methodology as stable as possible,

recognising that changes over time in approaches to diagnosis are likely to affect prevalence

and incidence but only one used a fixed algorithm method.[28] Further details of comparison of

study design and methodology are provided in the Appendix.

Results and interpretation: change over time?

Prevalence: The two studies of 65+ populations (CFAS and Zaragoza) with independent

sampling over time reported lower prevalence, in Zaragoza the reduction in men reached

significance although the reduction in overall prevalence did not. Stable prevalence of

dementia over time was reported in both the Swedish studies. Age- and gender-specific

estimates of prevalence for the three comparison studies are shown in Figure 2 and 3. Figure 2

shows the prevalence by five-year age groups and Figure 3 focuses on the estimates over time.

The findings suggest consistently greater changes in men than women particularly in those

studies from mainland Europe. The UK-based study found decline in prevalence in both

sexes.

Incidence: The Rotterdam study is the only study reporting incidence data. A reduction in incidence over 10 years, although not significant, was detected. The Stockholm study inferred changes in incidence over 20 years by integrating prevalence and mortality and also suggests a reduction.

Mortality with dementia: Two studies examined mortality and both report declining trends for the whole population.[24,25] Only the Stockholm study compared changes in mortality of people with dementia and found a decreasing trend across two cohorts.

More detailed information is provided in supporting information (Table S1 and S2).

Thus, despite methodological and operational differences between the studies (see Appendix), there is no evidence in any of these studies of any increase in prevalence when diagnostic method are stabilised. On the contrary, prevalence decreases by up to 20~25% over the last 20~30 years with much of this change influenced by changes in older men. A reduced incidence is also suggested by two studies, one using indirect methods.

The strength of the selected studies is that they are population-based and attempt to retain similar study methods over time. Using stable methods suggests actual reduction in

prevalence and incidence across time and generations. This is by far the most compelling

evidence from a major global region to provide an indication of population changes affecting

prevalence, potentially incidence and mortality of dementia.

A potential limitation of these Western European studies was lower response rates in more

recent cohorts with the UK and Spain suffering particularly from drop in response.[27,28] The

CFAS analysis provided extensive sensitivity analyses to address potential impact of

dropouts.[28] The response rates in Dutch and Scandinavian studies have been steady although

differential response within the refusal groups is still possible.[24-26] Another additional factor

which could have influenced the estimated prevalence and incidence is the likelihood of

dementia being mentioned in medical records if these are used to supplement partial

information. Medical records data were used in some studies (not the Stockholm and CFAS

study) which could be expected to increase estimates as this method will be subject to change

diagnostic boundaries and greater likelihood of contact with services across time. These data

are not provided so that its impact cannot be assessed. Although each study remained

consistent methodologies over time, study designs and research methods were different across

the five studies and therefore meta-analysis is not possible.

What might be influencing these findings? Lifecourse perspectives

What might the reasons for reduction be, when differences in methodology and diagnostic processes have been controlled for? The first of these could be a survivor effect of some kind due to variation in life expectancy. Those individuals in these five prevalence or incidence studies were born in the first half of the 20th century and will have experienced major historical events, which could influence survival at different life stages (Figure 4). Life expectancy at birth in the four countries is related to the influence of wars (World War I and II), famine (Dutch famine 1944, Spanish Civil War 1930s) and infectious diseases (the 1918 Influenza). Although life expectancy at birth continues to show considerable variation in social environment across countries, previous research shows that the combined prevalence estimates in Western Europe are reasonably consistent across countries.[7] Trends in prevalence and incidence of dementia are likely to be moderated by a complicated combination of societal changes on influencing survival, lifestyle factors and health profiles across life stages (Box 3).

From a lifecourse perspective, these historical events seem likely to have had a profound influence on living conditions, growth and development, physical and mental health in earlier life and cognition in older age across different generations.[9] In the two Swedish studies, first cohorts born before 1915 could have experienced worse education, living conditions and threat of influenza in their early age compared to the second cohorts. In Spain, although there

was only 7 year difference between the two cohorts, however the civil war and continual famines in late 1930s could have had considerable impacts on the nutrition and primary or secondary education of the younger cohorts.[32] The two Dutch cohorts which experienced the 1944 famine at different life stages and survived through war periods have indeed been reported to have different later life health profiles.[33] Compared to the other cohorts, the second cohort in the CFAS can be considered as a "post-war generation", with better survival, education, cognitive and physical development in early age and health status throughout their life.

Adverse environments in earlier eras will have influenced survival and may be different according to gender and deprivation. A greater reduction in dementia prevalence was found in men than women. Since the 19th century, women in Western Europe started to have longer life expectancy than men but this gender difference decreased in recent decades.[34] Although the improvement of living conditions, education and healthcare may have a positive influence on reducing dementia occurrence in younger generations, societal changes might have more complicated influences on women's behaviour and life experience. Changes in behaviour and lifestyle, such as smoking, drinking and employment outside home, have been suggested to have a substantial impact on premature mortality and the occurrence of non-communicable diseases in women.[35,36] Some of these factors are known to increase the risk of dementia and

might moderate the time trends in dementia prevalence. People with better education, socioeconomic status and health conditions are usually more resilient and have a higher probability of survival to older ages.[37,38] The impact of changed behaviours such as smoking and risk factors for vascular diseases was very much focused on men in the last century.

In additional to demographic and lifestyle factors, observational studies have consistently highlighted the strong relationship between vascular risk factors and cognitive decline/dementia. Incidence and mortality of major cardiovascular diseases have decreased in high-income countries since the 1980s.[39] Prevention and treatments of vascular diseases and chronic conditions may play an important role in reduced or stable occurrence of dementia over the last decades. Compression of morbidity with shorter periods of physical and cognitive infirmity may be occurring and our data concur with this.[40]

How to assess and interpret epidemiological evidence?

Although epidemiologists have been working for decades to carry out population-based cohorts to enumerate the size of dementia in the population, it is important to remember that such research is, as all research is, locked in time and space. Policy makers need to be careful about the evidence provided to them on dementia- what is its provenance and its relevance.

The interpretation of scientific findings could be various depending on different perspectives and contexts. An illustration of the difficulty inherent in interpretation of new findings in relation to old, or comparisons across geography is putting two systematic reviews of Chinese prevalence studies of dementia side by side.[41,42] In one, much promoted, the conclusion is that dementia prevalence is increasing in China.[41] In the other, which takes methodological variation into account, the increase in prevalence is attenuated and non-significant because the methodological factors, including introduction of new diagnostic criteria, appear to have been instrumental in the increase.[42] Such results provide a cautionary note about the interpretation of potential changes in dementia occurrence. Any studies which are based on current diagnostic practices and contact with health services are likely to reflect increased attention and awareness of people with dementia as well as potential increase in prevalence due to shifting diagnostic boundaries. This will counter the impact of reduction in actual occurrence through increased detection of milder "cases", previously not recognised as meeting dementia criteria. Inconsistent methodologies as well as enormous political interests, stakeholder and public awareness could influence the interpretation of scientific evidence on dementia. Catastrophic estimates of dementia in future ageing society serve current political and charity campaigns, encourage investment into pharmaceutical and healthcare business and are maintained by sustained attention of social and general media. Scientific evidence needs to match this excitement in order to continue to secure research funding and resources.

Evidence-based policy is not only to consult the evidence but also needs to further assess the provenance of evidence taking the quality of research and potential influences of social contexts into account.

In addition to the source of evidence, policy makers also have to assess the evidence and its relevance to diverse settings. Is the estimate from Western Europe generalisable across geographies and time? Up to the last decade, there was very little evidence of systematic variation in prevalence or incidence of dementia between high income countries where life expectancy is high. This is in contrast to considerable variation reported from low- and middle-income countries, where life expectancy is still below the median age of dementia incidence in high income countries (around aged 83 years).[43] For example, higher estimated prevalence has been reported in Latin America, which also have high vascular risk profiles. Difference in economic development, population structure, societal and cultural contexts across the globe could limit the application of scientific evidence, which is mainly from high income countries with a Western perspective. Policy making needs to assess the relevance of evidence to correspond to different contexts, time and geography.

Implication for policy: every life stage matters

This review provides a very positive and encouraging message in terms of possibilities of prevention and future perspectives within the dementia field. A possible decline in dementia occurrence underlines the potential long term benefits of national policies related to education, social determinants of health influencing inequalities, and health behaviours for future generations. Cognitive and brain health in later life are rooted in physical and mental health from earlier life stages so that every life stage matters. Policies aimed at whole populations, such as effective prevention policies, health promotion and health care provisions across the lifecourse are likely to be important over many decades and even into the next century.[44] The evidence from European studies reinforces the potential of preventive strategies across the lifecourse to reduce dementia risk rather than over-emphasises on pharmaceutical interventions and biomedical mechanisms in later life. Global societies need to bear this "lifecourse approach" in mind when drafting their current plans for investment.

The European studies synthesised here present a rather different picture from the "dementia epidemic" reported in existing systematic reviews and meta-analyses[3,41] and suggest that the number of people with dementia in European countries are stabilising despite population ageing. However, dementia care will remain a lasting challenge for many years in the future across the world. In particular, the oldest old (e.g., 85+) is the fastest increasing segment in the population, with up to 40% of affected and many more with cognitive decline and

frailty.[45,46] The case for balanced investment in research across primary (prevention), secondary (early detection/screening) and tertiary support (care once present) has never been stronger. The Organisation for Economic Co-operation and Development (OECD) response to addressing dementia mentioned that health systems across the member countries spend less than 3% on dementia prevention.[47] However, the strategies of dementia research still emphasise on biomarkers, biochemical mechanisms, treatments and cure.[47] In the UK, the research impact report from Alzheimer's Society shows 5% of research funding between 1990 and 2012 were invested to risk factors and preventive strategies, 11% in dementia diagnosis, 20% in care and support while nearly 65% in aetiology, cure and treatment development.[48]

Scientific evidence needs to be assessed for the strength and weakness that it will undoubtedly have with contextualisation the level of population in order to provide greatest value for the investments made. The existing strength of these Western European studies, including stable study methods, appropriate and representative population sampling, good enough response rate and repeated, fresh sampling on a regular basis, needs to be sustained and developed further. The advance of epidemiological research may inform not only policy and practice but also our understanding of health in older age in general across generations, geographies and futures.

Box 3 Dementia, epidemiological evidence and policy implications

(1) Definition of dementia: a syndrome of decline in cognitive function, such as memory, language and executive function.

(2) Risk factors: despite changes in diagnostic criteria, some consistent risk factors have emerged for dementia over the last decades[29-31]

- Demographic factors: older age, being female, low education, low social class
- Co-morbidity of chronic conditions: diabetes, vascular diseases, stroke, hypertension, depression
- Lifestyle factors: smoking, low level of physical activity

(3) Results:
- European population-based studies on dementia occurrence indicate a decline in age specific of up to 25%, most marked in men.
- The numbers of people with dementia in some European countries are stabilising despite population ageing.
- Health in early and middle life stage may be influencing this emerging pattern.

(4) Strengths and limitations of the study:
- Epidemiological studies remained the same study methods to compare changes in dementia occurrences over the last few decades.
- Meta-analysis is not possible. Response rates vary across countries and are generally lower in more recent cohorts with the UK and Spain suffering particularly from drop in response.

(5) Policy implications:
- All policies aiming to tackle dementia need to take lifecourse impact of early life health influence into account. Policy planning must be balanced across primary, secondary and tertiary prevention.
- Primary prevention, promoting healthy lifestyle factors and prevention in chronic conditions, has the largest modelled potential impact on dementia and disability in societal terms
- Policy makers need to assess carefully the evidence provided to them on dementia taking into account changes in diagnostic procedure, context, time, geography, provenance and relevance for current and future populations.
- Population-based epidemiological research, using consistent methodologies across geography, time and culture, provides robust evidence for policy making, dementia care planning and a comprehensive understanding of health in older age.

Authors' contributions

Carol Brayne developed original idea and designed the approach. Yu-Tzu Wu conducted literature search, data collection and reviewed the studies. Yu-Tzu Wu, Carol Brayne, Laura Fratiglioni, Fiona E Matthews, Antonio Lobo, Monique Breteler and Ingmar Skoog contributed to writing the paper.

Declaration of interest

We declare that we have no conflicts of interest.

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Figures

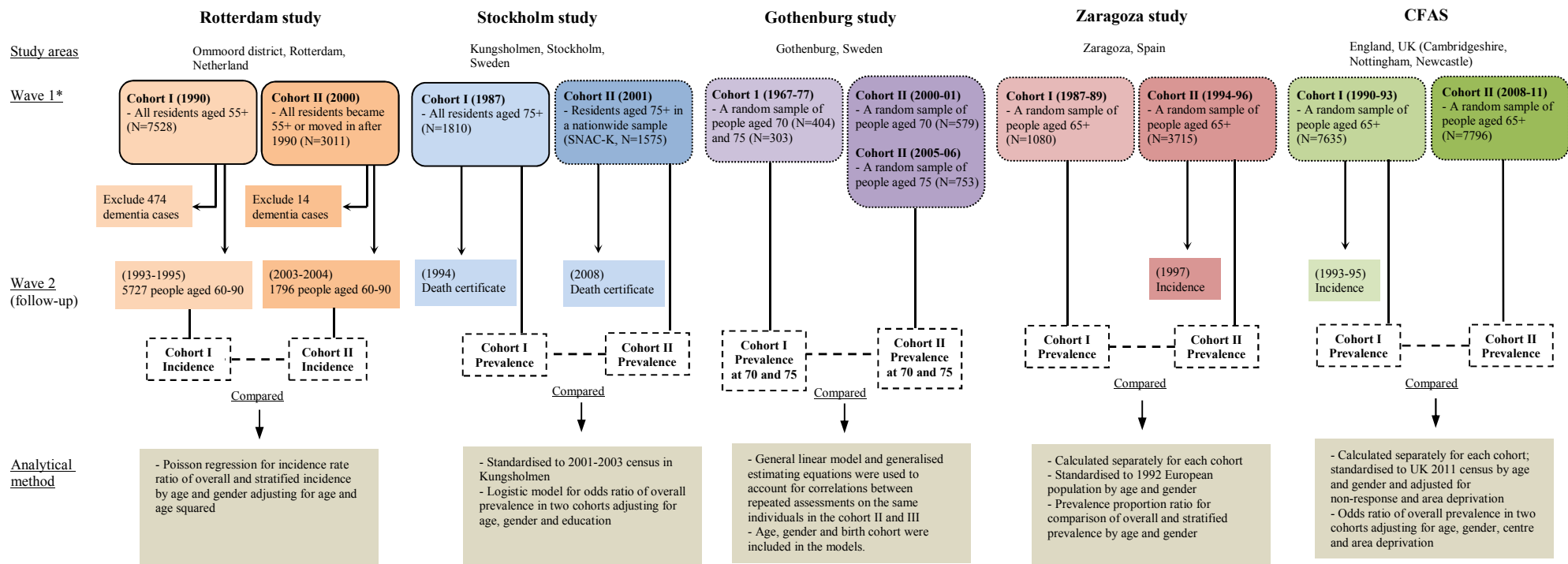**Figure 1.** Study designs of the five European studies

Figure 2 Comparison of age-specific prevalence of dementia (%) in three European studies

Figure 3 Age-adjusted prevalence of dementia by the year of investigation

Figure 4 Life expectancy at birth and the birth years of the study cohorts

Figure 1 Study designs of the five European studies

	Rotterdam study	Stockholm study	Gothenburg study	Zaragoza study	CFAS
Study areas	Ommoord district, Rotterdam, Netherland	Kungsholmen, Stockholm, Sweden	Gothenburg, Sweden	Zaragoza, Spain	England, UK (Cambridgeshire, Nottingham, Newcastle)

Wave 1*

- **Cohort I (1990)** - All residents aged 55+ (N=7528)
- **Cohort II (2000)** - All residents became 55+ or moved in after 1990 (N=3011)
- **Cohort I (1987)** - All residents aged 75+ (N=1810)
- **Cohort II (2001)** - Residents aged 75+ in a nationwide sample (SNAC-K, N=1575)
- **Cohort 1 (1967-77)** - A random sample of people aged 70 (N=404) and 75 (N=303)
- **Cohort II (2000-01)** - A random sample of people aged 70 (N=579)
- **Cohort II (2005-06)** - A random sample of people aged 75 (N=753)
- **Cohort I (1987-89)** - A random sample of people aged 65+ (N=1080)
- **Cohort II (1994-96)** - A random sample of people aged 65+ (N=3715)
- **Cohort I (1990-93)** - A random sample of people aged 65+ (N=7635)
- **Cohort II (2008-11)** - A random sample of people aged 65+ (N=7796)

Exclude 474 dementia cases
Exclude 14 dementia cases

Wave 2 (follow-up)

- (1993-1995) 5727 people aged 60-90
- (2003-2004) 1796 people aged 60-90
- (1994) Death certificate
- (2008) Death certificate
- (1997) Incidence
- (1993-95) Incidence

Cohort I Incidence — Cohort II Incidence
Cohort I Prevalence — Cohort II Prevalence
Cohort I Prevalence at 70 and 75 — Cohort II Prevalence at 70 and 75
Cohort I Prevalence — Cohort II Prevalence
Cohort I Prevalence — Cohort II Prevalence

Compared

Analytical method

- Poisson regression for incidence rate ratio of overall and stratified incidence by age and gender adjusting for age and age squared

- Standardised to 2001-2003 census in Kungsholmen
- Logistic model for odds ratio of overall prevalence in two cohorts adjusting for age, gender and education

- General linear model and generalised estimating equations were used to account for correlations between repeated assessments on the same individuals in the cohort II and III
- Age, gender and birth cohort were included in the models.

- Calculated separately for each cohort
- Standardised to 1992 European population by age and gender
- Prevalence proportion ratio for comparison of overall and stratified prevalence by age and gender

- Calculated separately for each cohort; standardised to UK 2011 census by age and gender and adjusted for non-response and area deprivation
- Odds ratio of overall prevalence in two cohorts adjusting for age, gender, centre and area deprivation
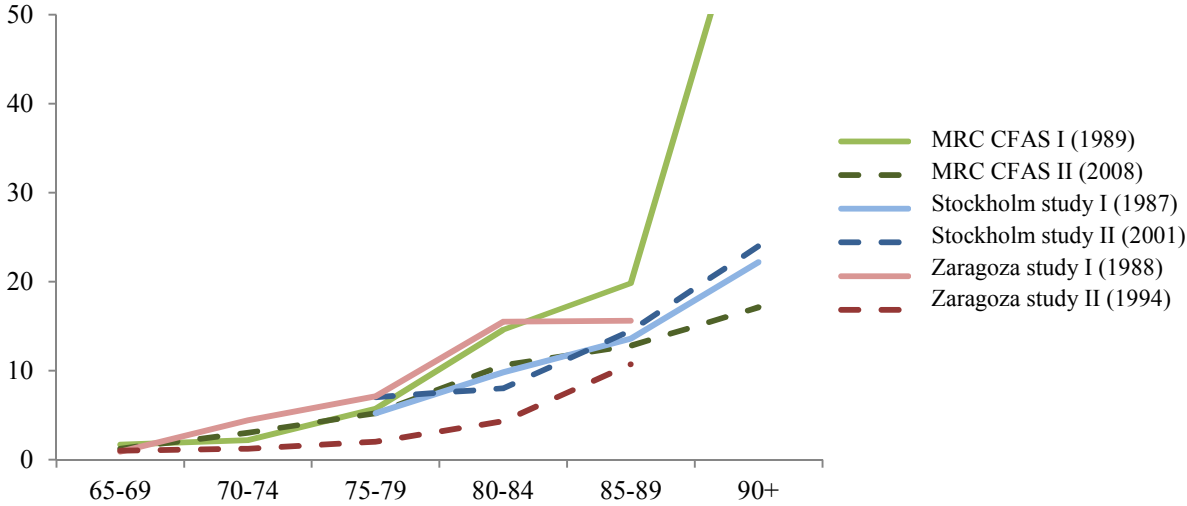
*: the boxes with dot lines indicate a random sample of people in the study areas.

Figure 2 Comparison of age-specific prevalence of dementia (%) in three European studies

Prevalence (%) in total population
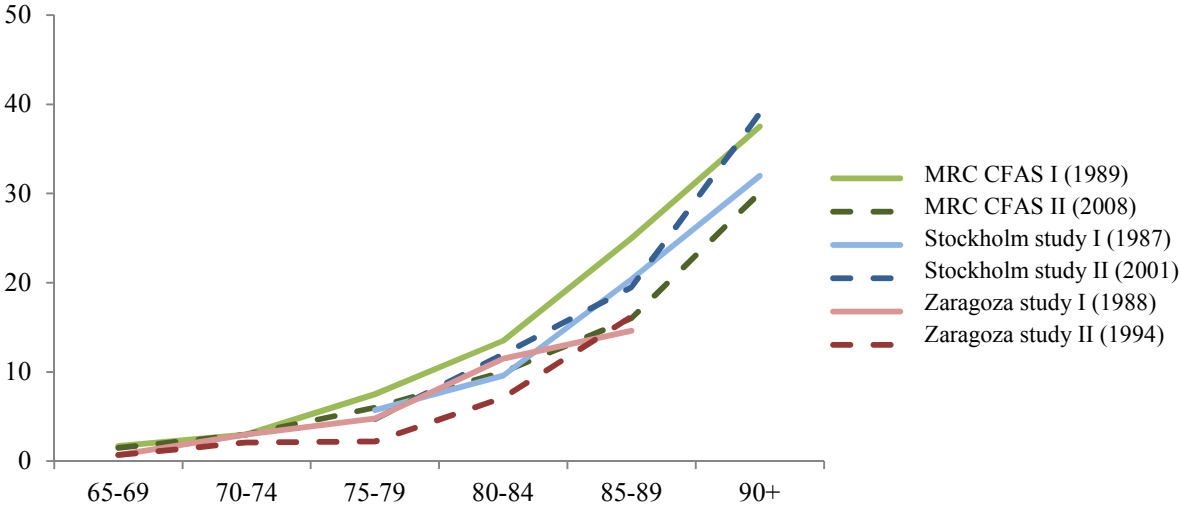
MRC CFAS I (1989)
MRC CFAS II (2008)
Stockholm study I (1987)
Stockholm study II (2001)
Zaragoza study I (1988)
Zaragoza study II (1994)

Prevalence (%) in men

68.2

MRC CFAS I (1989)
MRC CFAS II (2008)
Stockholm study I (1987)
Stockholm study II (2001)
Zaragoza study I (1988)
Zaragoza study II (1994)

Prevalence (%) in women

MRC CFAS I (1989)
MRC CFAS II (2008)
Stockholm study I (1987)
Stockholm study II (2001)
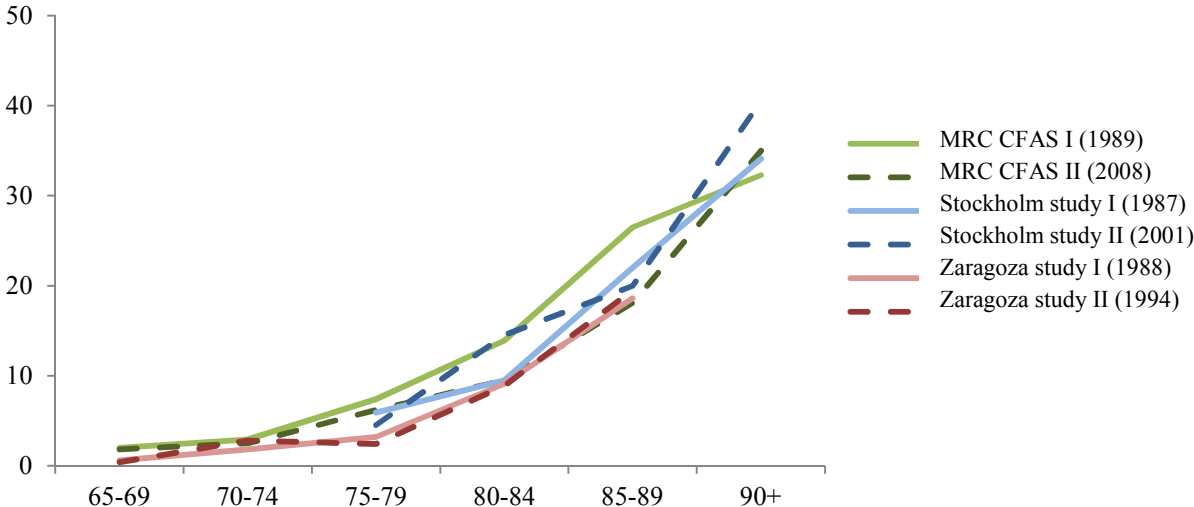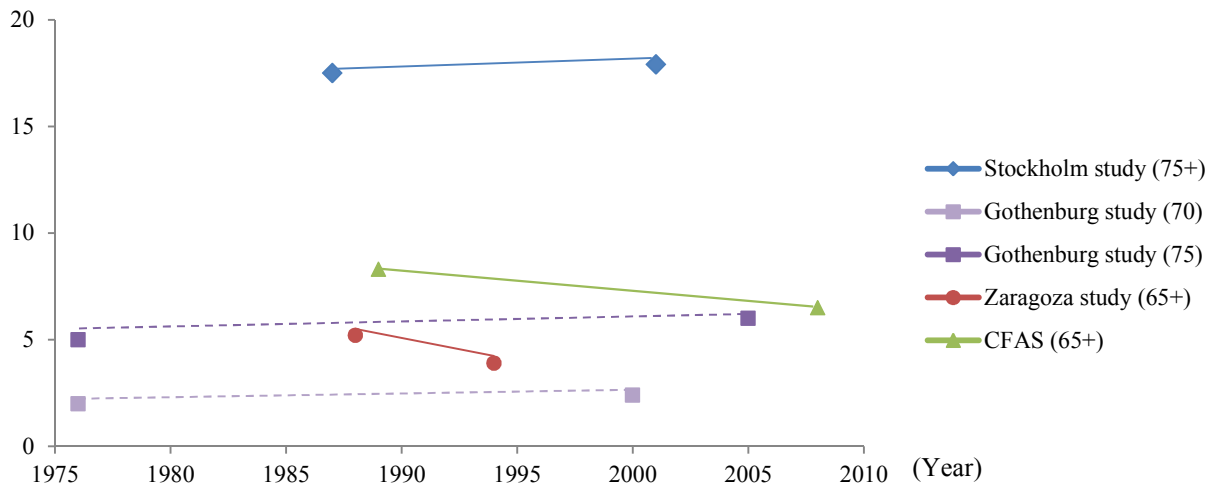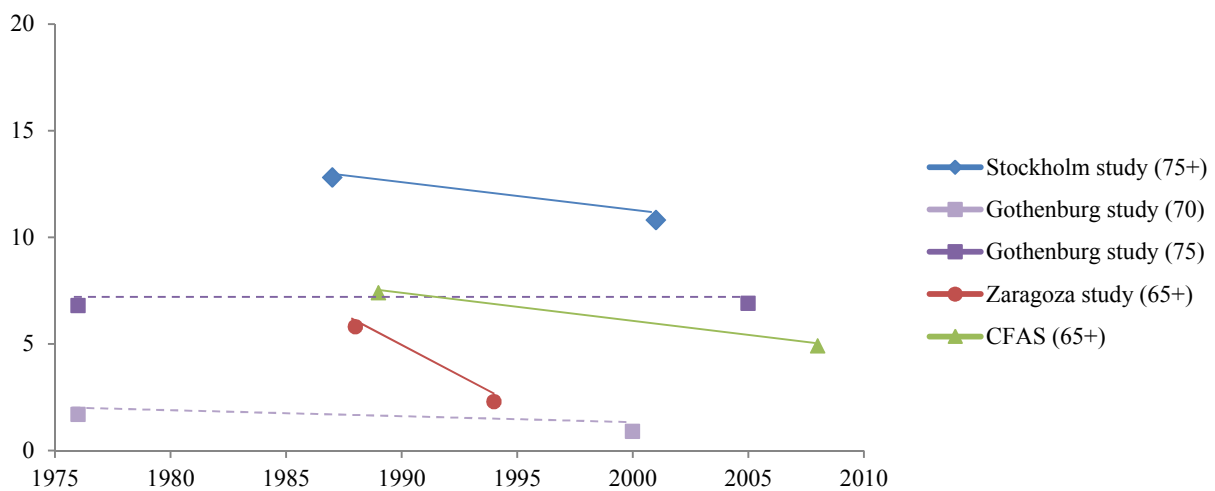Zaragoza study I (1988)
Zaragoza study II (1994)

Figure 3 Age-adjusted prevalence of dementia by the year of investigation

Prevalence (%) of dementia in total population

Prevalence (%) of dementia in men

Prevalence (%) of dementia in women

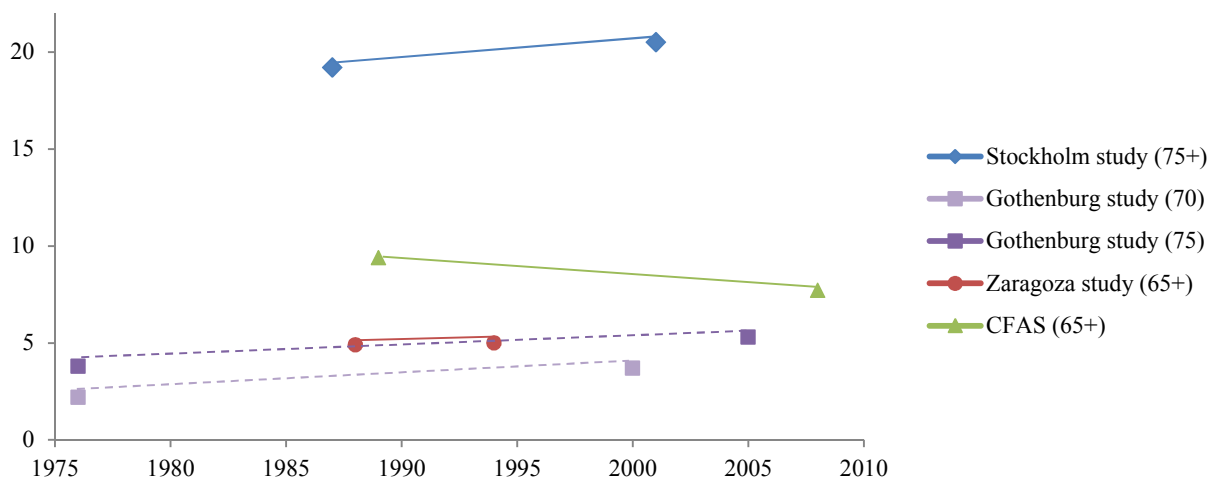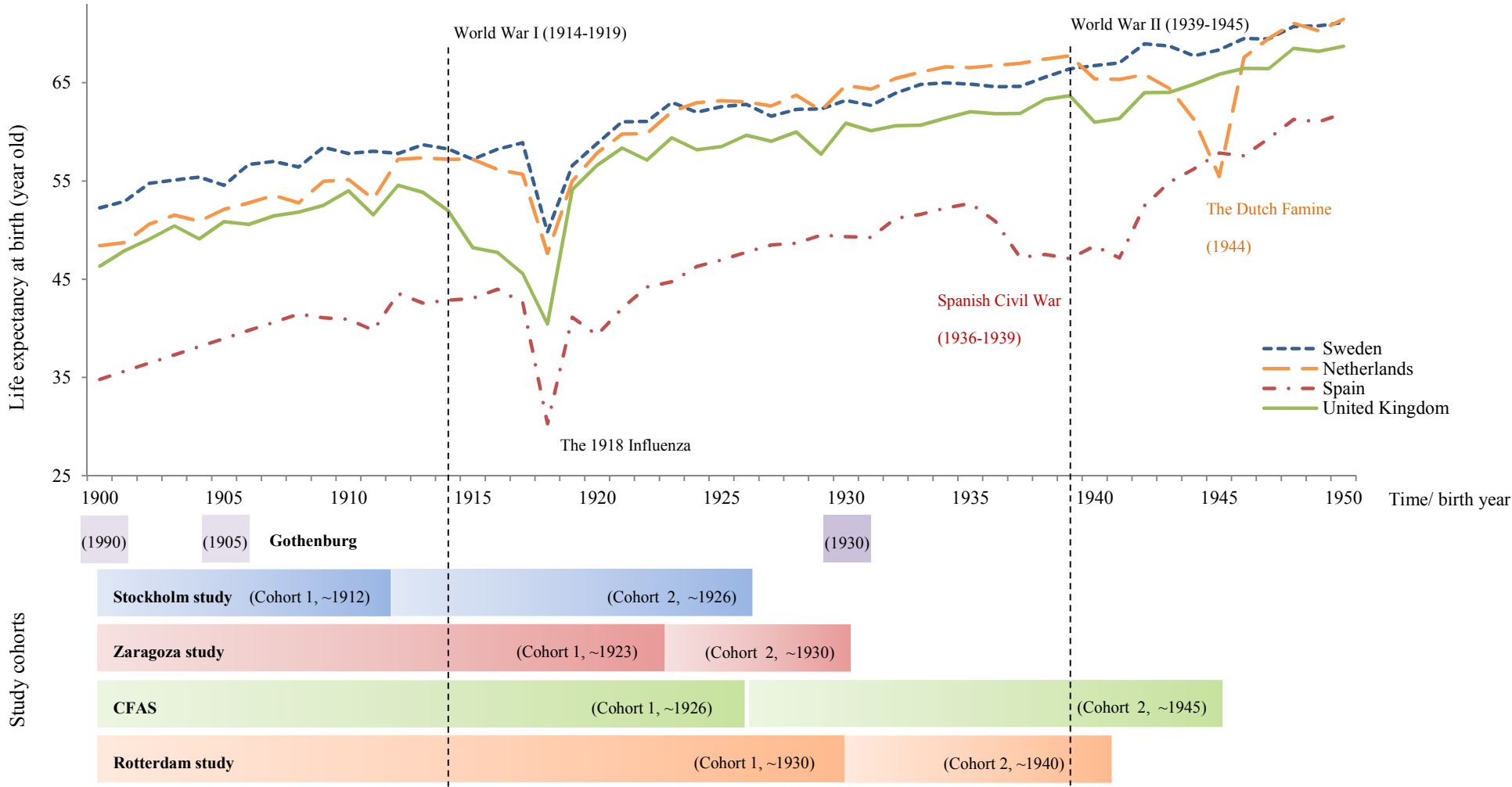**Figure 4** Life expectancy at birth and the birth years of the study cohorts

The upper half is life expectancy at birth from 1900 to 1950 in four European countries and shows the impact of historical events on health. The bottom half is birth years of the study cohorts. The most recent birth years is indicated in each cohort. The Gothenburg study specifically focused on the cohorts born in1900, 1905 and 1930.

Dementia occurrence in Europe: epidemiological evidence and implications for current policy making

Supporting information

S1. Detailed information for the European study comparison

Terminology

Varying terms used in different studies to describe the designs and different stages. A consistent terminology for this paper was developed to reduce confusion and shown below and in the illustrations.

(1) Phase: the investigation of prevalence or incidence generally included two phases, a screening phase and a diagnosis phase. Some recent studies used one-phase only combining screening and diagnosis.

(2) Wave: follow-up investigations for incidence or mortality; the studies which focused on the prevalence of dementia had only one wave, with one or two phases as described above.
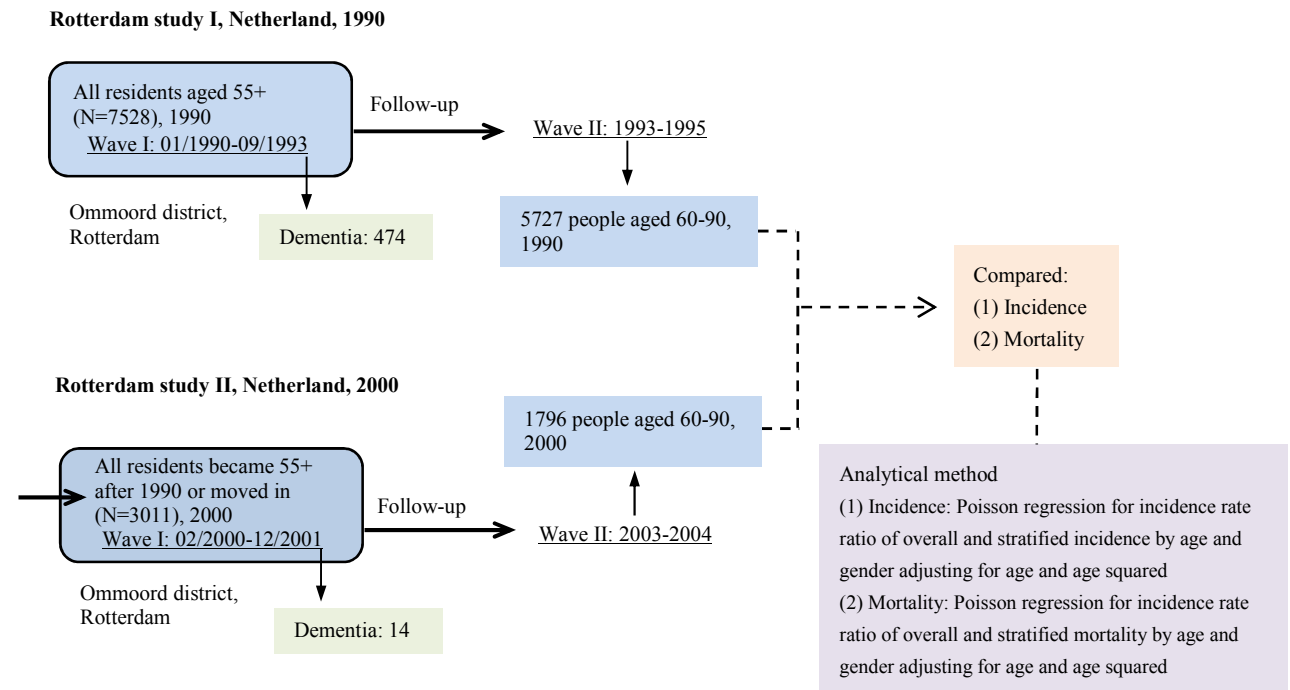
(3) Cohort: the time period of the study for comparison; either two cohorts can be recruited at different times (two fixed cohorts) or dynamic cohorts where one base cohort has additional people newly recruited.

Study design and population sampling

Figure S1 presents the designs and population sampling of the five selected studies.[24-28] Study populations were generally sampled from administrative data, census list or GP registration in the defined areas and stratified by age, varying in their representation of the general population of the relevant age in local areas but kept stable over the two time periods in all cases. All included people living in communities and institutions. Three of the studies were direct comparisons of new cohorts.[1-3] The other two were not such direct comparisons: the Stockholm study compared a local cohort at first time period with those drawn for a national study from the relevant geographical and age specific population;[4] the Rotterdam study is a dynamic cohort with the comparison population formed through recruitment of in-migrants into the geographical area of the relevant age as well as existing residents who had reached 65 and over in the intervening period.[5] The response rate of the first cohort was generally over 70%. In the second cohort, three of the studies had lower response rates ranging from 56% (CFAS II), 63% (Gothenburg) and 64% (Zaragoza).[1-3] Two achieved similar response at both time points (73% Stockholm, 90% Rotterdam).[4-5]
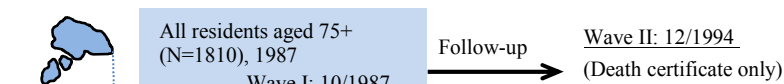
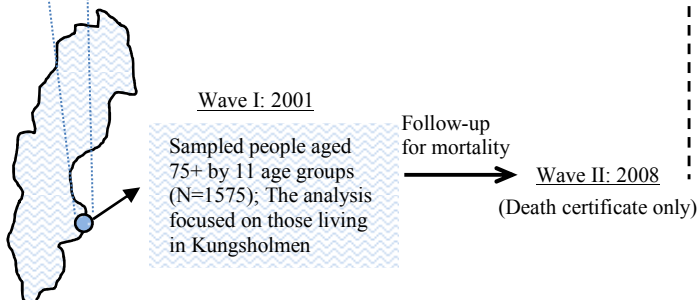**Figure S1 Study designs of the five European studies**

Rotterdam study, Netherland

Rotterdam study I, Netherland, 1990

All residents aged 55+
(N=7528), 1990
Wave I: 01/1990-09/1993

Follow-up

Wave II: 1993-1995

Ommoord district,
Rotterdam

Dementia: 474

5727 people aged 60-90,
1990

Compared:
(1) Incidence
(2) Mortality

Rotterdam study II, Netherland, 2000

All residents became 55+
after 1990 or moved in
(N=3011), 2000
Wave I: 02/2000-12/2001

Follow-up

Wave II: 2003-2004

Ommoord district,
Rotterdam

Dementia: 14

1796 people aged 60-90,
2000

Analytical method
(1) Incidence: Poisson regression for incidence rate
ratio of overall and stratified incidence by age and
gender adjusting for age and age squared
(2) Mortality: Poisson regression for incidence rate
ratio of overall and stratified mortality by age and
gender adjusting for age and age squared

Stockholm study, Sweden

Stockholm study I, Sweden, 1987

Kungsholmen, Stockholm

All residents aged 75+
(N=1810), 1987
Wave I: 10/1987

Follow-up

Wave II: 12/1994
(Death certificate only)

Compared:
(1) Prevalence (phase I)
(2) Mortality
(3) Incidence inferred

Stockholm study II, Sweden, 2001

Sweden National Study on Aging and Care whole
country in Kungsholmen, Stockholm (SNAC-K)

Wave I: 2001

Sampled people aged
75+ by 11 age groups
(N=1575); The analysis
focused on those living
in Kungsholmen

Follow-up
for mortality

Wave II: 2008
(Death certificate only)

Analytical method
(1) Prevalence: standardised to 2001-2003 census in
Kungsholmen; Logistic model for odds ratio of
overall prevalence in two cohorts adjusting for age,
gender and education
(2) Mortality: Kaplan-Meier survival curves; Cox
model for hazard ratio of mortality in two waves
adjusting for age, gender, education and MMSE score
(3) Incidence: inferred by prev./(1-prev.)/duration

Gothenburg study, Sweden

Gothenburg study I, Sweden, 1976-1977

404 people aged 70
(Random sample by
birth date)
303 people aged 75
(Random sample by
birth date)
Wave I: 1976-1977

Gothenburg, Sweden

Gothenburg study II, Sweden, 2000-2001

579 people aged 70
(Random sample by
birth date)
Wave I: 2000-2001

Gothenburg, Sweden

Gothenburg study II, Sweden, 2005-2006

753 people aged 75
(Random sample by
birth date; involved 371
people in the second
cohort 2000-2001)
Wave I: 2005-2006

Gothenburg, Sweden

Compared:
(1) Prevalence at age 70/ 75

Analytical method
(1) Prevalence at age 70/75 : General
linear model and generalised estimating
equations were used to account for
correlations between repeated assessments
on the same individuals in the cohort II
and III; age, gender and birth cohort were
included in the models.

Zaragoza study, Spain

ZARADEMP-0, Spain, 1987-1989

1080 people aged 65+
(Random sample by
age and sex)
Phase I: 1987-1989

Zaragoza, Spain

ZARADEMP-I, Spain, 1994-1996

4803 people aged 55+
(Random sample by
age and sex)
Phase I: 1994-1996

Follow-up

3715 people aged 65+

Phase II: 1997
(ZARADEMP-II)

Zaragoza, Spain

Compared:
(1) Prevalence

Analytical method
(1) Prevalence: calculated separately for
each wave; standardised to 1992 European
population by age and gender; prevalence
proportion ratio for comparison of overall
and stratified prevalence by age and gender

CFAS, UK

CFAS I, UK

7635 people aged 65+ from
Cambridgeshire, Nottingham and
Newcastle (Random sample)
Phase I: 02/1991-09/1994

Follow-up

Phase II: 02/1993-07/1996

Cambridgeshire,
Nottingham,
Newcastle

Compared:
(1) Prevalence

CFAS II, UK

7796 people aged 65+
(Random sample)
Phase I: 2008-2011

Cambridgeshire,
Nottingham,
Newcastle

Analytical method
(1) Prevalence: calculated separately for each
wave; standardised to UK 2011 census by age
and gender and adjusted for non-response and
area deprivation; odds ratio of overall prevalence
in two waves adjusting for age, gender, centre
and area deprivation

Study methods including diagnostic proceeding and criteria

A comparison of methodological features is reported in Table S1. In the analysis of the recent cohorts, most studies attempted to address the problem of drop out from screening to diagnostic phase either through study design or analytical approach. The Stockholm study and CFAS combined two-phase processes into a one-phase interview. The Zaragoza study conducted clinical examination in all suspected cases the day after screening. Apart from the first cohort in Gothenburg study and second cohort in Zaragoza study (ZARADEMP-I), the criteria for dementia diagnosis was DSM-III-R or equivalent (GMS-AGECAT algorithm). The first cohort (1976-1977) of the Gothenburg study used the historical criteria, which was confirmed to have high agreement with DSM-III-R in the second cohort. For the purpose of comparison, the diagnosis of the first cohort in Zaragoza study (ZARADEMP-0) was mapped to DSM-IV.

Table S1 Comparison of methodologies

Study	Population sampling		Screening phase			Criteria to next phase	Diagnosis phase			Follow-up wave
	Method	RR.[e]	Methods	Trained[d]	Instruments (cut-offs)		Methods	Trained[d]	Criteria /instruments	
Rotterdam study I, Netherland, 1990	People aged 55+ living in Ommoord district	73·3%	Interview by research assistants and physician[b]	Yes	MMSE(<26); GMS-A (organic level>0), CAMDEX	(1) All positive cases (2) Suspected cases	Examined by neurologist, neuropsychologist, research physician;	-	DSM-III-R, NINCDS-ADRDA, NINDS-AIREN Informant interview, MRI, medical record	3-4 years
Rotterdam study II, Netherland, 2000	The sub-cohort in 2000; People who became age 55+ after 1990 and moved in the district	89·5%	Interview by research assistants and physician[b]	Yes	MMSE(<26); GMS-A (organic level>0), CAMDEX	(1) All positive cases (2) Suspected cases	Examined by neurologist, neuropsychologist, research physician;	-	DSM-III-R Informant interview, MRI, medical record	3-4 years
Stockholm study I, Sweden, 1987	People aged 75+ in Kungsholmen	76·4%	Interview by two nurses	-	MMSE<24	(1) All positive cases (2) A sample of negative cases	Examined by physicians	Yes	DSM-III-R Clinical examination[a], family interview	6 years
Stockholm study II, Sweden, 2001	Random sample of people living in the same area; stratified by age and time of assessment	73·3%	-	-	-	One-phase interview	Conducted by physicians	Yes	DSM-III-R Interview, cognitive test, clinical examination[a] family interview	6 years
Gothenburg study I, Sweden, 1976-1977	Random sample of people aged 70 and 75 in Gothenburg by birth dates	78·8%	-	-	-	One-phase interview	Interview by a nurse and psychiatrists	Yes	Historical criteria[6], similar to DSM-III-R Psychiatric, physical, neuropsychological examination	-
Gothenburg study II, Sweden, 2000-2001	Random sample of people aged 70 in Gothenburg by birth dates	66·4%	-	-	-	One-phase interview	Interview by psychiatric nurses	Yes	Historical criteria[6] and DSM-III-R Psychiatric, physical, neuropsychological examination	-
Gothenburg study III, Sweden, 2005-2006	Random sample of people aged 75 in Gothenburg by birth dates	63·4%	-	-	-	One-phase interview	Interview by psychiatric nurses	Yes	Historical criteria[6] and DSM-III-R Psychiatric, physical, neuropsychological examination	-
ZARADEMP-0, Spain, 1987-1989	Random sample of people in Zaragoza city; stratified by age and gender with two substitutes	95·2%	Interview by lay interviewers (medical students)	Yes	MMSE (<24/35)[c]; GMS-B (threshold global score>1)	(1) All positive cases (2) A sample of negative cases	Examined by research psychiatrists; two months after screening;	Yes	DSM-III-R AGECAT, HAS, medical reports, IADL	-
ZARADEMP-I, Spain, 1994-1996	Random sample of people living the same area; stratified by age and gender	63·6%	Interview by lay interviewers (medical students)	Yes	MMSE (<24/35)[c]; GMS-B (threshold global score>1)	All "doubtful cases"	Examined by psychiatrists; the next day of screening;	Yes	DSM-IV AGECAT, HAS-AGECAT, medical report, IADL	3 years
CFAS I, UK, 1989-1994	Random sample of GP registration in the defined areas; stratified by age groups	80·0%	Interview by interviewers	Yes	MMSE, ADL, AGECAT items	(1) All AGECAT O3+ (2) 20% of baseline stratified by MMSE score	One month later conducted by interviewers	Yes	DSM-III-R GMS (B3)-AGECAT, CAMCOG, CAMDEX, HAS, HIS, BDS	2 years
CFAS II, UK, 2008-2011	Random sample of GP registration; stratified by age groups in the same areas	56·0%	-	-	-	One-phase interview	Conducted by interviewers	Yes	DSM-III-R GMS (B3)-AGECAT, HAS, HIS, BDS	2 years

[a.] Clinical examination including medical history, physical and neurologic examination, cognitive examination, assessment of depression; [b.] The participants were first screened by MMSE and GMS-B. If the results were positive, CAMDEX was conducted by physician. The participants with both positive results in screening and CAMDES entered diagnosis phase.; [c.] Spanish version of MMSE (Mini-Examen Cognoscitivo) with maximum score 35, suggested cut-off 23 to 24; [d.] Trained in administration of standardised methods; [e.] Response rate (%)

Analytical strategy

Four studies provided a comparison of prevalence.[1-3] The Gothenburg study compared the prevalence at specific ages: 70 and 75 in three cohorts over 30 years.[1] The Zaragoza study and CFAS calculated prevalence separately for each cohort as the sampling was completely independent. Since a one phase and two phase study have different analytical implication, CFAS I and II analyses were structured to identify whether change in design across time required specific adjustment. The Stockholm study and Gothenburg study pooled the data from the two cohorts for comparison and examined for cohort differences in one model. Prevalence was adjusted for age and gender in the three studies with a range of ages.[2-4] The Stockholm study additionally adjusted for education in the model and CFAS conducted extensive analysis on non-response and area deprivation with multiple sensitivity analyses. The incidence of dementia over time was compared in the Rotterdam study.[5] The Stockholm study estimated incidence over two decades using prevalence and mortality.[4]

Comparison of prevalence, incidence and mortality across cohorts

Table S2 reports prevalence estimates in the four European studies by men and women. The conclusion (C.) in the table was based on the interpretation in original papers. The study may suggest stable (S) or decreased (D) prevalence although the difference did not achieve statistical significance. The decrease achieving statistical significance is underlined (D). Similar information was extracted from the Rotterdam Study and Stockholm Study for comparison of incidence (Table S3) and mortality (Table S4).

Limitations of the studies

This analysis has shown considerable variation in methodology across the studies, with some achieving comparison through inference of prevalence and others carrying out direct comparisons. Meta-analysis is not therefore possible. Populations vary in their responses more recently with the UK and Spain suffering particularly from drop in response – the UK from a higher original point. The CFAS analysis provided extensive sensitivity analyses to address potential impact of dropouts. The response rates in Scandinavian studies have been steady although differential response within the refusal groups is still possible. Another additional factor which could have influenced the estimated prevalence and incidence is the likelihood of dementia being mentioned in medical records if these are used to supplement partial information. Medical records data were used in some studies (not the Stockholm and CFAS study) which could be expected to increase estimates as this method will be subject to change diagnostic boundaries and greater likelihood of contact with services across time. These data are not provided so that its impact cannot be assessed.

Table S2 Comparison of prevalence in the four European studies

Prevalence (%)		Cohort (yr.)	N	All	65-69	70-74	75-79	80-84	85-89	90+	C.[1]
Stockholm study	Total	I (1987)	1739	17.5	-	-	5.7	9.6	20.4	32.0	S
		II (2001)	1575	17.9	-	-	4.7	12.0	19.5	39.0	
	Men	I (1987)	549	12.8	-	-	5.2	9.8	13.6	22.2	S
		II (2001)	422	10.8	-	-	7.0	8.0	14.5	24.0	
	Women	I (1987)	1748	19.2	-	-	5.9	9.5	22·0	34.1	S
		II (2001)	1153	20.5	-	-	4.5	14.5	20.0	40.5	
Zaragoza study	Total	I (1988)	1080	5.2	0.7	3.0	4.8	11.5	-	-	S
		II (1994)	3715	3.9	0.7	2.1	2.2	7.1	16.2	-	
	Men	I (1988)	435	5.8	0.9	4.4	7.1	15.5	15.6	-	D
		II (1994)	1516	2.3	1.0	1.2	2.0	4.3	10.7	-	
	Women	I (1988)	645	4.9	0.6	1.8	3.2	9.1	18.6	-	S
		II (1994)	2199	5.0	0.4	2.8	2.4	8.9	19.5	-	
CFAS	Total	I (1989)	7635	8.3	1.7	3.0	7.5	13.5	25.0	37.5	D
		II (2008)	7796	6.5	1.5	3.0	6.0	10.0	16.0	30.1	
	Men	I (1989)	3045	7.4	1.7	2.2	5.7	14.6	19.8	68.2	D
		II (2008)	3550	4.9	1.2	3.0	5.2	10.6	12.8	17.1	
	Women	I (1989)	4590	9.4	2.0	2.9	7.4	13.9	26.5	32.3	D
		II (2008)	4246	7.7	1.8	2.5	6.2	9.5	18.1	35.0	
Gothenburg study	Total (age 70)	I (1976)	404	2.0	-	-	-	-	-	-	S
		II (2000)	499	2.4	-	-	-	-	-	-	
	Men (age 70)	I (1976)	177	1.7	-	-	-	-	-	-	S
		II (2000)	229	0.9	-	-	-	-	-	-	
	Women (age 70)	I (1976)	277	2.2	-	-	-	-	-	-	S
		II (2000)	270	3.7	-	-	-	-	-	-	
	Total (age 75)	I (1976)	303	5.0	-	-	-	-			S
		II (2005)	753	6.0	-	-	-	-	-	-	
	Men (age 75)	I (1976)	117	6.8	-	-	-	-	-	-	S
		II (2005)	321	6.9	-	-	-	-	-	-	
	Women (age 75)	I (1976)	186	3.8	-	-	-	-	-	-	S

[1.] C: Conclusion of the comparison papers; S: the study suggested stable prevalence over time; D: the study suggested decreased prevalence, over time; D̲: the decrease of overall estimates achieved statistical significance.

Abbreviation: yr.: year; -: no information in the papers

Table S3 Comparison of incidence in the Rotterdam study

Incidence (per 1000 person-year)		Year	p-y	All	60-69	70-79	80-89	Conclusion
Rotterdam study	Total	I (1990)	25696	6.6	1.3	9.7	31.5	Decreased
		II (2000)	8384	4.9	1.1	6.4	26.4	
	Men	I (1990)	-	6.3	1.8	9.8	30.9	Decreased
		II (2000)	-	4.5	1.4	4.7	30.4	
	Women	I (1990)	-	6.8	0.9	9.5	31.8	Decreased
		II (2000)	-	5.2	0.8	7.8	24.2	

Table S4 Comparison of mortality in the Rotterdam and Stockholm study

Mortality (per 1000 p-y)		Year	p-y	All	60-69	70-79	80-89	C.[1]
Rotterdam study	Total	I (1990)	25696	22.0	11.1	25.1	69.3	D
		II (2000)	8384	14.0	6.4	21.7	33.1	
	Men	I (1990)	-	29.0	16.4	32.4	109.1	D
		II (2000)	-	18.5	11.8	28.4	38.9	
	Women	I (1990)	-	22.0	6.7	19.8	50.8	D
		II (2000)	-	14.0	2.1	15.7	29.0	
Stockholm study[2]	Total	I (1987)	8551	95.5	-	-	-	D
		II (2001)	6672	105.7	-	-	-	
	Men	I (1987)	-	112.9	-	-	-	D
		II (2001)	-	106.4	-	-	-	
	Women	I (1987)	-	90.4	-	-	-	D
		II (2001)	-	105.4	-	-	-	

[1.] C: Conclusion of the comparison papers; D: the decrease of overall estimates achieved statistical significance.

Abbreviation: p-y: person-year; yr.: year; -: no information in the papers

[2.] The figures are different from the original paper (Qiu et al., 2013) as they are corrected by the authors of Stockholm study; after adjusting for age, gender and education, the hazard ratio of two cohort (II vs. I) was 0.88 (95% CI: 0.79, 0.98), which indicated that the younger cohort had significantly longer survival time than the older cohorts.

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