Department of Public Health Sciences

Degree Project for the Master's Program in Global Health

Temporal trends in the incidence of dementia hospitalisations in Sweden

Based on the Swedish National Inpatient Register (Hospital Discharge Register) during 1980-2011

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ABSTRACT

BACKGROUND**:** Dementia imposes a significant burden to global health with currently 47 million people in the world suffering from it. It is estimated that by 2050 the number of people affected will increase to 135 million, of which 71% will be living in lower and middle income countries. Temporal trends in dementia incidence are a useful tool to understand the disease epidemiology. Yet, for most countries dementia data is limited or incomplete. In Sweden dementia incidence trends can be calculated using hospitalisations with reported dementia from the Swedish National Inpatient Registry.

AIM: To describe and compare dementia incidence temporal trends within Sweden from 1980 to 2011, and to explore the relationship between incidence of dementia and sociodemographic and diagnostic factors.

METHODS: 2,549,857 men and women with information regarding hospitalisation with reported dementia from the Swedish birth cohorts 1920-1940 were followed for 31 years. Outcome was ascertained through linkage to the Swedish National Inpatient Registry via lopnr (a unique personal serial number). Dementia hospitalisation, sex and educational level were classified into categorical variables. Dementia incidence rates were obtained through Poisson regression model. Cox regression analyses were performed to determine risk hazard ratios (HR) with 95% confidence intervals (CI). Descriptive statistics were used to explain the temporal trends.

RESULTS: In Sweden overall dementia hospitalisations and crude incidence trends (not adjusted for age) increased during 1980-2011. Women and individuals with low educational level showed the highest incidence rates. Yet, during 1997-2011 the risk of being hospitalised with dementia was lower for women (HR: 0.94; 95% CI: 0.93 to 0.96) and was lower among individuals with high educational level (HR: 0.91; 95% CI: 0.90 to 0.93), age-adjusted. Throughout the studied period age was a driver for dementia incidence trends: the oldest age categories consistently presented the highest dementia incidence rates.

CONCLUSION: Swedish dementia incidence trends continued to rise from 1980 to 2011 but differed depending on sex and education. These findings will inform public health policy regarding temporal trends and may help direct the global action against dementia.

Key words: Dementia; Incidence; Time Trends; Registries; Epidemiology.

CONTENTS

ABBREVIATIONS

AD   Alzheimer's Disease

ADL   Activities of Daily Living

CI   Confidence Interval

DALYs   Disability-Adjusted Life Years

DLB   Dementia with Lewy bodies

DSM   Diagnostic and Statistical Manual of Mental Disorders

GBD   Global Burden of Disease

HIC   High Income Countries

HR   Hazard Ratio

ICD   International Classification of Diseases

IPR   Swedish National Inpatient Register

LISA   Longitudinell integrationsdatabas för sjukförsäkrings och arbetsmarknadsstudier
            (*Longitudinal integration database for health insurance and labour market studies*)

LMIC   Lower and Middle Income Countries

MMSE   Mini Mental State Examination

NCDs   Non-Communicable Diseases

NPR   National Patient Registry

PY   Person-Years

RTB   Registret över totalbefolkningen (*Total Population Register*)

SveDem   Swedish Dementia Registry

UN   United Nations

YLDs   Years Lost to Disability

YLLs   Years of Life Lost

LIST OF FIGURES AND TABLES

INTRODUCTION

An ageing world

The world has experienced an unprecedented population growth in the last century. In line with the epidemiological transition outlined by Omran (1) the world has moved from infectious diseases epidemics to extended non-communicable diseases (NCDs); this has resulted in a bigger world population, living longer and suffering from long-lived chronic illnesses. In the last decade, the United Nations (UN) has manifested that "ageing presents social, economic and cultural challenges to individuals, families, societies and the global community" (2,3). These challenges are enhanced and felt more acutely in societies of low and middle income countries (LMIC) where, due to complex epidemiological trends, populations are ageing at faster rates. By year 2050, 80% of the world's older population is expected be concentrated in LMIC regions (2).

Amongst all the conditions and diseases linked to ageing, dementia is one of the most alarming and it is deemed to be one of the most pressing social and health crises of the 21st century. The combined effects of longer lives and increased population has made dementia a so-called "Silent Epidemic" (4). Dementia is an overarching term for a decline in mental ability severe enough to interfere with daily life, it includes Alzheimer's disease (AD), vascular dementia, dementia with Lewy bodies (DLB) and Parkinson's disease amid others (5). AD is the most prevalent accounting for 50%-75% of the total cases (6). Currently it is estimated that 47 million people in the world suffer from dementia (Figure 1) – incidentally, every 3 seconds a new case of dementia is diagnosed (7). These numbers are projected to increase to 135 million in 2050, with 71% of the affected people living in LMIC (8,9).
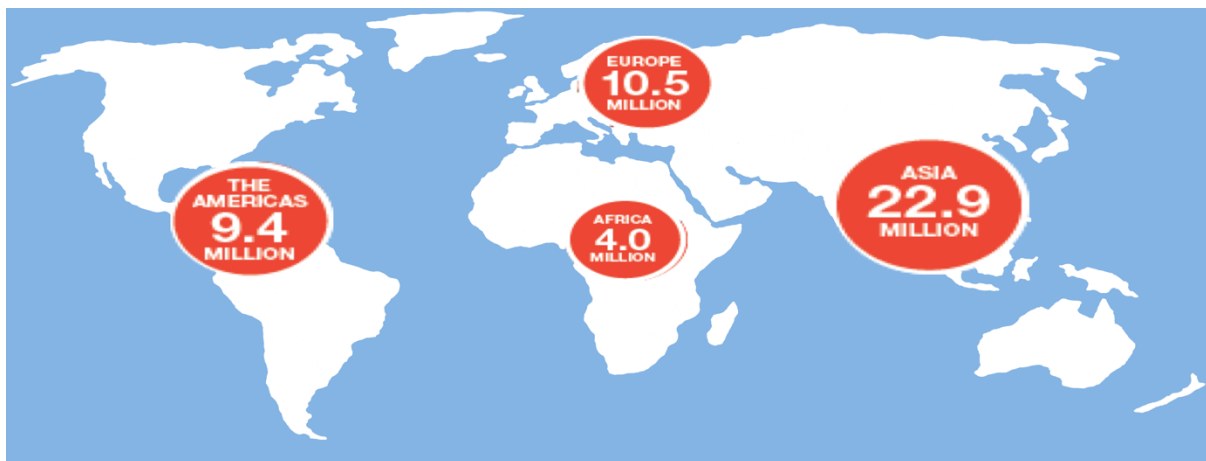
Figure 1| Estimated number of people with dementia in each world region in 2015. (Adapted World Alzheimer Report (5)).

The burden of dementia: disability and cost

Among the world's oldest, dementia is one of the the principal chronic disease contributor to disability, burden of disease and need for exhaustive and personal care (9). People that suffer from dementia usually struggle with cognitive functions such as thinking, language, memory, personality, understanding and everyday activities (6). The burden of a disease is commonly expressed in disability-adjusted life years (DALYs), which quantify both premature mortality in years of life lost (YLLs) and disability in years lost to disability (YLDs) within a population (10). In 2010, NCDs accounted for 54% of the global burden of disease (GBD) compared to 43% just two decades earlier. Neurologic disorders and cerebrovascular diseases combined accounted for 7.1% of the total GDB measured in DALYs (all causes and ages), of which AD and other dementias were responsible for 0.46% (11). In Sweden, Alzheimer's disease appeared in the top 10 leading causes of DALYs in 2010 but not back in 1990 (12). Inexorably, the marked increase in dementia-related DALYs results in heightened needs from patients which challenge the world's healthcare systems and societies both socially, scientifically and economically to meet those needs.

The care for dementia is costly and exerts a burden both on the family nucleus and on the healthcare providers. Globally, in 2010 around US$ 604 billion dollars were spent in dementia related care (13), in 2015 the cost increased to US$ 818 billion and it is estimated that by 2018 dementia care will cost 1 trillion US$ (8). In Sweden, the cost of illness of dementia was estimated to 6,186.8 millions € in 2008 (14) and by 2012 it rose to 7,070.4 millions € (15); more specifically to establish a dementia diagnosis costs 849 € per diagnosed patient in primary care and 1,334 € within a specialised unit (16). Countries, such as many LMICs, with an already weak healthcare system and strained social services cannot adequately provide for those living with dementia and their caregivers with suitable support. Thus, dementia is a pressing issue that needs to be tackled globally in order to counteract its social, economic and health consequences.

Dementia demographics and trends

Given the rising numbers of elderly people both in high income countries (HIC) and LMIC (Figure 2.a), it is important to understand how the number of cases and incidence rates of dementia are changing. Moreover, certain groups within society are at higher risk of suffering from dementia, and thus policy makers should be aware of dementia demographics

in order to make informed decisions. Dementia is considered to be a gendered epidemic because women carry the biggest burden of disease (17) having higher age-specific prevalence and incidence of dementia (8). Similarly, it is believed that secular improvements in education in HICs might result in a progressive decline in age-specific incidence of dementia (8) since years of formal education may be a protective factor against dementia (8,18). Therefore, analysis of incidence trends and associated sociodemographic variables in the past decades can provide insightful information in order to implement tailored prevention strategies and promote effective policies for dementia care and treatment in the coming years.

Unfortunately, in most, if not all LMICs, there are not wide databases of patients' diagnoses or representative population based studies, and if so the accounts are either partly incomplete or not detailed enough to include dementia diagnosis (19). Thus, LMICs can benefit from HICs' databases, experience and expertise of dealing with dementia epidemic (20), for example, by adjusting the national healthcare systems to make them ready and prepared and putting forward policies for dementia awareness.
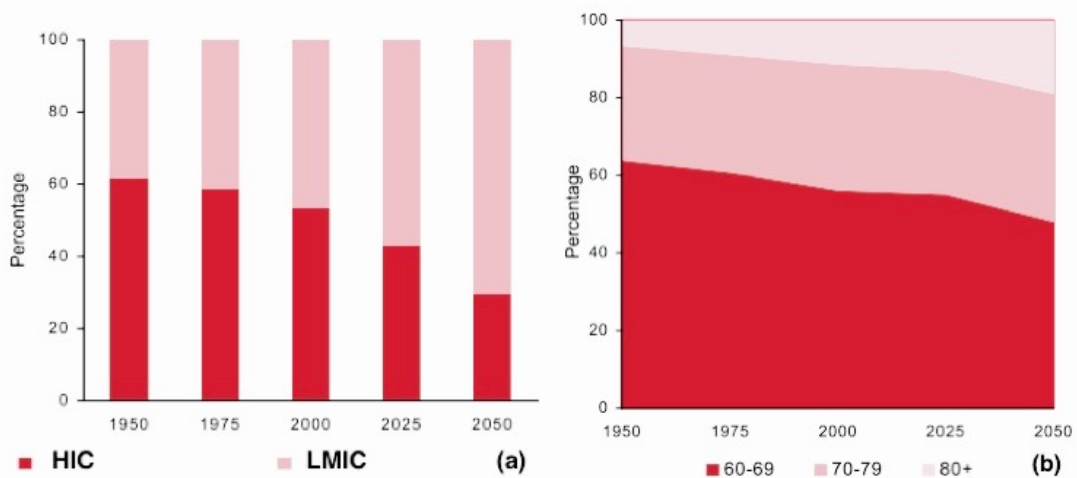
Figure 2| (a) Distribution of world population aged 80 or over by income regions, 1950-2050. (b) Distribution of population aged 60 or over by age groups: world, 1950-2050. Adapted from UN, Population Division (21).

According to the World Alzheimer Report 2015, the estimated worldwide crude prevalence of dementia was 5.2% (8), affecting roughly 5-8% of people over 65 years, 15-20% of people over 75, and about 25-50% of those aged 85 years or more (6,22). Sweden has a markedly aged population: the 65+ years old account for the 18% of the total

population. Moreover, currently it is the only country whose 80+ age group represents more than 5% of total population (23). Globally, only slightly more than 1.6% of the total human population is over 80 years old but this proportion is projected to increase up to 4.3% by 2050 (3,21). Also, the number of 80+ people, those with higher dementia prevalence, has been increasing more rapidly than the older population as a whole (Figure 2.b). Therefore, Sweden could be used as an epidemiological-template country and exploring Sweden's past decades might allow to model and understand future global dementia trends.

Applicably, since 1964 the Swedish National Inpatient Register (IPR), part of the National Patient Registry (NPR), was gradually implemented to cover hospital discharges and all doctors in Sweden, public and private, are obliged to deliver data to the IPR. With reference to dementia, by 1973 national coverage of psychiatric clinics was achieved and in 1987 the IPR had full national coverage (24). Yet, this resource has been underused until now with regards to dementia. Thus, better understanding of what the Swedish registers entail, is likely to help our understanding of what might happen in other countries, in the future. The knowledge gap addressed in this thesis is both using IPR to evaluate dementia trends and whether dementia incidence is indeed increasing, has become stagnant or on the contrary has started to decrease. In other words, the thesis addresses trends of dementia, which is currently a contested topic (25–28).

Given the above outlined importance of dementia and understanding future trends, this project aims to analyse the cases of dementia during the period from 1980 to 2011 in the IPR, also called the Hospital Discharge Register, within Swedish cohorts born from 1920 to 1944.

BACKGROUND

Temporal trends in the incidence of disease over time may help to indicate alterations in risk factors (27). In Sweden, to the best of our knowledge, data from the IPR has never been used before to study time trends in the incidence of dementia. Previous studies have considered the viability of using Swedish registers to detect dementia by looking at the sensitivity and specificity of dementia. The NPR had a sensitivity of 33% and specificity of 98% (29) and an overall positive predictive value of diagnoses in the register of 85-95% (24). Moreover, it is believed that the low sensitivity differs with different categories of people (30). Overall, the aforesaid studies agree that despite moderate sensitivities, based on the high specificities, the quality of dementia coding in the registries is acceptable (29) and that is safe to use register-based data in certain epidemiological studies of dementia (30). Recently, Swedish registries have begun to be used in studies that explore marital status, cardiovascular and cognitive fitness as risk factors for dementia (31–33).

However, there is limited literature available on country-specific incidence of dementia (34), and often studies analysing incidence trends offer a conflicting and contradicting picture (27). Within Sweden a previous population study found no statistically significant trend in dementia's incidence between the period 1947-1957 and 1957-1972 (35). Yet a study carried out in central Stockholm observed stable dementia prevalence from late 1980s to the early 2000s suggesting a reduced incidence rate (4,36). Thus the present study using IPR for dementia hospitalisations explores the following decades' incidence of first hospitalisation with reported dementia diagnosis for the whole population during the period 1980-2011. Besides, through the period being studied, the International Classification of Diseases (ICD) diagnosis of dementia changed (ICD8, ICD9 and ICD10). It has been established that coding changes between revisions of the ICDs can result in significant changes in long-term trends in diagnosis (37) and that diagnostic criteria influences prevalence (38). Therefore, analysis of the dementia hospitalisation incidence trends should consider ICDs' amendments.

The thesis aims to identify the temporal trends in absolute numbers of first hospitalisation with reported dementia diagnosis in the IPR; determine using incidence rates whether these trends can be explained by sheer population size changes and to obtain age-standardized trends of dementia hospitalisations over time to determine whether the trends can be explained by changes in the age structure of the population. Moreover, the thesis will analyse the effects of sociodemographic factors such as gender and education on dementia trends.

RESEARCH QUESTION

What is the time trend in the incidence of first-time hospitalisations with reported dementia diagnoses in the Swedish National Inpatient Register (1980-2011) and how should it be understood in relation to changing population size, age structure, gender, levels of educational attainment and within ICD-systems?

AIM AND SPECIFIC OBJECTIVES

The aim of the thesis is to describe and compare dementia incidence trends within Sweden from 1980 to 2011, and to explore the relationship between incidence of dementia and sociodemographic and diagnostic factors.

i.   To determine the absolute number of dementia hospitalisations per year and the dementia hospitalisations crude incidence rate assessing whether there is a time trend during 1980-2011.

ii.   To determine the dementia hospitalisation incidence rate and assess whether there is a time trend during 1980-2011 within different categories with regards to sex, education and age.

iii. To account for diagnostic factors, determine the dementia hospitalisation incidence rate, assess whether there is a time trend during the ICD10 period (1997-2011) and establish how sociodemographic factors such as sex, education and age may affect it.

METHODOLOGY

Study setting

The study used the data from the Swedish Inpatient Registry (IPR) for the birth cohorts from 1920 through 1944. Individuals were followed up for dementia diagnosis during 31 years: from 1st January 1980 until 31st December 2011, when data availability ends. The total population in Sweden in 1980 was 8,317,937 and rose to 9,482,855 by 2011. The cohorts were compared against the Swedish total population for adequacy in age categories and sex (http://www.statistikdatabasen.scb.se) by calculating the relative percentage in each age category. No major discrepancies were found and thus the chosen cohorts were assumed to be representative of the total Swedish population within appropriate age categories.

Study design

This was a population-based cohort study of Swedish population born between the years 1920-1944. The cohorts were defined using Registret över totalbefolkningen (RTB) (*Total Population Register)* and individuals from correct cohorts were identified based on lopnr. Lopnr is a unique identifier, similar to the Swedish personal number, created when the dataset is provided to the researcher from Statistika Centralbyrån (*Statistics Sweden*). This way the lopnr can be used to find individuals across different registers and connect their information. For the study, individuals' sex and birth information was derived from RTB and the date of birth from Longitudinell integrationsdatabas för sjukförsäkrings och arbetsmarknadsstudier (LISA) (*Longitudinal integration database for health insurance and labour market studies*). Their records were linked to IPR through their lopnr and first hospitalisations with reported dementia were selected based on ICD codes. Date of the hospitalisation was registered as timing of dementia onset. The educational information was retrieved from the 1970 census. Observations were likewise linked to Cause of Death Register and the Immigration and Emigration Register for censoring purposes.

The total number of individuals included in the study from 1st January 1980 to 31st December 2011 was 2,549,857. The exclusion criteria used to define observations is illustrated in Figure 3. Excluded from the initial records of the RTB were those born before 1920 because for older cohorts the well established relationship of dementia increasing with age was not observed, it was assumed that older cohorts died prior to register start date and thus were not able to reliably represent dementia in old age; those that exited

(emigrated/died) the study before 1980 and those whose age at hospitalisation with dementia was <60. The study was limited to old-age dementia and thus familial cases, which account only to less than 5% of total dementia cases and have earlier onsets (13), and sporadic early-onset dementia were omitted by setting the age at ≥60. For studying the impact of education on dementia incidence, those lacking complete educational information were also excluded.

Total individuals in RTB
[n=4,220,467]

31.53% [n=1,330,812]
excluded because birth year <1920

Total individuals from
1920-44 birth cohorts
[n=2,889,655]

0.11% [n=3,189]
excluded because age at hospitalisation with dementia <60

Individuals diagnosed with
dementia at ≧60
[n=2,886,466]

7.97% [n=336,609]
excluded if observation exit (die or emigrated) prior to 1980

Total individuals in
incidence sample
[n=2,549,857]

4.76% [n=200,727]
excluded because educational information was missing in 1970 census

Total individuals with
educational information
[n=2,349,130]

Figure 3 | Flowchart with exclusion criteria for individuals to be included in the study.

The outcome for the study was the number of individuals hospitalized with reported dementia diagnosis during the period 1980–2011. Only first-time diagnoses were considered into the study in order to avoid repeated count of events, since dementias are neurodegenerative disorders from which patients do not get cured and cannot relapse into (39). During the timespan that the study encompassed the ICD coding changed twice: in 1986 from ICD8 to ICD9 and in 1997 from ICD9 to ICD10. Thus the codes considered for dementia diagnosis varied within periods, with a broad classification within ICD8 and more detailed one in ICD10 (Table 1).

The study design included the total target population thus no sampling strategy was used.

Table 1| ICD codes included in the study.

	Code	Description
ICD 8 **(1968-1986)**	290.0	Senile dementia
	290.1	Presenile dementia
ICD 9 **(1987-1996)**	290.0	Senile dementia, uncomplicated
	290.1	Presenile dementia
	290.2	Senile dementia with delusional or depressive features
	290.3	Senile dementia with delirium
	290.4	Arteriosclerotic dementia
	331.0	Alzheimer's disease
ICD 10 **(1997-present)**	F00	Dementia in Alzheimer's disease
	F01	Vascular dementia
	F02	Dementia in other diseases classified elsewhere
	F03	Unspecified dementia (including presenile and senile dementia)
	G30	Alzheimer's disease
	G30.1	Alzheimer's disease late onset
	G30.8	Other Alzheimer's disease
	G30.9	Alzheimer's disease, unspecified

Main study variables

Dependent Variable

Dementia hospitalisation: The outcome variable of the study was dementia hospitalisations, which were defined by ICD codes for dementia diagnosis presented in Table 1. Dementia was classified as a binary variable in which [0] referred to those who were never hospitalized with reported dementia diagnosis, emigrated, died or exited the study at the end of follow up (31st December 2011); and [1] as those hospitalized with any dementia code specified in Table 1.

Dementia incidence: Incidence was defined as "the rate of occurrence of new cases arising in a given period in a specified population" (10). The dementia hospitalisation incidence rates were presented per 10,000 person-years, yearly over time.

Independent variables

ICD codes: The criteria for the diagnosis of dementia can have a direct effect on the crude number of dementia cases and on temporal trends. Thus, the different ICD periods were categorised and highlighted to consider whether changes in incidence could be related to changes in ICD. Hospitalisations up to 31st December 1986 were coded as [1] for ICD8; from 1st January 1987 to 31st December 1996 were coded as [2] for ICD9 and from 1st January 1997 onwards were coded [3] for ICD10. More than 86% of subjects diagnosed with dementia entered the registry within ICD10 period (Table 2).

Table 2 | *Description of study individuals by ICDs.*

	Non-dementia	Dementia Diagnosis	Total
ICD8	109,973	719	110,692
%	99.35	0.65	100.00
ICD9	234,952	10,768	245,720
%	95.62	4.38	100.00
ICD10	2,075,502	117,943	2,193,360
%	94.63	5.37	100.00
Total	2,420,427	129,430	2,549,857
	94.93	5.07	100.00

Sex: was coded as a binary variable with men coded [0] and women [1].

Level of education: the data for this variable was retrieved from the 1970 census. The number of years of education were available divided in seven categories: 1)Folkskola (*primary school*) ≤7 years, 2)Folkskola (*primary school*) =8 years, 3)Folkskola (*primary school*) ≥9 years, 4)Realskola (*junior secondary school*), 5)Allmänt gymnasium (*senior secondary school)*, 6)Eftergymnasial (*after high school)* and 7)Forskarutbildning (*doctoral studies*). For the purpose of the study three new different categories were created: categories 1-4 were placed under low educational level (*förgymnasial=pre-high school*) coded [1]; 4-5 under middle educational level (*gymnasial=high school*) coded [2] and 6-7 under higher educational level (*eftergymnasial=after high school*) coded [3]. Those without information on education level were excluded from the study (see Figure 3 for the exclusion rationale).

Analysis

Incidence rate was calculated for both sexes, with individual participants contributing person-years (PY) from entry in 1980, or in the year they turned 60 (whichever came first), until they were diagnosed with dementia, died free of dementia, emigrated or follow up ended on December 31st 2011. For the analysis, the study period was divided into five years' intervals, 1980-84, 1985–89, 1990–94, 1995–99, 2000–04, 2005–09 and 2010-11. The last category includes only 2 years due to data availability. The population was divided into seven age groups, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89 and 90-92 years. The last category includes only 3 years. The lower margin was delimited at 60 because it is the cut-off generally accepted by the UN when referring to older population (3,40) and also dementia presents different aetiology for early onset (13). The upper limit was based on the study observations in which the oldest participant was 92 years old. For the age stratified categories, the incidence rate was age standardised to the general population in Sweden as 31st December 2000 (http://www.statistikdatabasen.scb.se), to have a standard rate for each age category.

Bearing in mind that 86% of the total cases occur within the ICD10 (Table 2), in order to perform a more detailed analysis of the period 1997-2011 the age categories and time intervals were adjusted to every two years' intervals as follows:

-age (60-62, 63-64, 65-66, 67-68, 69-70, 71-72, 73-74, 75-76, 77-78, 79-80, 81-82, 83-84, 85-86, 87-88, 89-90,91-92);

-years (1997-1998, 1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011).

The crude incidence of dementia for the general population and the incidence rate according to sex, education and age were calculated for 5-years intervals. Poisson regression model was used to estimate dementia incidence rate and assess temporal trends (41,42). The two-sample t-test was used to compare incidence rates in men and women, and educational levels. Significance was set at $\alpha=0.05$.

A survival analysis Cox regression model was used to study the difference in risk of hospitalisation within calendar years during the ICD10 period (1997-2011). The model was adjusted for age as an underlying factor, that is individuals became at risk at their age at study entry, in this case at the start of ICD10 (1997). In this way, the fact that older people will have higher dementia risk was accounted for. The initial model was further adjusted, in a stepwise manner, for the categorical variables of sex and educational attainment as independent covariates. All statistical analyses were performed with the statistical software Stata (Version 14.1, Stata Corporation, and College Station, TX, USA).

However, it is important to note that some statisticians argue that inferential statistical tests are not pertinent when interpreting time trends findings that include the total target population (27,43). The aim of the thesis is mainly descriptive, thus descriptive statistics and trend interpretation were the primary analyses performed.

Ethical considerations

Permission was granted for the student to use the data for purposes of the Master's thesis by the Public Health Sciences Department at Karolinska Institutet. The main ethical concern raised within the study was to preserve the individuals' identity anonymous. The use of the lopnr did not allow the researcher to identify an individual's personal details. However, one might argue that when many subcategories are used identification may be possible. Here, relatively large groups based on sex, age, dementia diagnosis and educational level were used. Thus, it is highly unlikely that individuals could be identified.

RESULTS

Descriptive statistics and crude numbers of dementia hospitalisations

Table 3 | Descriptive characteristics of study population.

Characteristic	Subgroup	All (N=2,549,857)
Sex (%)		
	Men	1,282,726 (50.3)
	Women	1,267,131 (49.7)
Age (Mean, SD)		78.7 (6.6)
Educational attainment (%)		
	Low Level	1,440,961 (56.53)
	Middle Level	685,858 (26.89)
	High Level	222,311 (8.71)
	Unknown	200,727 (7.87)
Dementia status (%)		
Dementia hospitalisations		129,347 (5.07)
Dementia-free individuals		2,420,510 (94.93)

The total number of first dementia hospitalisations for the whole period (1980-2011) was 129,347 (Table 3) and the crude trend showed a massive continuous increase: from 13 hospitalisations with dementia in 1980 to 14,492 in 2011 (Figure 4). Yet, the lower number at the begging of the study could be misleading since the oldest participants were only 60 years old and dementia risk increases with age. Overall, the average age at hospitalisation with reported dementia for the study population was 78.7 (± 6.6) (Table 3). Looking at separate decades without adjusting for age, within the last 10 years there was an increase of 213% in cases from 4,635 in 2001 to 14,492 in 2011. Moreover, the last 6 years alone (2006-11) accounted for 56% of all the hospitalisations with reported dementia within the studied period.
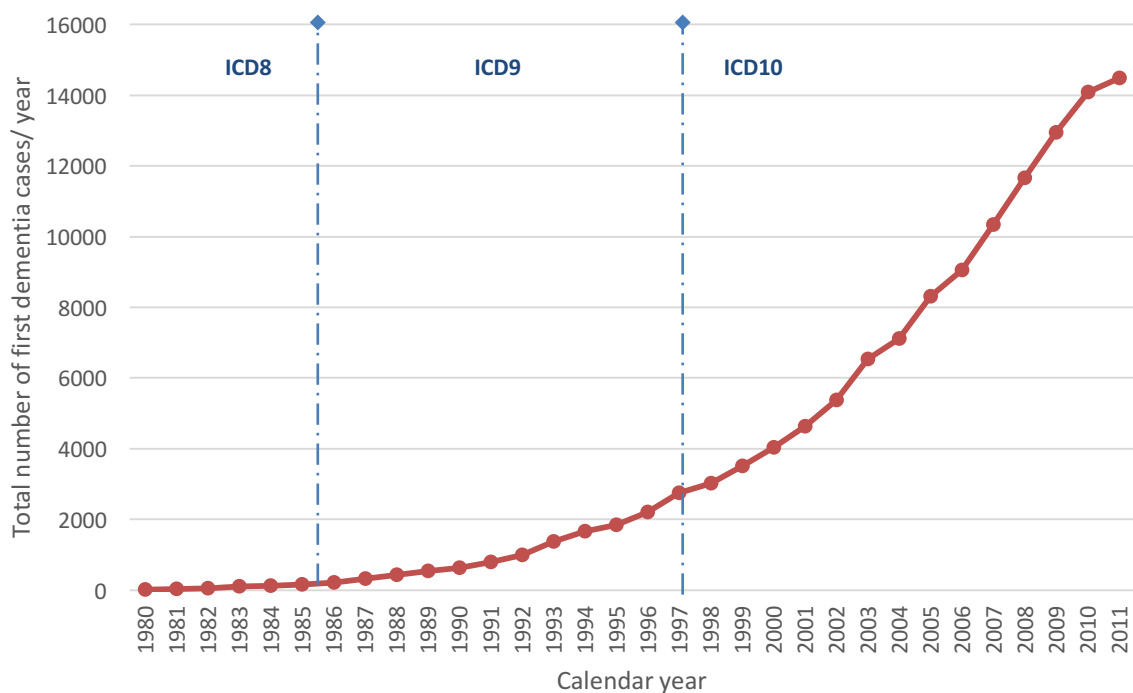

Figure 4 | Annual first time cases of dementia for men and women in Sweden (birth cohorts 1920-1944), from 1980 to 2011.

Incidence rates of dementia hospitalisation

Table 4 | Time interval-specific number of person-years at risk, number of dementia hospitalisations, and incidence rates (per 10,000 person-years, with 95% confidence interval (CI), in Swedish population (birth cohorts 1920-1944).

Years	Persons years at risk	Dementia hospitalisations	Incidence rate	95% CI
1980-84	12,495,059	338	0.3	0.2-0.3
1985-89	12,078,615	1,679	1.4	1.3-1.4
1990-94	11,540,010	5,436	4.7	4.6-4.8
1995-99	10,805,352	13,317	12.3	12.1-12.5
2000-04	9,834,830	27,669	28.1	27.8-28.5
2005-09	8,571,819	52,295	61.1	60.5-61.5
2010-11	3,008,825	28,612	95.1	93.9-96.2

The five-year period incidence of hospitalisations with reported dementia (not age-adjusted) increased substantially during the study period (Table 4). The incidence rose from 0.3 (95% CI:0.2-0.3) per 10,000 person-years in the first 5-year interval of the study period to 95.1 (95% CI: 93.9-96.2) per 10,000 person-years in the last interval (Table 4). In Figure 5, the change from ICD8 to ICD 9 did not seem to affect the incidence trends substantially (3.6-fold increase in incidence rate), after 1997 with the implementation of ICD10 the incidence rate appeared to increase more steeply (7.7-fold increase in incidence rate).
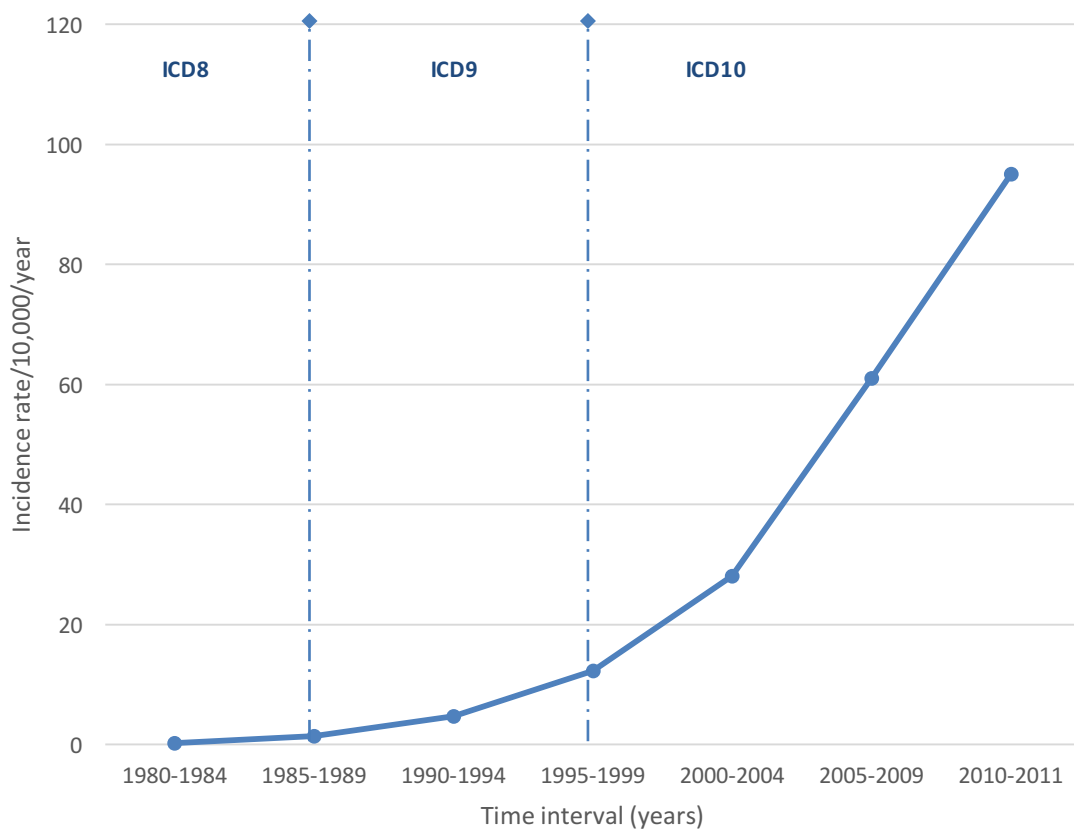

Figure 5 | Incidence rates of dementia per 10,000 person-years in men and women in Sweden (birth cohorts 1920-1944), from 1980 to 2011, averaged for five-year time intervals.

Table 5 | Cox regression model for risk of dementia hospitalisation for two-year intervals during 1997-2011[a]

Year	Hazard Ratio	Lower 95% CI	Upper 95% CI
1997-1998	1	-	-
1999-2000	0.96	0.92	0.99
2001-2002	0.96	0.91	1.01
2003-2004	1.01	0.95	1.08
2005-2006	1.04	0.96	1.13
2007-2008	1.11	1.01	1.23
2009-2010	1.20	1.07	1.35
2011	1.20	1.05	1.36

a. Cox regression model controlled for sex and education level. 1997-1998 reference category.

The trend observed within the ICD10 period was analysed in more detail by preforming a Cox regression analysis, adjusting for age. The model compared the risk for dementia hospitalisation between the different two year periods. Overall, the hazard ratio (HR) increased with time: from HR: 0.96; 95% confidence interval (CI): 0.92 to 0.99 in 1999-2000 to the maximum observed value of HR: 1.20; 95% CI: 1.05 to 1.36 in 2011 (Table 5). That is, from 2009 to 2011 there was a 20% increased risk of being hospitalised with dementia when compared to 1997-1998.

Dementia incidence and sociodemographic variables - *by sex*

Table 6 | Hospitalisations with reported dementia with regard to sex.

	Non-dementia	Dementia Diagnosis	Total
Men (%)	1,225,672 (95.55)	57,054 (4.45)	1,282,726
Women (%)	1,194,838 (94.29)	72,293 (5.71)	1,267,131
Total (%)	2,420,510 (94.93)	129,347 (5.07)	2,549,857

Sociodemographic variables such as sex are thought to affect dementia incidence and thus it was analysed in more detail. Of the total number of incident hospitalisations with reported dementia 44.1% were men and 55.9% were woman (Table 6). The average male to female ratio within the study population was 1.01 and did not change significantly during the study period. Figure 6 presents the corresponding time trends of dementia hospitalisations incidence specific for men and women, not adjusted for age. Up to the year 2000, the incidences rates for both sexes were virtually identical, and only from 2000 onward the trends became distinct one from another. In men, the incidence increased from 0.27 per 10,000 person-years in the first interval (1980-1984) to 84.4 per 10,000 person-years in the last interval (2010-2011) ($p<0.001$), and in women from 0.26 to 102.6 per 10,000 person-years in the same respective time intervals ($p<0.001$).
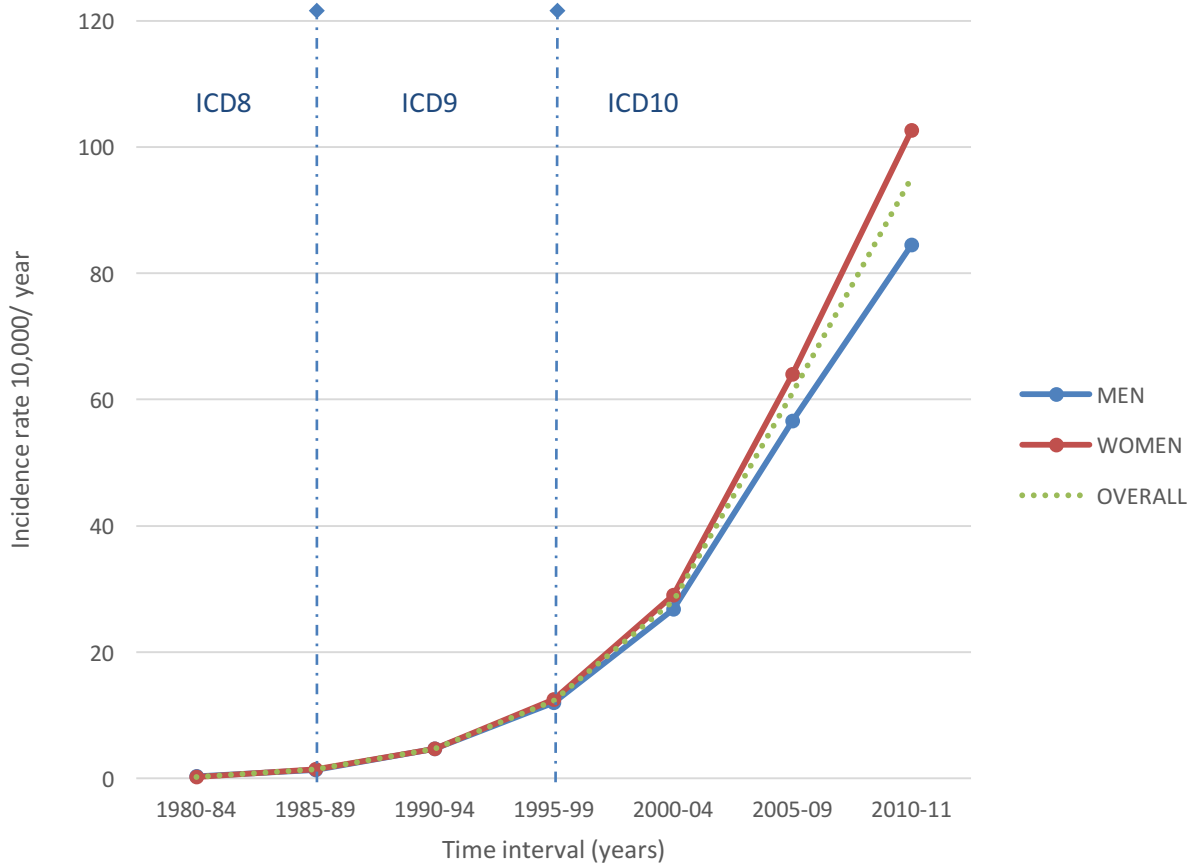
Figure 6 | Time trends in incidence rates of dementia in women, men and all separately from 1980 through 2011 (moving 5-year average incidence rates per 10,000 person-years): Sweden (birth cohorts 1920-1944)

Moreover, to study the effect of the sex variable on the incidence rate for dementia hospitalisations within the ICD10 period, the Cox regression model was further adjusted. The Cox model inherently adjusted for the fact that women live longer. Over the 1997-2011 period, women had a 6% (95% CI: 0.93 to 0.96) reduced risk of being hospitalised with dementia compared to men (Table 7).

Table 7 | Multivariate Cox regression model for risk of dementia hospitalisation during the ICD10 period (1997-2011)

Characteristic	Subcategory	No-incident dementia n=2,075,502	Incident dementia n=117,858	Hazard Ratio	Lower 95% CI	Upper 95% CI
Sex (%)	Women	1,065,345 (51.31)	66,415 (56.36)	0.94	0.93	0.96
Educational Level (%)	Low	1,154,367 (55.62)	75,345 (63.93)	1	-	-
	Middle	577,148 (27.81)	28,678 (24.33)	0.96	0.95	0.98
	High	344,070 (16.58)	13,837 (11.74)	0.91	0.90	0.93
a. Cox regression model was controlled for sex and education level. Men and low educational level were the reference categories.						

Dementia incidence and sociodemographic variables - *by educational level*

Table 8 | Hospitalisations with reported dementia regarding educational level.

Educational Level	Non-dementia	Dementia Diagnosis	Women	Men	Total
Low (%)	1,357,691 (94.47)	83,270 (5.53)	774,153 (53.72)	666,808 (46.28)	1,440,961 (61.34)
Middle (%)	654,762 (95.47)	31,096 (4.53)	296,520 (43.23)	389,338 (56.77)	685,858 (29.20)
Higher (%)	213,095 (95.85)	9,216 (4.15)	196,458 (46.44)	226,580 (53.56)	222,311 (9.46)
Total (%)	2,225,548 (94.74)	123,582 (5.26)	1,267,131 (49.69)	1,282,726 (50.31)	2,349,130 (100.00)

According to educational attainment, more than half of the study's individuals had low level education, 29.20% had middle level and only 9.46% had higher level education. More women than men had lower education and men had both more middle and higher education (Table 8). The 5-year period, not age-adjusted, incidence of hospitalisations with reported dementia increased significantly for all educational levels from 1980-4 to 2010-11, from 0.37 to 111.47 per 10,000 person-years in low level, from 0.74 to 79.93 per 10,000 person-years in middle level and from 0.18 to 65.90 per 10,000 person-years in higher level (Figure 7).
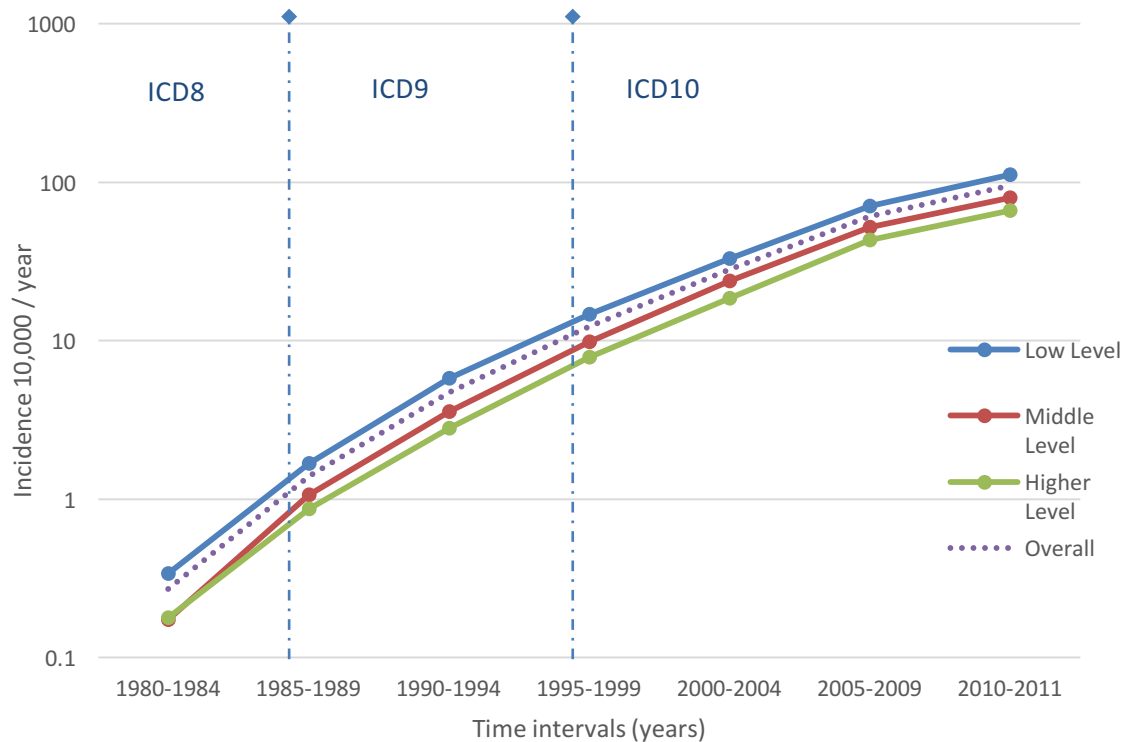

Figure 7 | Time trends in educational level specific incidence rates of dementia (men and women) from 1980 through 2011 (moving 5-year average incidence rates per 10,000 person-years): Sweden (birth cohorts 1920-1944). Logarithmic scale.

Moreover, educational differences between incidence rates in dementia hospitalisations decreased over time within the period. Comparison of incidence rates within the last year interval showed that incidence of dementia was lowest for those with higher level education compared to overall rates (p=0.003). Similarly between 1997-2011, the Cox regression model showed that within educational levels categories, those with high level education had a 9% (95% CI: 0.90 to 0.93) reduced risk of being hospitalised with dementia compared to those with low educational level. Meanwhile, those with middle educational level presented a smaller protective effect, with only a 4% (95% CI: 0.9 to-0.98) reduced risk of being hospitalised with dementia compared to those with low educational level (Table 7), even after adjusting for the fact that older people had overall lower education (56.33 % of individuals aged 80+ had only low education level, age is inherent in Cox model).

Age-stratified incidence rates of dementia hospitalisation

Figure 8 | Time trends in age-specific incidence rates of dementia in men and women combined from 1980 through 2011 (moving 5-year average incidence rates per 10,000 person-years): Sweden (birth cohorts 1920-1944). Logarithmic scale.

Once the incidence rate during the studied period was determined and the effect of sociodemographic factors on dementia established, it was necessary to analyse such trends

within stratified age categories. Figure 8 shows the trend over 31 years for dementia in seven age groups: 60 to 64, 65 to 69, 70 to 74, 75 to 79, 80 to 84, 85 to 89, and 90 to 92 years. For all the three youngest age groups (60-64, 65-69, 70-74), the incidence rates exhibited an average of 1.6-fold increase from the beginning of the study until 2011: from 2.8 to 5.2, 7.8 to 11.5 and 19.6 to 31.2 per 10,000 person-years respectively. The age categories of 75-79 and 80-84, showed a 1.4-fold increase from 2000 to 2011. Lastly, the oldest age categories, 85-90 and 90-92 presented an average 1.7-fold increase in incidence rates between 2000 and 2011: from 184.6 to 301.5 and from 195.7 to 346.4 per 10,000 persons-years, accordingly. These results suggest that hospitalisations for dementia became more common over time, irrespective of age and dementia incidence rates increased similarly across age categories.
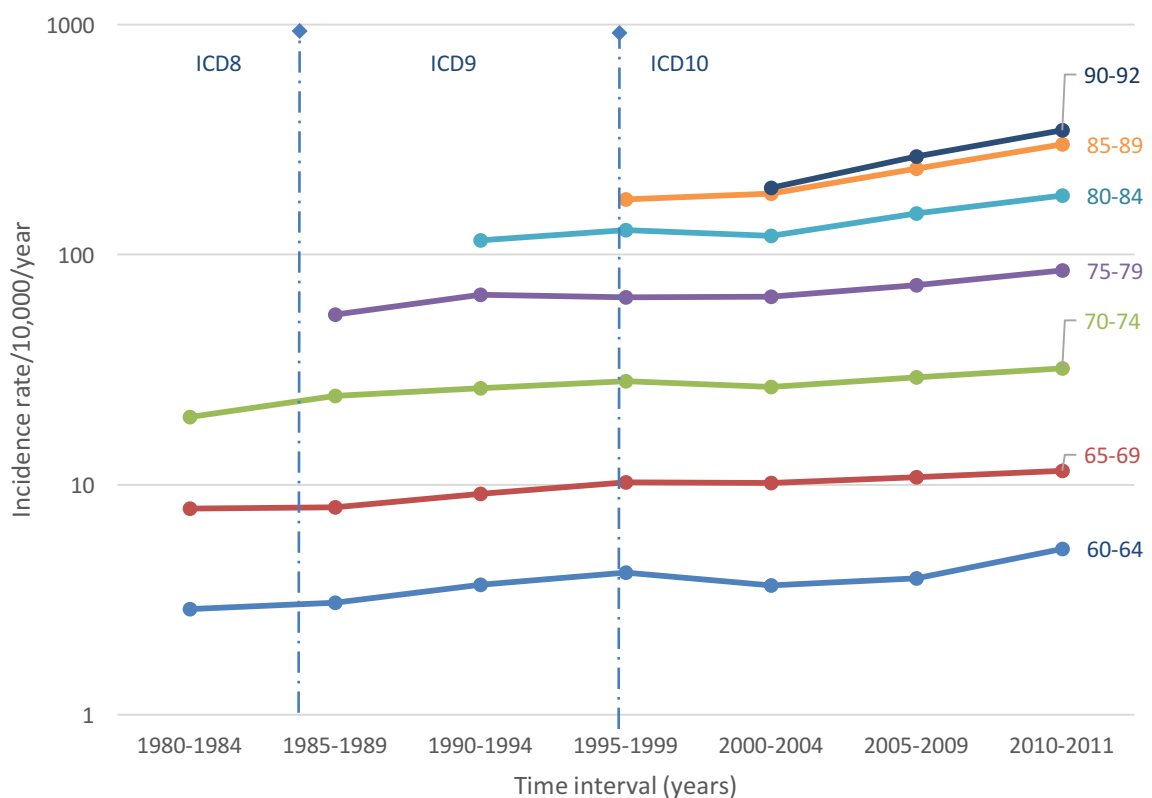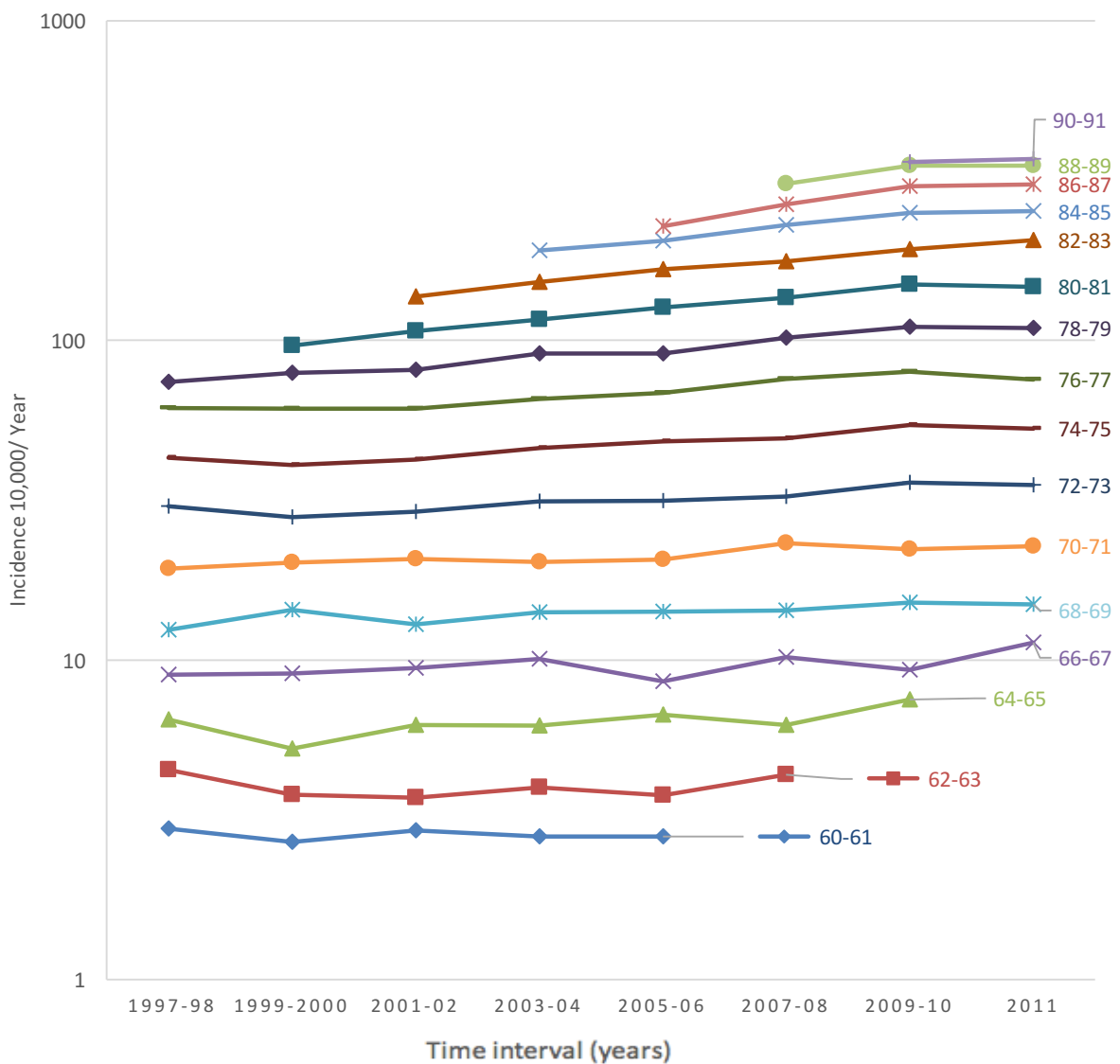

Figure 9 | Time trends in age-specific incidence rates of dementia in men and women combined from 1997 through 2011 (moving 2-year average incidence rates per 10,000 person-years): Sweden (birth cohorts 1920-1944). Logarithmic scale.

Based on the trends observed in Figure 8 a more detailed analysis of incidence rate trends within ICD10 was necessary. Figure 9 presents the age-specific dementia incidence rates throughout the ICD10 period (1997-2011). For all the six youngest age groups (60-71), the incidence rates remained low throughout the ICD10 period, with the maximum being 23.19 per 10,000 person-years for 70-71 years in 2007-2008. The incidence rates within the age groups 60-1, 62-3, 64-5, 66-7, 68-9 and 70-1 showed in average 1.12-fold increase: from 3 to 2.8, 4.5 to 4.4, 6.5 to 7.5, 9.0 to 11.3, 12.4 to 14.9 and 19.3 to 22.7 per 10,000 person-years respectively.

The age categories 72-77, also showed rather constant incidence trends with 1.16-fold increase at 72-73 (from 30.2 to 35.2 per 10,000 person-year), 1.23-fold increase at 74-75 (from 43 to 53 per 10,000 person-years) and an increase of 1.22-fold at 76-77 (from 61.5 to 75.5 per 10,000). The age categories of 78-79, 80-81 and 82-83 showed a marked increase (average 1.5-fold increase) in incidence rate (1997-2011): from 74.2 to 109.5, 96.3 to 147.2 and 137 to 205.5 per 10,000 person-years respectively. The relative percentage increase for the the last decade (2001-2011) was 35.5 % in 78-79 age category, 40 % in 80-81 age category and 50.1% for the ages 82-83. Dementia incidence rates experienced higher increases within older age categories.

Moreover, the older age categories (84-85, 86-87, 88-89 years old) presented an average 1.28-fold increase in incidence rates up to 2010: from 191.5 to 250.4, 227.3 to 303.6 and 309.1 to 351.9 per 10,000 person-years, respectively. From 2010 to 2011 the trends seemed to level off with minimal changes in incidence rates, with an average 1.01-fold increase. This pattern was also observed in the oldest group (90-92), for which the incidence only increased by 2.5% (from 361.5 to 370 per 10,000 person-years) during 2009-2011.

Lastly, looking at a single year, in 2011 the incidence rate of dementia steeply increased with age from 11.3 (95% CI: 9.8 to 13.0) per 10,000 person-years at age 66–67 years to 370.1 (95% CI: 349.2 to 392.1) per 10,000 person-years at age 90-91 (Table 9). Incidence rates became remarkably high from 80-year-old onwards (147.2 (95% CI: 139.9 to 154.8) per 10,000 person-years). Thus, within the ICD10 period age was also a driver for dementia incidence trends: the older categories showed the highest dementia incidence rates.

Table 9 | Age-specific number of person-years at risk, dementia cases, and incidence rates (per 10,000 person-years, with 95% confidence interval (CI), in 2011, Swedish population (birth cohorts 1920-1944)

Age Category	Persons-years at risk	Number of cases	Incidence rate	95% CI
66-67	170,584	193	11.3	9.8-13.0
68-69	197,469	294	14.9	13.2-16.7
70-71	163,940	372	22.7	20.4-25.1
72-73	153,165	539	35.2	32.3-38.3
74-75	135,744	720	53.0	49.3-57.1
76-77	120,977	914	75.5	70.8-80.6
78-79	112,234	1229	109.5	103.5-115.8
80-81	101,762	1498	147.2	139.9-154.8
82-83	89,406	1837	205.5	196.2-215.1
84-85	77,808	1972	253.4	242.4-264.8
86-87	64,547	1989	308.1	294.8-321.9
88-89	50,778	1790	352.5	336.5-369.2
90-91	30,938	1145	370.1	349.2-392.1

DISCUSSION

Main findings

The main findings of this study were that during the period from 1980 to 2011 in Sweden the absolute number of dementia hospitalisations increased. Likewise, the crude incidence rate rose significantly in the past three decades. During the ICD10 period (1997-2011), there was a 20% increased risk of being hospitalised with dementia comparing the first interval 1997-1998 to the last year 2011. In terms of gender differences, for the whole period the incidence rate was similar up to 2005, after then women incidence rates were higher than those for men, albeit the time trends were not adjusted for age. Moreover, the analysis of sociodemographic variables during 1997-2011 showed that women compared to men had a 6% reduced risk of being hospitalised with dementia. Regarding educational attainment, incidence of dementia increased for all educational levels through the period when not controlling for age. Low educational level presented the highest incidence rates although differences amongst educational groups decreased over time. A more focused analysis was performed for the last 15 years (ICD10 period), the results showed that those with high level education had a 9% reduced risk of being hospitalised with dementia compared to those with low educational level. Finally, throughout the period age was associated with increasing dementia incidence trends, that is the older age categories consistently showed higher incidence rates. Yet, these trends may merely be a coincidental finding and could be rejected or reinterpreted if incidence rates for a longer time window were available.

Up to today dementia trends behaviour remains contested: some studies have suggested that dementia incidence is declining (25,26,36,44,45), meanwhile some maintain that trends have stagnated (27,46) and others argue that it is still on the rise globally (8,47–49). The study's results support the latter claim as both the crude numbers of hospitalisations with dementia between 1980 and 2011 and the incidence rate (1997-2011) increased in Sweden. Moreover, the study's trends are similar to real incidence trends in Sweden within the specified period. Wimo *et al.,* (50) estimated dementia incidence rates in both men and women of age 85+ in Sweden to be 382.73 per 10,000 person-years in 2000-2001, these numbers are comparable to the study's results which were 380.28 per 10,000 person-years[1] during 2000-2004, for both men and women in the same age category.

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[1] Incidence calculated from Figure 8, by combining the two age categories over 85: 85-89 and 90-92.

Sex differences in dementia

Firstly, the literature highlights the underlying neurobiological sex differences in dementia (51), as women's brains age earlier and follow a distinct pathological pathway from that of men (52,53). Moreover, dementia diagnosis differs in men and women mainly because of different symptoms: men are more likely to present aggressiveness and diurnal rhythm disturbances meanwhile women are more likely to have paranoia, affective disturbances, anxieties and phobias (54).

Globally, two-thirds of the 47 million people currently living with dementia are women (7). However, within the study population of all incident individuals with dementia diagnosis 44.1% were men and 55.9% were woman, thus the study population did not follow the aforementioned proportion. Besides, women's overall lifetime risk of developing Alzheimer's disease is believed to be almost twice that of a man (17). Within the literature, there is a prevailing idea that this increased burden on women is simply because, overall, women have greater life expectancy and thus are longer at risk of developing the disease (17), resulting in higher age-specific prevalence and incidence of dementia among women, particularly at older ages (9). Nevertheless, regarding sex-dependent incidence rates of dementia there are some discrepancies; whereas some studies suggest a higher incidence rate in women than in men, mainly amongst those 85 old and older (55–57); others indicate no gender difference (58,59). The study results showed that within the whole study period, not adjusting for age, women had higher incidence rates than men. When looking only at ICD10 and adjusting for age, the results showed that women compared to men had a 6% reduced risk of being hospitalised with dementia. Yet, it is important to note that previous population-based studies have found no gender differences up to 90 years, and after that AD incidence was higher in women but vascular dementia incidence was higher for men, irrespective of age (52). This study did not discriminate between the different types of dementia and the oldest individual in the study population was only 92 years old. Thus, these circumstances could account for the results' discrepancies.

Education and dementia

The cognitive reserve hypothesis implies that having more years of education allows the brain to compensate for early stage dementia neurobiological changes by utilising alternative neuronal pathways when completing a cognitive task (8,44). That is, people with lower

educational attainment are at higher risk for dementia than those with higher educational level (18,60,61), even as little as 3 years of education can be protective against dementia (62). The study's results showed that during the whole period those with higher level education had overall lower incidence rates, not adjusting for age which can significantly bias the results. The ICD10 analyses were adjusted for age and results showed that dementia hospitalisation is less common among those with middle (HR 0.96, 95% CI: 0.95 to 0.98) or highest level of education (HR 0.91, 95% CI: 0.90 to 0.93). Yet, even after adjusting for the fact that men (in these cohorts) have higher education dementia hospitalisation is less common among women (HR 0.94, 95% CI: 0.93 to 0.96). However, there might still be some other confounders not explored in this study that differentiate people with high, middle and low education levels. All in all, even if rather moderately the study's results seem to support the cognitive reserve hypothesis, both higher and middle education had a modest protective effect against dementia when compared to low education level.

Age as a driver for dementia incidence

Dementia's strongest risk factor is age, thus irrevocably dementia incidence increases substantially as one grows older (63). The results showed that throughout the study the older age categories (≥80 years) consistently presented the highest incidence rates. Also, the study's results showed that over the whole period, dementia incidence rates increased similarly across age categories. These results are in line with Rizzuto et al., who did not find a trend according to age in registers (30). Yet, within the ICD10 period results suggested that dementia incidence rates increased more within older age categories. Lastly, a Swedish study found that dementia diagnosis differs with age: the total number of tests used to diagnose dementia were less in the elderly when compared with younger patients (64). Thus, it is worth considering whether this diagnosis bias could have skewed the results.

Underlying factors and mechanisms

During the timeframe of the study, there were factors that might underlie the dementia incidence rate phenomena and thus should be taken into account, such as the Ädel Reform, implementation of Swedish Dementia Registry (SveDem) and the progressive changes in dementia awareness and advocacy.

First, in Sweden up to 1992 the vast amount of the dementia related geriatric care was registered through the hospitals; but after 1992, when the Ädel reform came into action, the

care for the elderly, including those suffering from dementia, was shifted to be under the municipalities responsibility (50). This shift might have resulted in a change of perception at a population level as to where to go in case of suspected dementia. Thus, after the reform the amount of people diagnosed with dementia at hospitals might have decreased as a consequence, and so the validity of hospital discharge as a method to study dementia incidence, may be compromised. Yet, the overall number of dementia hospitalisations more than doubled in the two years following the reform from 784 in 1992 to 1,670 in 1994 (Figure 4). Similarly, in May 2007 SveDem was launched with the aim to "improve quality of diagnostics, treatment and care of patients with dementia disorder" (65). Hence, dementia cases from 2007 onwards might have been affected by this new registry. Raised dementia awareness could potentially make people more likely to know their diagnosis and thus have an effect on patients' journals at hospitalisation. Within the study's results total number of hospitalisations increased 25% in the two years following SveDem, from 10,340 in 2007 to 12,937 in 2009 (Figure 4). Currently, 100% of all memory clinics in Sweden are participating in SveDem, and consequently it might affect the IPR's ability to detect dementia cases.

Secondly, dementia cases can go undetected for many years before being diagnosed. However, other than the vague and diffuse symptoms of dementia (66) the reasons for under-diagnosis are various and include: historical burden of dementia and stigma; dementia awareness within the greater society; medical uncertainty when diagnosing dementia and reluctance by the individual and/or family members to seek care (67). All of the aforementioned reasons could to a certain extent affect the validity of the thesis' results and thus they will be explored in more depth.

From a historical viewpoint, over the years dementia evolved from a vague, misunderstood, and often alienated concept linked to "foolishness" and inevitable mental decline in old age, to become a defined disease with certain clinical and pathological features (63,68). However, this historical negative conceptualisation still prevails and affects dementia by creating stigma within society (69). Part of the stigma exists due to lack of knowledge and understanding of what dementia really is and what it entails. In the last three decades, governments and public health organizations alike have worked towards increasing dementia awareness. Yet, so far these efforts have only moderately altered dementia perception (27) and thus further advocacy measures have to be put in place. In 2010, the Swedish National Board of Health and Welfare implemented the National Dementia Strategy, yet this measure

is very unlikely to have affected this thesis' results since the study finished in 2011. Still, it will surely have an effect on dementia reporting and detection in the years to come.

In line with the National Dementia Strategy, it is necessary to rise awareness not only within the general population but also within the medical body to enable doctors to make informed diagnosis. According to a qualitative study, Swedish doctors are not proactive in making a diagnosis and they rely greatly on family members or patients to bring to their attention dementia symptoms such as memory loss (70). Thus, the educational level of the patient, and by extension their relatives, can have an effect on dementia detection. This thesis showed a modest risk decrease on those with higher education, which may be partly counteracted by the same phenomenon: highly educated parents have highly educated children and partners that will detect even the smallest sign of dementia. Moreover, even within the medical community dementia is a stigmatised disease. Most Swedish doctors avoid using the word 'dementia' and were reluctant to speak to patients about their condition (70). This medical uncertainty might have affected the results by under-diagnosing incident dementia cases for hospitalized patients. Moreover, another limitation is that within the IPR only those dementia cases with causes related to hospitalisation are included, hence an individual might have dementia but not be recorded as a dementia hospitalisation case.

Finally, it is worth mentioning that in contrast with doctors' uncertainty, dementia diagnosis is becoming a more accessible procedure that other healthcare staff can perform. For example, dementia can be assessed with Mini Mental State Examination (MMSE) by occupational therapists, physiotherapists or speech therapists. However, MMSE are most likely not done at hospitalisation. Also, a wealth of new techniques such as MRI, CT, SPECT/PET, lumbar puncture or EEG are becoming more and more available and commonplace when diagnosing dementia (64). This advancements might lead to earlier diagnosis which can reduce dementia-related costs from delayed institutionalisation (71,72). All in all, dementia incidence trends derived from IPR might have been altered by these advancements, yet ascertainment of such effect is beyond this thesis scope.

Regarding the underlying neurobiological mechanisms that play a role in dementia pathology, research has suggested that healthier diets and increased physical activity could be protective against dementia (39,73,74). Moreover, public health interventions aimed at modifying cardiovascular risk factors could in turn also had repercussions in dementia

incidence, since cardiovascular disease is considered a risk factor for dementia (75,76). In short, the thesis did not account for changes in lifestyle trends that could have altered dementia risk and consequentially affect incidence temporal trends.

Strengths and Limitations

The main methodological limitation was using the IPR for studying time trends, since for any given change one can not determine whether it reflects true changes of incidence or changed sensitivity. Another limitation is that IPR had only complete national coverage since 1987 (24), thus the results from the first 7 years of the study might not be fully valid. Additionally, the core of the study relies on hospitalisations with reported dementia diagnosis to infer incidence; there are some inherent problems with using hospitalisation such as the amount of detail in diagnosing the patient. Moreover, these measures are just a mere approximation and not the "real" incidence as date of onset most likely differs from date of diagnosis. This mistiming can somehow be undermined as it is intrinsic in dementia's aetiology to present progressive and slow symptoms hard to diagnose ipso facto (7). Thus, dementia onset as used in the study (date of hospitalisation), even if delayed from probable clinical onset of dementia, is a reliable measure based on dementia's peculiar aetiology.

Another closely related limitation is dementia case ascertainment and the lack of consistency in dementia diagnosis throughout the study period due to changes in diagnostic registration systems. First, according to a study carried out in Gothenburg, Sweden, dementia prevalence varies extensively depending on which diagnostic classification system was use. Diagnostic and Statistical Manual of Mental Disorders (DSM) showed a higher case ascertainment than ICD (38). Thus, it might be that the use of ICD criteria excludes some cognitively impaired people from receiving appropriate and accurate diagnosis. Secondly, in Sweden the shift from ICD-8 to ICD-9 took place in 1986-1987 and the shift from ICD-9 to ICD-10 in 1996-1997. ICD8 did not specify Alzheimer's disease and all dementia cases fell either within pre-senile or senile dementia; ICD9 still maintained the senile/pre-senile dementia but included Alzheimer's disease, lastly ICD10 is the most complete and still in use today which makes it the most reliable and useful period to study. Moreover, due to the lack of reliable dementia biomarkers, behavioural aspects and performance of social roles are of great importance in diagnosis; for example decline of activities of daily living (ADL), which functions as an important criterion for the differentiation of the severity of the dementia (77), and personality changes (38) were only included in ICD10 (78). This thesis did not find that

the change from ICD8 to ICD9 affected the incidence trends for hospitalisations with reported dementia, yet the shift from ICD9 to ICD10 was substantial. All considered, the changes in dementia incidence within each period are much more valid than the whole period and therefore, the thesis analysed the ICD10 period more in depth in order to overcome the diagnosis inconsistency constraint.

Also, there is certain limitation when categorising the educational attainment. By reducing the census categories from seven to three broader categorical variables the scope of how finely tuned the effect of education on dementia incidence is, is limited. Moreover, the educational level categories do not take into consideration the different educational reforms that Sweden underwent in 1936-1949 (Folkskolan Reform) and 1949-1962 (Enhetskolan Reform) and how this secular changes might have affected the trends.

Lastly, a matter to be discussed is that hospitalisations for any cause in Sweden, for both men and women, decreased between 1989 and 2011 (79). Yet, the results showed that hospitalisations with reported dementia increased during the same period. Thus, the trends deviate for the norm and can not solely be explained in sociocultural aspects such as improvements of healthcare system or more health-aware population.

Future research

Having explored the methodological weaknesses and strengths of the thesis, and bearing in mind the aforementioned cardiovascular disease trends, it would have strengthened the study to compare the time trends of dementia in relationship with cardiovascular trends. In this manner, one would be able to discern whether those public health interventions implemented to reduce cardiovascular disease risk also affected incidence of dementia. Similarly, diagnosis and/or hospitalisation because of a cardiovascular event could be included in the Cox model in order to yield more valid results.

Furthermore, the study would have been more robust if data form the Cause of Death Registry was also included. Similarly, in the future to advance the research topic data from IPR will be ideally complemented by information from the Drug Registry (currently only data from 2011 onwards is available) and compared and contrasted with SveDem data.

CONCLUSIONS AND RECOMMENDATIONS

Given the world's increasing life expectancy and rising number of elderly people age-related diseases, such as dementia, are becoming widespread. Thus, epidemiological analyses of incidence trends are crucial in understanding the disease and determining future trends. This thesis findings showed that during the period 1980-2011 crude numbers of dementia hospitalisations continuously increased and overall incidence rates of dementia augmented. Also, the older ager categories consistently presented the highest incidence rates. Thus, dementia is an increasingly urgent political priority and healthcare systems around the world have to be prepared to buffer this "old-age boom". Moreover, during the ICD10 period both being female and having higher level education were moderately protective against dementia.

In light of increasing incidence rates, societies must invest in dementia research with the hope to reduce if not overall dementia incidence, at least its associated disability. The elaboration of plans, policies and interventions aimed at reducing dementia incidence should be based on evidence from epidemiological research. Considering the past three decades in the Swedish context, decision makers and stakeholders could address dementia at a population level by increasing sex-specific research, encouraging physically active and intellectually engaging lifestyles and raising awareness of dementia.

Increasing dementia incidence is also a matter of great concern for policy makers in LMIC. Although this thesis' findings may not necessarily be immediately transferable to LMIC settings, there are lessons that could be applied. Amongst those, the need to minimize dementia-related stigma by raising awareness both within the general population and medical staff; the necessity of an efficient diagnosis system in order to detect cases early on and the benefit of improving access to education to counteract dementia risk. In the years to come, it is imperative for health systems and private agents to be prepared to provide adequate and cost-efficient care and support both for dementia patients and their families.

Lastly, in order to contribute to the wealth of global dementia data, governments in LMICs should be encouraged to commission surveys to monitor trends and start, or maintain, registries such as the IPR. In the long run, these measures might be instrumental in understanding national dementia epidemiology within a broader global perspective.

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