Understanding Socioeconomic Disparities in Stroke: An international perspective

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Een internationale studie

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Para mis padres, Renato, Rolando y Carolina

'Let me tell you about the very rich. They are different from you and me. They possess and enjoy early, ad it does something to them, makes them soft where we are hard, and cynical where we are trustful, in a way that, unless you were born rich, it is very difficult to understand. They think, deep in their hearts, that they are better than we are because we had to discover the compensations and refuges of life for ourselves. Even when they enter deep into our world or sink below us, they still think that they are better than we are'.

F. Scott Fitzgerald, *The Rich Boy*, published in the *Collected Short Stories*

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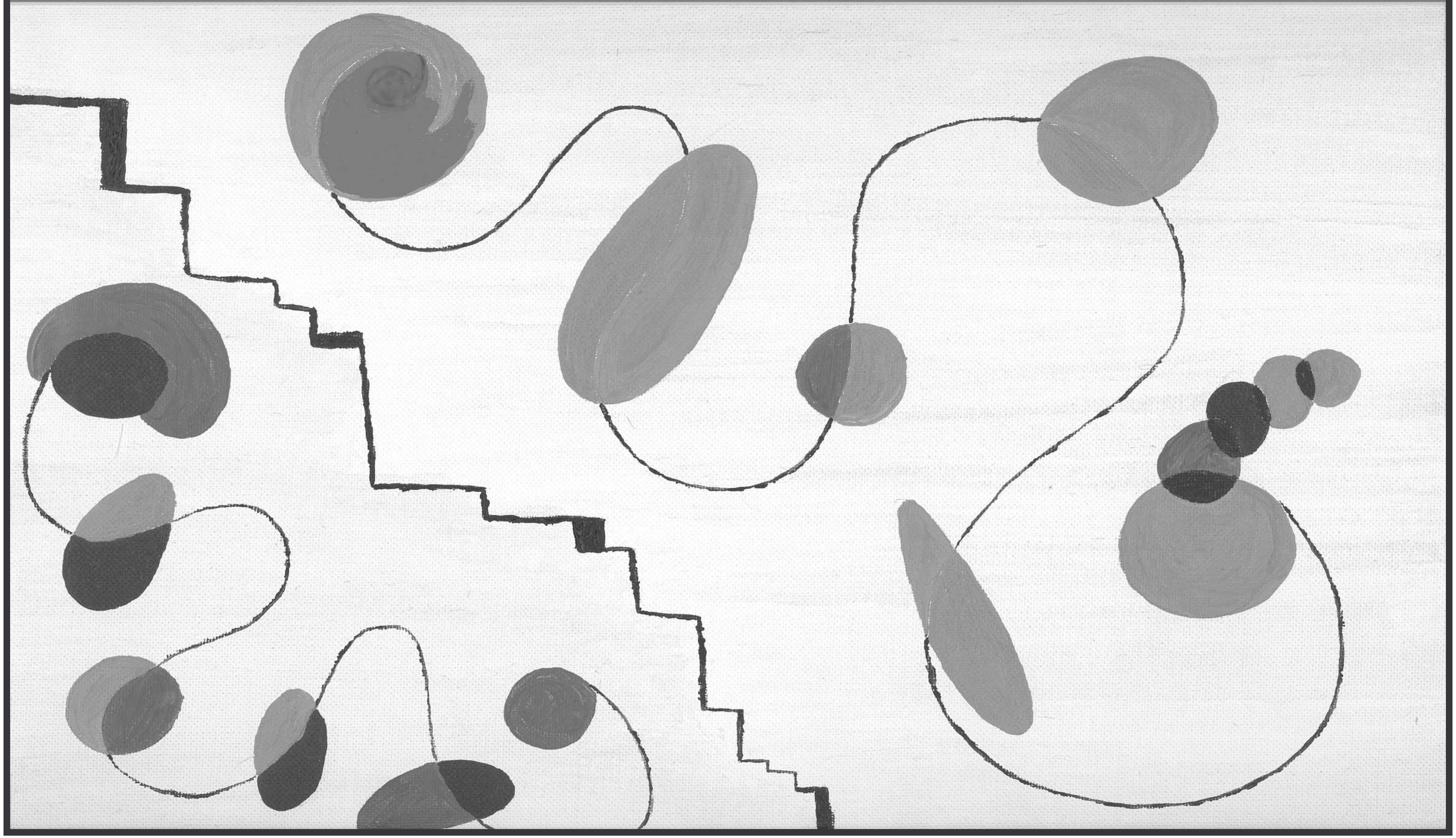

Chapter 1

Introduction

1.1 Stroke

Global trends in stroke: A complex epidemiological pattern

Stroke is a major chronic disease defined as the sudden onset of focal (or global) disturbance of cerebral function lasting more than 24 hours, with no other apparent cause than a vascular disturbance[1]. It is a major disorder that encompasses various subtypes comprising subarachnoid haemorrhage, intracerebral haemorrhage and cerebral ischaemic infarction[2,3], the latter accounting for about 80% of all strokes. Stroke is the second leading cause of death worldwide and the third most common cause of death in the developed world[4]. It accounts for about 4.3 million deaths every year[5] and is one of the major causes of long-term disability worldwide[6]. While approximately one third of stroke patients die within the first 12 months, another third will be permanently disabled and dependent on the assistance of others[6]. Stroke carries enormous emotional and socioeconomic consequences for patients and their families. Lifetime costs for stroke patients are high and range from US$91,000 for ischaemic stroke to US$228,000 for subarachnoid haemorrhage[4,7,8]. It is estimated that stroke accounts for about 3% of total health care costs[9], representing a major burden for the healthcare system.

Stroke mortality rates are generally higher in men than in women in most countries, but these differences narrow considerably above the age of 75 years[10]. There is evidence of significant variation in the burden of stroke around the globe[6]. In Europe, stroke incidence rates vary from 101 to 285 in men and from 47 to 198 in women per 100,000 at ages 35 to 64[1]. Only in this region, the case-fatality rate at 28 days varies from 15% to 49% among men and from 18% to 57% among women[1]. Estimates for the entire world indicate that stroke mortality among those aged 35 to 74 is highest in Eastern Europe and former Soviet Union countries, ranging from 156 to 309 among men and 101 to 222 among women per 100,000 per year. In contrast, relatively low stroke mortality rates have been observed in Western European countries, where stroke mortality rates below 100 among men and 70 among women per 100,000 per year have been reported during recent years. The countries with the lowest stroke mortality rates during the mid-1990s were Switzerland, Canada, the United States, France and Australia[10].

Variations between world populations are also evident in stroke mortality trends. Countries with low stroke mortality rates have experienced steep stroke mortality declines for several decades, followed by a plateau in mortality rates during the last years. For instance, in the United States, a decline in the age-adjusted rate of stroke mortality began in 1924 for non-white women and in 1930 for non-white men[11,12]. The rate of decline accelerated in the 1970s, but slowed down during the 1980s for reasons that remain unclear[13]. Recently published statistics suggest that the long-term decline in stroke mortality rates in the United States may have ceased[11]. In contrast, stroke mortality has increased in less favourable economies such as those in the Eastern European region, especially during the last decade[10].

Risk factors for stroke

As 75% of strokes are first-ever events, effective prevention among individuals who had not had a previous stroke i.e., primary prevention, can have the greatest impact on reducing the burden of stroke[14]. Age is the single most important risk factor for stroke. For each successive 10 years after age 55, the stroke rate more than doubles in both men and women[15,16]. Other non-modifiable risk factors for stroke comprise gender (male), ethnicity (black, Hispanic and Asian), heredity and geographical location[16].

Conventional stroke risk factors

Table 1.1 summarizes the major well-established modifiable risk factors for ischaemic stroke, subarachnoid and intracerebral haemorrhage. The proportion attributable risk for different stroke subtypes are presented based on current reviews and on guidelines provided by the American Heart Association[16-25]. These are largely based on United States and European longitudinal cohorts, which comprise predominantly Caucasian populations such as the Framingham study and the European Monica cohorts. As ischaemic strokes represent approximately 80% of all strokes, most evidence concerns the occurrence of ischaemic events. Hypertension is the most consistent powerful predictor of all stroke subtypes[26], accounting for as much as 40% of ischaemic strokes around age 70[14,20,27]. Smoking accounts for about one fifth of ischaemic strokes[14,20] and subarachnoid haemorrhages[17,23], and as much as 27% of ischaemic strokes are attributable to diabetes mellitus[14,20]. Obesity and physical inactivity are major risk factors for ischaemic stroke[14,20], and atrial fibrillation is involved in about one fifth of all ischaemic events[14,20]. Alcohol consumption is a major risk factor for haemorrhagic stroke, with as much as 21% of all subarachnoid haemorrhage cases been attributable to consumption of more than 100-299 g/week of alcohol[23]. Although light and moderate alcohol consumption seems to be associated with a decreased risk of ischaemic stroke[14,20], excessive alcohol consumption increases the risk of ischaemic events[14,20]. Increasing levels of total cholesterol as associated with higher rates of ischaemic stroke, and low HDL is a risk factor for ischaemic stroke in men[14]. Recent meta-analyses indicated that consumption of more than five servings of fruits and vegetables per day is associated with as much as 26% reduction in the risk of stroke[28], which association displays a dose-response relationship[29].

Other major risk factors for ischaemic stroke include a history of coronary heart disease, heart failure and peripheral artery disease, atrial fibrillation, asymptomatic carotid stenosis, higher sodium (Na) and lower potassium (K) intake[14,20]. A positive family history and autosomal dominant polycystic kidney disease (ADPKD) have also been associated with an increased risk of subarachnoid haemorrhage[17,23], whereas a history of ischaemic stroke is associated with increased risk of intracerebral haemorrhage. Finally, about 10% of all intracerebral haemorrhages and as much as one third of lobar intracerebral haemorrhages seem to be attributable to possession of an apolipoprotein E4 or E2 allele[25].

Novel stroke risk factors: From biomarkers to psychosocial determinants

Despite major evidence of their impact on stroke, conventional risk factors predict less than one half of future cardiovascular events[18,30,31]. Furthermore, these risk factors may have a different causal effect in different ethnic groups[18]. Evidence has accumulated that factors other than conventional risk factors may contribute to the development of atherosclerosis[14,18], which precedes most cerebral thromboses. Novel risk factors for stroke include hyperhomocysteinemia (elevated homocysteine levels), fibrinogen[32], impaired fibrinolytic activity, platelet reactivity, hypercoagulability, lipoprotein(a), small dense low-density lipoprotein, infectious agents, and markers of inflammation including C-reactive protein and soluble intercellular adhesion molecule 1 (ICAM-1)[14,18].

In addition to these novel risk factors, evidence has accumulated during recent years on the role of psychosocial risk factors in the development of stroke. Psychosocial factors encompass sources of prolonged stress throughout life that can have a negative impact on health. Research indicates that depression is a strong predictor of stroke risk[33-36]. Most convincingly, studies speak to the seriousness of poststroke depression, which confers a high risk for subsequent mortality independently of conventional risk factors[37-41], and is associated with increased disability and cognitive impairments after stroke[42-44]. Studies also indicate that socially isolated men have an increased stroke risk[45], and larger social networks are associated with fewer limitations in physical function among stroke patients[46].

Another potential psychosocial risk factor is severe psychological stress, which has been found to predict stroke mortality[47-49]. The mechanisms through which these factors increase stroke risk are not well understood, and might involve more proximal stroke determinants such as increased blood pressure as mediating pathways. Independently of the underlying mechanisms, psychosocial risk factors are modifiable and amenable to interventions, and can be considered as important risk factors for stroke.

Table 1.1. Modifiable risk factors and their population attributable risk (PAR) for ischaemic stroke, subarachnoid haemorrhage and intracerebral haemorrhage

Risk factor	Population attributable risk*		
	Ischaemic stroke[14,16,20,26]	Subarachnoid haemorrhage[16,17,23]	Intracerebral haemorrhage[16,24,25]
Hypertension	20-40	17	34
Diabetes mellitus	5-27	-	-
Smoking	12-18	20	-
Cardiovascular disease		-	-
Coronary heart disease	8-6	-	-
Heart failure	2-3	-	-
Peripheral artery disease	5	-	-
Hypercholesterolemia		-	-
High total cholesterol	15	-	-
Low HDL cholesterol	10	-	-
Obesity	12-20	-	-
Physical activity	30	-	-
Atrial fibrillation	2-23	-	-
Excessive alcohol consumption	1-32	11	6
Asymptomatic carotid stenosis	2-7	-	-
Dietary factors		-	-
Na intake >2300 mg	Unknown	-	-
K intake >4700 mg	Unknown	-	-
Positive family history	Unknown	11	-
Autosomal dominant polycystic kidney disease (ADPKD)	-	0.3	-
Previous ischaemic stroke	-	-	13
ApoE2 or E4	-	-	10

*Population-attributable risk is the proportion of ischemic stroke in the population that can be attributed to a particular risk factor. Estimates come from the American Heart Association stroke council statements and systematic reviews largely based on United States and European longitudinal cohorts, which comprise predominantly Caucasian populations such as the Framingham study and the European Monica cohorts.
Dashes indicate none or insufficient evidence of the contribution of a risk factor to a specific stroke subtype; values indicate the range of the population attributable risk as reported in several studies or for different age-groups.

Understanding international variations and trends in stroke: A role for social and economic circumstances?

The causes behind international variations and trends in stroke mortality remain largely unknown. Nevertheless, a potential role for changes in overall social and economic circumstances in different world regions can be hypothesised. Overall, a widening gap has emerged between two groups of nations: Those with low and declining stroke mortality and those with high and increasing mortality[10,50]. The highest to lowest ratio between countries is as high as 9:1 for the group 35 to 74 and 5:1 for the group aged 75 to 84 years[10]. Absolute rate differences between the countries with the lowest and highest stroke mortality are around >200 deaths per 100,000 population per year in the younger age group and >2000 per 100,000 population per year in those aged 75 to 84[10]. Interestingly, the international pattern of stroke mortality rates seems to be associated with the overall level of social and economic growth in European established marked economies. Figure 1.1 shows that the log of gross domestic product is negatively correlated with the stroke mortality rate in European countries (r= -0.75, p<.0001). Variations between countries in stroke mortality rates might thus reflect differences in the level of socio-economic development and stability during the last decades. Similarly, the steady stroke mortality decline in developed countries may reflect major improvements in social and economic circumstances for several decades. Against this background of ecological associations at the aggregate level, the question on the role of social and economic circumstances at the individual level on stroke risk arises as an important one.

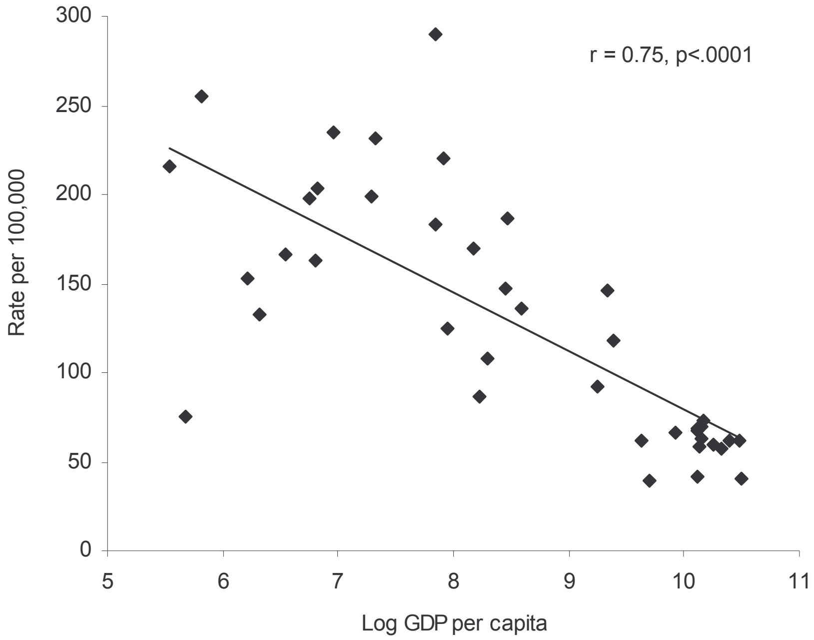

Figure 1.1. Scatter-plot of national stroke mortality rate against the log of national gross-domestic product (GDP) per capita in 1999 among 40 European countries (sources: WHO health for all database, own calculations)

1.2 Socioeconomic status and stroke: An introduction

A consistent social gradient around the world

Socioeconomic status is inversely associated with stroke incidence and mortality in most developed countries including the United States, Canada, Australia and European populations[51-62]. Although there are variations between countries[51], socioeconomic differentials in stroke have been found to be consistent and possibly larger than those in coronary heart disease (CHD)[51,63]. Socioeconomic status is a major predicator of stroke, so that up to 36% of incident ischaemic strokes can be attributable to low socioeconomic status in both men and women[54]. Overall, socioeconomic status might play a major role in explaining trends and the distribution of stroke in the population.

In relative terms, socioeconomic differences in stroke appear to be larger at ages 30 to 59. Although differences remain after this age, relative disparities seem to be less pronounced in the older age groups[51,55,56,63]. However, due to the fact that around 89% of strokes occur after age 65[64], socioeconomic differentials in stroke might be largest at older ages. No studies have yet systematically assessed the age-pattern in socioeconomic differentials in stroke.

In the Netherlands, socioeconomic differentials in stroke have been reported[60,61]. The Rotterdam study found a clear socioeconomic gradient for stroke risk among elderly women, which remained largely unchanged after adjusting for established cardiovascular risk factors[60]. In a separate study, socioeconomic status of small postcode areas was significantly related to stroke incidence in the Netherlands[61]. In areas with relatively low income, the incidence of stroke was about 25% higher than the incidence in areas with an average or high income[61]. Overall, these studies suggest that there is an association between socioeconomic status and stroke, which remains largely unexplained.

Socioeconomic status and stroke-subtypes

The largest impact of stroke stems from ischemic stroke, which represents 80% of all stroke cases, whereas intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH) contribute about 10% each to the total burden of stroke[3]. Results from the FINMONICA Stroke Register comprising a large population suggested that socioeconomic status is associated with ischaemic stroke[54], IH[55] and SAH[56], and that associations are of a similar magnitude for these major stroke sub-types. Furthermore, this study indicated that case-fatality rates for both ischemic stroke and SAH –but not for ICH- are higher among lower socioeconomic status groups[54-56]. In agreement with these findings, the Swedish MONICA study found that SES was similarly associated with the three subtypes of stroke[65]. In short, results from these studies suggest that socioeconomic position is negatively associated with all stroke subtypes, and that no major difference seem to exist in the magnitude of these associations.

International variations in socioeconomic differentials in stroke

Few systematic international comparisons of socioeconomic differentials in stroke have been conducted. The most important contribution comprises an overview of the association between occupational class and stroke mortality in Western Europe during the 1980s. During this period, relatively small occupational differences in stroke mortality were observed in most northern Scandinavian countries (Sweden, Norway and Denmark), Italy and Spain, whereas larger differences were reported in England/Wales, Ireland and Finland. It is not known whether these international variations have persisted into more recent dates.

It has been hypothesised that southern European countries may be lagging behind in the epidemiological transition earlier experienced by northern Europe and the United States[66,67]. Consequently, no socioeconomic differences in risk factors such as smoking would have yet emerged in southern populations. As a consequence, socioeconomic differentials in cardiovascular disease would be expected to be larger in northern than southern Europe. However, studies during the 1980s suggested that the north-south gradient observed for socioeconomic differentials in ischaemic heart disease (IHD) e.g., larger differentials in northern than southern populations, has not been observed for stroke[51,68,69]. The explanation of this differential pattern for stroke and IHD remains unknown, and might be due to limitations in data quality for southern populations in previous studies[51]. Further research is necessary to replicate these findings and to elucidate the causes of this pattern.

Stroke mortality has declined considerably during recent decades[10]. However, no studies have assessed variations in socioeconomic differentials in stroke mortality in more recent periods. Previous studies were also limited to middle-aged men[51,68]. Research on inter-country variation can contribute to the identification of risk factors and policies through which the excess stroke mortality among lower socioeconomic groups can be reduced. This can in turn contribute to an overall reduction in stroke mortality across Europe.

Socioeconomic status and stroke trends

Despite the declining trends in stroke mortality during the last decades[10], socioeconomic inequalities in stroke have persisted and may have widened during the last 40 years in some populations[68,70]. Populations that have shown different levels of decline in stroke mortality may have experienced different trends according to socioeconomic status. In particular, larger stroke mortality declines may have occurred among those with a high socioeconomic status. Overall, a less favourable relative decline in cardiovascular disease mortality has generally been observed among lower than higher socioeconomic groups in European populations, Australia and the United States[68,70-76]. However, trends in the two main cardiovascular diseases, stroke and IHD, differ substantially within and between populations[75-77], as does their association with socioeconomic status[51,67,68]. Furthermore, European countries have experienced changes in the prevalence of classical cardiovascular risk factors such as smoking and hypertension during recent decades[78,79]. International studies on trends may point at specific policies and risk factors that may have had an impact on socioeconomic differences in stroke mortality. This may elucidate ways through which socioeconomic disparities can be reduced in order to sustain the stroke mortality decline in European countries. There have been no studies focused on trends in stroke mortality according to socioeconomic status in different European populations.

Explaining socioeconomic differences in stroke: How does socioeconomic status gets into the brain?

The role of conventional risk factors

The higher rates of stroke in lower socioeconomic groups are likely to be the direct result of higher prevalence of stroke risk factors in these groups. In general, two major groups of conventional stroke risk factors might be considered as potential mediators of the association between socioeconomic status and stroke: (1) *Biological determinants* encompass blood pressure and hypertension, cholesterol level, body mass index (including overweight and obesity), diabetes mellitus, general and central adiposity, fibrinogen (serum lipids), previous cardiovascular disease and genetic factors; and (2) *behavioural determinants* comprise smoking, alcohol consumption, physical activity and nutritional factors.

Research conducted in the UK indicates that these factors can only explain about half of the association between socioeconomic status and stroke among middle-aged men and women[52,53]. Risk factors included in these studies comprise blood pressure, smoking, height, forced expiratory volume and body mass index, among others. Most dramatically, among Dutch elderly women, these factors explained almost none of the association between socioeconomic status and stroke[60]. Risk factors that mediate socioeconomic differentials in stroke at young ages might not necessarily mediate associations among the elderly. Furthermore, different socioeconomic indicators might increase stroke risk through different causal pathways.

It is unclear whether findings from existing studies can be generalized to other populations. International studies have documented large socioeconomic differentials in the prevalence of risk factors favouring the high socioeconomic groups for several risk factors including smoking, hypertension, body mass index and nutrition[80-85]. However, there is evidence of substantial differences between countries in the social patterning of these factors. For instance, socioeconomic differentials in smoking and fruit and vegetable consumption are known to be larger in northern than southern European populations[82,84,86]. This pattern is particularly marked in women, among whom reverse social differences in smoking remain in the south[82,84,86]. Thus, the causal pathways through which socioeconomic status increases stroke risk might differ for different populations, with factors such as smoking contributing to socioeconomic differentials in stroke in northern but not in southern Europe.

In summary, the mechanisms through which different socioeconomic status indicators have an impact on stroke risk in different populations remain largely unclear[52,53,60]. Although conventional cardiovascular risk factors are potential explanatory factors, further research on the role of alternative explanations of socioeconomic differentials in stroke is warranted.

Psychosocial risk factors: The alternative mechanism?

Psychosocial factors such as emotional support and depression are related to stroke[33-36,45], and can contribute to socioeconomic differentials in all-cause mortality[87]. Most importantly, psychosocial risk factors such as control at work might account for the unexplained share of the association between socioeconomic status and coronary heart disease[88]. However, no studies have examined whether psychosocial risk factors also play a role in the explanation of socioeconomic differences in stroke. Of particular interest is the role of depression, which has been found to be a strong and independent psychosocial predictor of stroke incidence, post-stroke survival and functioning[33-44], and is related to socioeconomic status[89]. Furthermore, the extent to which individuals maintain social networks at later ages has been associated with stroke risk as well as fewer post-stroke limitations[45,46]. Given their strong and independent association with both socioeconomic status and stroke, psychosocial factors are interesting candidate explanations of socioeconomic differentials in stroke.

Quality of care: Preventive vs. post-stroke secondary care

Despite a long tradition of universal health care coverage, socioeconomic differences in access to care remain across Europe[90,91]. While individuals with lower socioeconomic status visit their GP more often, those in higher socioeconomic groups use more specialist care[90,91]. Thus, better health care access in higher socioeconomic groups after adjustment for need -health care inequity- could contribute to socioeconomic differentials in stroke.

Studies on the role of healthcare in explaining socioeconomic differences in stroke have focused on the role of post-stroke secondary care. Even in populations with universal health care access, better post-stroke care has been reported in higher socioeconomic groups. Finnish, Swedish and Canadian stroke patients with higher socioeconomic status are more often treated at a University hospital, examined by a neurology specialist, and examined with computed tomography (CT) or magnetic resonance Imaging (MRI)[54,56,59,65]. However, a study conducted among Dutch stroke patients examined whether socioeconomic differentials in healthcare utilization remained after adjustment for health-need. Although patients with a low socioeconomic status experienced more disabilities, no inequity in healthcare utilization was observed in these patients[92].

Stroke is a condition to a large extent preventable. Therefore, the quality of care for the management of risk factors is likely to play a major role in the prevention of stroke in the population. A recent audit among general practitioners (GPs) in the Netherlands found a substantial number of shortcomings in the quality of care for the prevention of stroke, particularly in the domain of hypertension control and the assessment of patients' risk profile[93]. Most interestingly, patients living in socially deprived areas were more likely to have a poor management of cardiovascular risk factors[94]. These findings suggest a great potential for the reduction of socioeconomic differentials in stroke by improving the delivery of general practice care for stroke prevention.

Due to their gate-keeping role in the Dutch healthcare system, GPs play a major role in the management of cardiovascular risk factors in the Netherlands. Since 1989, the Dutch College of general practitioners has introduced guidelines for the management of cardiovascular risk factors[95]. These guidelines aim to improving the quality of GP care for stroke precursors such as hypertension, diabetes mellitus and transient ischaemic attack (TIA). Little is known about systematic socioeconomic variations in GP's adherence to guidelines relevant for the prevention of stroke. Research on these disparities may reveal specific aspects of care that can help prevent socioeconomic disparities in stroke occurrence.

1.3 This thesis

This thesis aims to contributing to the understanding of socioeconomic differences in stroke from an international and explanatory perspective. The overall aim of the thesis is *to estimate the magnitude of socioeconomic differences in stroke across different world populations, and to assess the contribution of biological, behavioural, psychosocial and preventive health care related risk factors to socioeconomic differentials in stroke.*

An international perspective

Several studies have shown that lower socioeconomic status is associated with higher stroke rates in specific populations[51-62,68]. However, these studies are largely based on data from northern European countries, the United States and Australia, whereas few studies have examined socioeconomic differentials in stroke in other populations such as those in southern Europe. Socioeconomic differences in risk factors for stroke such as smoking and fruit and vegetable consumption vary substantially across populations[82,84,86]. Therefore, results for northern European countries and the United States might not be generalizable to other European populations. The present study attempts to overcome these issues by assessing socioeconomic differentials in northern and southern European populations and the United States.

An international perspective in analysing socioeconomic differentials is of particular importance for stroke. There is evidence of enormous variation between world populations in stroke mortality rates[10]. Similarly, whereas some countries have experienced steep stroke mortality declines, countries such as those in Eastern Europe have experienced increases in stroke mortality during recent decades[10]. These variations might reflect major differences between countries not only in the prevalence of stroke risk factors but also in the organization of stroke care services[6], which might have an impact on the magnitude of socioeconomic differentials in stroke. Only by comparing countries is it possible to elucidate healthcare and social policies at the national level that might be associated with the magnitude of socioeconomic differences in stroke.

Research questions

The distinctive nature of this thesis lays in the combination of an international perspective, the assessment of the contribution of multiple stroke risk factors, and the emphasis on the role of preventive care in general practice in explaining socioeconomic differences in stroke. The specific research questions addressed in this thesis are:

1. What is the international pattern of socioeconomic differences in stroke mortality during the last decades among men and women at middle and old ages in Europe and the United States?

2. What is the role of biological, behavioural and psychosocial risk factors in the explanation of socioeconomic differences in stroke?

3. What is the impact of inequity in the quality of preventive care and cardiovascular risk management on socioeconomic differences in stroke?

Methods and data sources

This thesis has the advantage of comprising multiple data sources from different world populations and a variety of methods of analysis. Table 1.2 presents an overview of data sources from studies included in this thesis. Overall, seven data sources are used in this study:

- *Socioeconomic differences in healthy aging (SEDHA) project.* The SEDHA project comprises longitudinal data at the national or regional level on mortality by socioeconomic status for 10 European populations including Finland, Norway, Denmark, England/Wales, Belgium, Switzerland, Austria, Turin (Italy), Barcelona (Spain), and Madrid (Spain). This study is based on linkage of census and mortality registry data and comprises approximately 5 years of follow-up for each population.
- *The Monitoring of Socioeconomic inequalities project.* This study comprises data on mortality by educational level and occupational class in the period 1981-1985 to 1991-1995 in 6 European populations including Norway, Finland, Sweden, Denmark, England and Wales, and Turin (Italy).
- *The Health and retirement survey (HRS) study.* Data came from 19,565 participants in the Health and Retirement Study who provided information on demographics and cardiovascular risk factors. Individuals were followed for stroke incidence (fatal and non fatal) for an average of 8.5 years.
- *The Globe study*. Data came from 3,339 individuals in the south of the Netherlands aged 40-74 years among whom information on biomedical, behavioural and psychosocial risk factors were obtained through baseline interview. Stroke incidence was ascertained during 12 years of follow-up through linkage with the national hospital diagnosis registry.
- *Established Populations for the Epidemiologic Studies of the Elderly (EPESE) study.* Data comprised a sample of 2,812 men and women aged 65 years and over from the New Haven cohort of the EPESE study. Individuals provided baseline information on demographics, functioning, cardiovascular and psychosocial risk factors in 1982 and were followed for 12 years.
- *The European Prospective Investigation into Cancer (EPIC) study.* This study comprised data from 507,000 men and women aged 30 to 74 years in nine European countries (Denmark, France, Germany, Greece, Italy, the Netherlands, Spain, Sweden and United Kingdom) who completed a validated diet and health questionnaire at baseline and were followed for mortality (mean 5.3 years).
- *The Second National survey of General practice.* This study comprises data from approximately 400,000 patients of general practice in the Netherlands collected during a one-year period. Data were collected on diagnoses, referrals, prescriptions and diagnostic procedures.

Table 1.2. Overview of data sources: Study name, population, period, follow-up and outcome

Study	**Population and age**	**Data collection Period**	**Follow-up**	**Outcome**	**Thesis Chapter**
Socioeconomic differences in healthy aging (SEDHA)	Entire or representative population in 9 European countries (30 year or older)	1990-1997	5 years	Stroke mortality	2, 4
The Monitoring of Socioeconomic inequalities project	Entire or representative population in 6 European countries (30-74 years)	1981-1985, 1986-1990, 1991-1995	5 years	Stroke mortality	3
The Health and retirement survey (HRS) study	19,565 men and women in the United States (50 years or older)	1992-2004	12 years	Fatal or non-fatal stroke incidence	5
The Globe study	3,339 men and women in the South of the Netherlands (Eindhoven) (40 to 74 years)	1991-2003	13 years	Fatal or non-fatal stroke incidence	6
Established Populations for the Epidemiologic Studies of the Elderly (EPESE) study	2,812 men and women from the New Haven cohort, United States (65 years or older)	1982-1994	12 years	Fatal or non-fatal stroke incidence	7
The European Prospective Investigation into Cancer (EPIC) study.	507,000 men and women in 9 European countries (40 years or older)	1992-2002	5 years	Stroke mortality	8
The Second National survey of General practice	400,000 patients in general practice in the Netherlands (25 years or older)	2000-2002	1 year	Fatal or non-fatal stroke incidence	9,10

Structure of thesis

Further to the introduction of research question and methods (chapter 1), this thesis is divided into three sections. The first section comprises four chapters aimed to examining the international pattern of socioeconomic differentials in stroke mortality. Firstly, Chapter 2 provides an overview of socioeconomic differentials in stroke mortality in 9 European countries among men and women, and analyses age-variations in these differentials in each population. This chapter places socioeconomic differentials in stroke into context by describing their contribution to socioeconomic differences in life expectancy in Europe. Chapter 3 describes time trends in stroke mortality by socioeconomic status in 6 European countries during recent decades. In an attempt to raise hypotheses on the causes of international variations, Chapter 4 compares socioeconomic differences in ischaemic heart disease (IHD), stroke and lung cancer mortality in 9 European countries. This section ends with chapter 5, which assess the impact of wealth, income and education on stroke incidence in US adults, and describes the age-pattern of socioeconomic differentials in stroke at old age in a representative sample of US citizens.

The second section comprises three chapters and aims to contributing to the explanation of socioeconomic differentials in stroke. Firstly, chapter 6 depicts the potential impact of modifying conventional and psychosocial risk factor on socioeconomic differentials in stroke incidence in the Netherlands, looking at their impact on both relative and absolute measures of effect. Chapter 7 aims at assessing the impact of income and education on stroke incidence and how this varies at early and late old age, and to estimate the role of conventional and psychosocial risk factors in a sample of US elderly. Chapter 8 concludes this section by examining the contribution of nutritional and conventional risk factors to socioeconomic differences in stroke and IHD mortality in Europe, comparing their differential role in northern and southern populations.

The third and last section of this thesis concentrates on the role of socioeconomic variations in the quality of preventive care for stroke in explaining socioeconomic stroke differentials. Firstly, chapter 9 assess how socioeconomic disparities in stroke incidence relate to systematic socioeconomic variations in the quality of preventive care for precursors of stroke provided by GPs in the Netherlands. Based on evidence-based guidelines, quality indicators were developed and systematic deviations from general practice guidelines relevant for stroke prevention assessed. This section ends with chapter 10, which examines socioeconomic differences in the prescription for statins for primary and secondary prevention in general practice, and assesses GP adherence to guidelines for statin prescriptions in the Netherlands.

This thesis concludes with a general discussion of the findings, their policy implications and recommendations for tackling socioeconomic differences in stroke worldwide.

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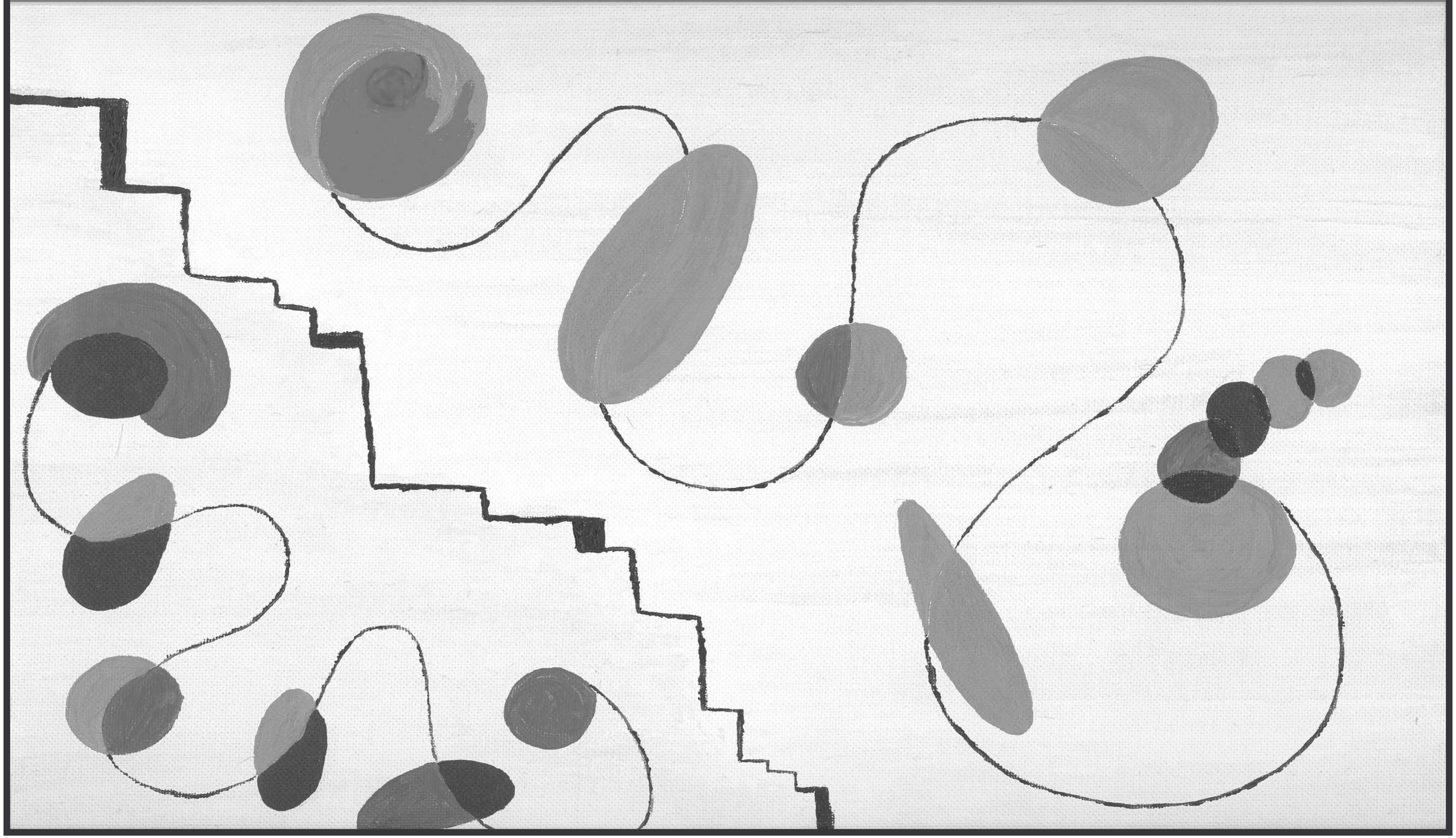
Part II

Socioeconomic disparities in stroke: An international perspective



Chapter 2

Educational level and stroke mortality: A comparison of 10 European populations during the 1990s

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(http://stroke.ahajournals.org/cgi/content/full/35/2/432)

Abstract

Background and purpose: Variations between countries in occupational differences in stroke mortality were observed among men during the 1980s. This study estimates the magnitude of differences in stroke mortality by educational level among men and women aged 30 years and older in 10 European populations during the 1990s.

Methods: Longitudinal data from mortality registries were obtained for 10 European populations, namely Finland, Norway, Denmark, England/Wales, Belgium, Switzerland, Austria, Turin (Italy), Barcelona and Madrid (Spain). Rate ratios were calculated to assess the association between educational level and stroke mortality. The life-table method was used to estimate the impact of stroke mortality on educational differences in life expectancy.

Results: Differences in stroke mortality according to educational level were of a similar magnitude in most populations. However, larger educational differences were observed in Austria. Overall, educational differences in stroke mortality were of similar size among men (Rate Ratio [RR], 1.27; 95%CI, 1.24 to 1.30) and women (RR, 1.29; 95%CI, 1.27 to 1.32). Educational differences in stroke mortality persisted at all ages in all populations although they generally decreased with age. Eliminating these differences would on average reduce educational differences in life expectancy by 7% among men and 14% among women.

Conclusions: Educational differences in stroke mortality were observed across Europe during the 1990s. Risk factors such as hypertension and smoking may explain part of these differences in several countries. Other factors such as socioeconomic differences in healthcare utilization and childhood socioeconomic conditions may have contributed to educational differences in stroke mortality across Europe.

2.1 Introduction

Research has shown that individuals with a low socioeconomic status experience higher stroke mortality than those with a high socioeconomic status[1-8]. During the 1980s, relatively small occupational differences in stroke mortality were observed in most Nordic countries (Sweden, Norway and Denmark), Italy and Spain, whereas larger differences were reported in England/Wales, Ireland and Finland[1]. However, it is not known whether these international variations persisted into the 1990s.

Welfare and healthcare systems vary across European countries[9,10]. Similarly, the magnitude of socioeconomic differences in the prevalence of risk factors for stroke such as hypertension[11], smoking[12] and diet[13] varies by country. Research on inter-country variation can contribute to the identification of risk factors and policies through which the excess stroke mortality among lower socioeconomic groups can be reduced. This would in turn contribute to an overall reduction in stroke mortality across Europe.

The aim of this paper is to assess stroke mortality differences according to educational level across Europe during the 1990s. Previous studies were limited to middle-aged men and based on cross-sectional data for some countries[1]. This is the first longitudinal study of the association between educational level and stroke mortality in 10 European populations among men and women aged 30 years and older. This is also the first study to assess the impact of stroke mortality on educational differences in life expectancy, providing a broader public health perspective.

2.2 Methods

Data and Subjects

Longitudinal data on mortality by educational level, sex and five-year age group were obtained for ten European populations. Participants were enumerated during a census in the early 1990s and followed-up for different periods (Table 2.1). Most studies covered the entire national population, except Madrid (regional), Barcelona and Turin (urban), Switzerland (population living in German speaking areas) and England/Wales (1% representative sample of the population). Studies included individuals aged 30 years and older (age specified at the start of follow-up), except in Denmark, where data on education were not available for those aged 70 years and older.

Table 2.1. Follow-up period, number of person-years at risk and stroke deaths among men and women aged 30 years and older

Population	Follow-up period	Number of person-years		Number of Stroke deaths	
		Men	Women	Men	Women
Finland	1991-1995	6,758,254	7,690,004	10,245	16,824
Norway	1990-1995	5,622,530	6,106,085	10,822	15,463
Denmark*	1991-1995	6,157,669	6,242,145	3,111	2,458
England/Wales	1991-1996	796,618	894,517	1,336	2,298
Belgium	1991-1995	13,047,398	14,587,998	18,050	28,309
Switzerland	1991-1995	5,673,634	6,747,784	7,118	10,541
Austria	1991-1992	2,092,646	2,459,626	3,520	6,356
Turin	1991-1996	1,276,242	1,532,676	2,563	3,672
Barcelona	1992-1996	2,263,963	2,798,811	3,505	5,497
Madrid	1996-1997	2,047,073	2,398,763	1,389	2,156

* Data available for ages 30-69 years only

Educational level was used as an indicator of socioeconomic status. In contrast to occupational class, this indicator can be applied equally to both men and women and is more comparable between age groups[14,15]. Education is considered a more reliable indicator of socioeconomic status among the elderly, because it includes the large proportion of economically inactive individuals that would be excluded when using occupational class[15]. Educational level is also more comparable between European countries and more stable over time than other indicators such as occupational class and income[14,15].

Educational level was first coded according to national classification schemes. In order to enhance comparability between countries, education was subsequently reclassified into three equivalent categories so that the proportion of individuals with a low educational level was similar across populations. These groups approximately corresponded to levels 0-2 (pre-primary, primary and lower secondary education), 3 (upper secondary education) and 4-6 (postsecondary education) of the UNESCO Standard Classification scheme. In most countries, about 65-80% of the population had a low educational level, 15-30% had a middle level and about 10-15% had a high educational level.

Stroke (cerebrovascular disease) was defined as code numbers 430-438 of the 9th revision of the International Classification of Diseases (ICD-9), except in Denmark and Switzerland, where both ICD-8 (430-438) and ICD-10 (I60-I69) codes were used.

Methods of analyses

Age-standardized stroke mortality rates were calculated for gender and education strata distinguishing three age groups: 30-59, 60-74 and 75 years and older. Rates were standardized by five-year age groups using the direct method with the European population of 1995 as the standard[16]. Age-adjusted rate ratios (RR) were calculated using Poisson regression. This summary index compared the mortality rate of the low education group with the combined rate of the middle/high education group, using the latter as the reference category. These two upper levels were combined in order to obtain more precise estimates, given the small size of these education groups. Analyses were performed using SAS, version 6.12.

In order to estimate the impact of eliminating educational differences in stroke mortality on educational differences in life expectancy at age 30, the cause-elimination life table method was applied. Firstly, the difference in life expectancy between the low and middle/high education groups was calculated. This was compared with predicted differences in life expectancy, as they would have been if the low education group had the same stroke mortality rate of the middle/high education group.

Analyses were performed separately for each population and for a pooled dataset weighted on the size of each cohort. This was done in order to take into account differences in population size in the pooled analysis.

2.3 Results

The age-standardized stroke mortality rates among men and women with low education were higher than the mortality rates among those with a middle or high educational level in all populations (Tables 2.2 and 2.3, respectively). This pattern was consistent in all age groups. A clear educational gradient was generally observed among middle-aged men and women, although this was less consistent among the younger and older age groups in some populations.

Table 2.2. Age-standardized stroke mortality rates (per 100,000 person-years) by educational level among men aged 30-59, 60-74 & ≥75

Population	Standardized Mortality Rate		
	30-59 years	60-74 years	75+ years
Finland			
Low	40.8	368.5	1766.4
Middle	30.6	318.5	1609.5
High	19.2	260.7	1612.1
Norway			
Low	19.9	295.3	1931.2
Middle	7.0	215.2	1686.3
High	7.8	164.4	1712.5
Denmark			
Low	22.5	135.2*	N.A.†
Middle	19.9	114.9*	N.A.†
High	15.9	108.4*	N.A.†
England/Wales			
Low	23.3	275.8	1843.7
Middle	18.5	196.3	1268.1
High	20.3	135.0	1669.0
Belgium			
Low	19.8	249.3	1551.1
Middle	13.6	207.6	1409.3
High	11.2	175.5	1201.6
Switzerland			
Low	14.1	218.8	1396.3
Middle	8.9	153.8	1232.2
High	6.6	125.7	1146.6
Austria			
Low	19.8	266.1	1825.8
Middle	10.9	159.3	1310.0
High	6.0	162.7	1676.3
Turin			
Low	20.8	294.9	2561.2
Middle	15.5	216.2	2058.2
High	18.5	163.2	2054.2
Barcelona			
Low	23.7	199.6	990.4
Middle	11.3	163.8	771.7
High	13.7	148.6	989.9
Madrid			
Low	8.8	104.4	739.6
Middle	7.1	111.6	675.7
High	7.2	100.2	454.9
All populations			
Low	21.3	259.1	1608.6
Middle	14.7	189.3	1286.2
High	11.9	156.5	1271.2

* Men aged 60-69 years
† Not available

Results shown in Figure 2.1 indicate that men and women with a low educational level had significantly higher mortality rates than those with a middle/high educational level. Educational differences in stroke mortality were of a similar magnitude in most populations. However, in Austria, differences were larger than the European average among both men and women, although this difference was only statistically significant among women. Overall, men and women with a low educational level had approximately a 26-28% higher risk of dying from stroke than those with a middle/high educational level.

Table 2.3. Age-standardized stroke mortality rates (per 100,000 person-years) by educational level among women aged 30-59, 60-74 & 75 years and older

Population	Standardized Mortality Rate		
	30-59 years	60-74 years	75+ years
Finland			
Low	22.5	250.0	1758.3
Middle	15.6	190.2	1573.4
High	10.0	138.9	1334.6
Norway			
Low	12.8	194.3	1747.2
Middle	6.1	127.8	1530.9
High	5.9	163.8	1470.1
Denmark			
Low	18.1	94.3*	N.A.†
Middle	14.8	71.9*	N.A.†
High	11.2	65.8*	N.A.†
England/Wales			
Low	19.2	222.9	1772.7
Middle	9.5	200.3	1426.7
High	0.0	103.3	1605.1
Belgium			
Low	13.6	172.1	1400.8
Middle	9.1	122.9	1180.4
High	8.2	95.2	1170.6
Switzerland			
Low	8.2	114.0	1133.9
Middle	6.1	79.4	964.9
High	3.4	77.6	851.4
Austria			
Low	12.4	157.4	1710.6
Middle	8.6	91.7	1152.7
High	2.3	81.0	1254.5
Turin			
Low	12.1	175.8	1870.1
Middle	8.3	141.9	1368.9
High	10.1	129.0	1656.8
Barcelona			
Low	10.8	115.2	971.6
Middle	4.4	64.1	742.2
High	9.8	95.6	786.0
Madrid			
Low	6.4	55.9	666.0
Middle	3.5	33.5	596.5
High	4.7	55.6	516.2
All populations			
Low	13.6	168.7	1433.6
Middle	9.2	115.0	1145.7
High	7.5	103.7	1051.3

* Women aged 60-69 years
† Not available

Differences in stroke mortality according to educational level were similar among men (RR, 1.27; 95%CI, 1.24 to 1.30) and women (RR, 1.29; 95%CI, 1.27 to 1.32) (figure 1). Although in most populations educational differences in stroke mortality were somewhat larger among women than among men, these variations were generally small and not significant.

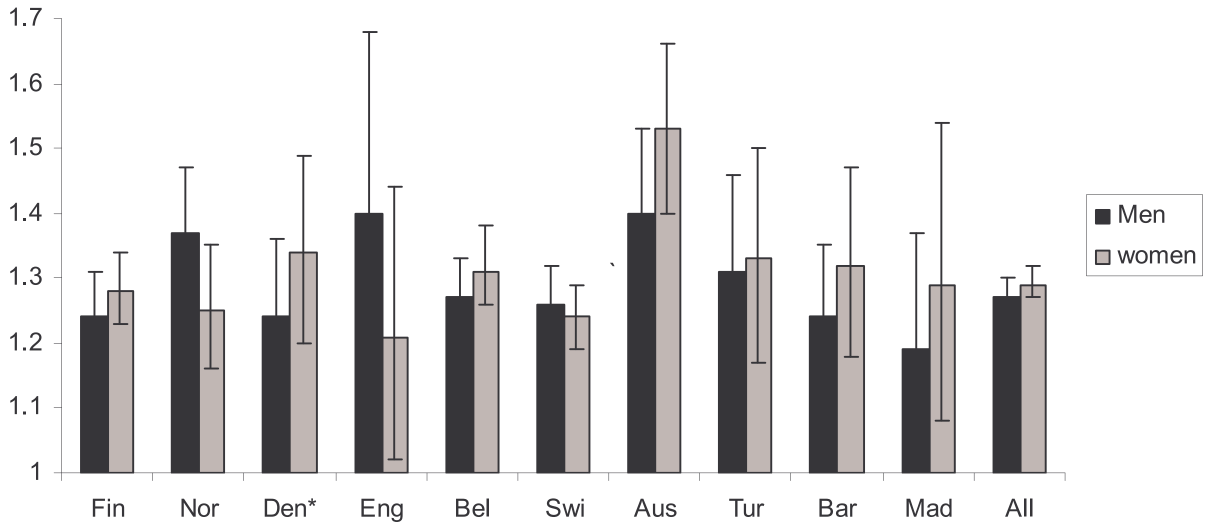

Figure 2.1. Stroke mortality: RR between low and middle/high educational levels among men and women aged _30 years.

Fin indicates Finland; Nor, Norway; Den, Denmark; Eng, England/Wales; Bel, Belgium; Swi, Switzerland; Aus, Austria; Tur, Turin (Italy); Bar, Barcelona (Spain); and Mad, Madrid (Spain).

*Data available for ages 30 to 69 years only.

Figure 2.2 shows the RRs for stroke mortality rates in low compared to middle/high education groups for each age category. As results were similar for men and women, RRs were calculated for both groups combined. Differences in stroke mortality between education groups were generally present in all age groups (Figure 2). However, differences decreased with age in most populations and in Europe as a whole. RRs in the pooled analysis were 1.52 (95%CI, 1.45 to 1.59) among those aged 30-59 years, 1.37 (95%CI, 1.33 to 1.41) among those aged 60-74 years and 1.19 (95%CI, 1.17 to 1.21) among those aged 75 years and older. A sharper decline with age was observed in Norway, Austria and Barcelona. In contrast, in England/Wales, Turin and Madrid, educational differences did not decrease consistently with age. However, in all populations, absolute rate differences increased with age and were largest among those aged 75 years and older (Tables 2.2 and 2.3, respectively).

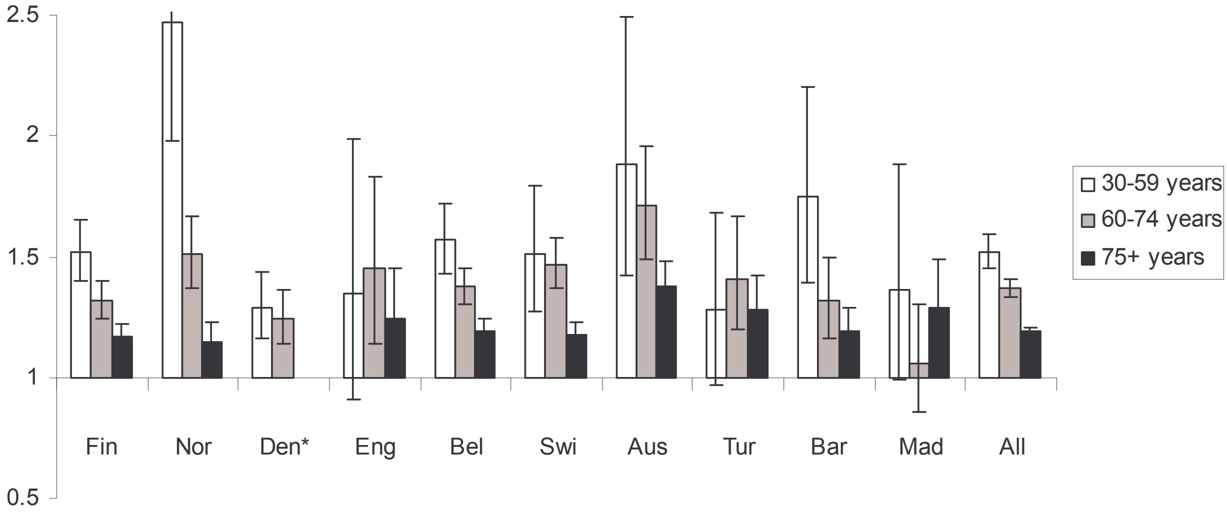

Figure 2.2. Stroke mortality: RR between low and middle/high educational levels among both men and women aged 30 to 59, 60 to 74, and _75 years.

Fin indicates Finland; Nor, Norway; Den, Denmark; Eng, England/Wales; Bel, Belgium; Swi, Switzerland; Aus, Austria; Tur, Turin (Italy); Bar, Barcelona (Spain); and Mad, Madrid (Spain).

*Data available for ages 30 to 69 years only.

Differences in life expectancy at age 30 between low and middle/high education groups were on average 3.22 years among men and 2.18 years among women (Table 2.4). Eliminating educational differences in stroke mortality would on average reduce educational differences in life expectancy by 7% (.24 years) among men and 14% (.31 years) among women. The largest reduction would be achieved among both men and women in Turin (9% and 18% respectively) and Austria (7% and 18% respectively), as well as among men in Norway (7%) and England/Wales (7%).

Table 2.4. The impact of eliminating educational differences in stroke mortality on educational differences in life expectancy at age 30 among men and women

Population	Men			Women		
	Differences in LE (years)	LE differences after elimination (years)	Reduction in years (%)	Differences in LE (years)	LE differences after elimination (years)	Reduction in years (%)
Finland	3.68	3.49	.19(5%)	2.37	2.09	.28(12%)
Norway	3.59	3.34	.25(7%)	2.45	2.19	.26(11%)
England/W	3.27	3.05	.22(7%)	2.26	2.00	.26(11%)
Belgium	3.31	3.16	.15(5%)	2.43	2.20	.23(9%)
Switzerland	3.84	3.68	.16(4%)	1.86	1.67	.19(10%)
Austria	4.19	3.89	.30(7%)	2.31	1.89	.42(18%)
Turin	2.57	2.34	.23(9%)	1.78	1.46	.32(18%)
Barcelona	4.02	3.83	.19(5%)	2.67	2.40	.27(10%)
Madrid	2.41	2.32	.09(4%)	1.37	1.20	.17(12%)
All	3.22	2.98	.24(7%)	2.18	1.87	.31(14%)

* LE indicates life expectancy

2.4 Discussion

Differences in stroke mortality between education groups were of a similar magnitude across populations. Larger disparities were however observed in Austria. Educational differences in stroke mortality were similar among men and women and generally decreased with age. Eliminating differences in stroke mortality between education groups would on average reduce disparities in life expectancy by 7% among men and 14% among women.

Evaluation of Data

Some limitations of this study should be considered. Firstly, countries might differ in the practices and accuracy of death registrations, which might have influenced results for some countries. However, our results would only be biased if misclassification of stroke occurred differentially across educational levels. There is no evidence to suggest that this has occurred in any of the countries. Therefore, any bias caused by this problem is likely to be small.

Secondly, national education levels were reclassified so that the proportion of participants with low education was similar across countries. This was not possible in Switzerland, where a larger proportion of participants had a high educational level. However, as this was possible in most populations, educational levels were generally comparable across countries. Nevertheless, low education groups were relatively large in each country. We do not know whether similar results would be observed when dividing this group into more specific levels.

Finally, we assessed whether data problems might explain the results for Austria. However, such problems were not identified. Although the follow-up period was shorter in Austria and Madrid, previous evaluations indicate that mortality differences by education are unrelated to follow-up time[17]. Instead, the pattern for Austria might resemble that of Middle European countries such as the Czech Republic and Hungary, where socioeconomic differences in stroke mortality were larger than in Western Europe[7,17].

Comparison with previous studies

In contrast to previous research during the 1980s among men[1], we found similar educational differences in stroke mortality across Europe. Populations with small occupational differences during the 1980s such as Turin, Spain and most Nordic countries had similar educational disparities as other populations during the 1990s. Similarly, whereas the largest disparities were observed in Finland during the 1980s, these were around the European average in our study. These discrepancies might be explained by improvements in the quality of our data, which comprised broader age groups. Previous studies in some countries used cross-sectional data in which the number of deaths was not directly linked to data on the population at risk. These studies might also have been biased by the use of occupational class due to the exclusion of economically inactive men[15,17].

Furthermore, different mechanisms might account for the effect of educational level and occupational class[14,15]. Whereas education might influence mortality primarily through factors such as health behaviour, occupation might also represent exposure to the psychosocial and physical dimensions of work arrangements[14]. Finally, widening socioeconomic differences in stroke mortality in some southern European countries[3] may have contributed to a more homogeneous international pattern during the 1990s.

Explanation of results

Hypertension is the most important risk factor for stroke. A higher hypertension prevalence has been observed in Northern countries such as Finland and England, as compared to Mediterranean states[18]. However, socioeconomic differences in hypertension prevalence have been reported both in Northern[11] and Southern European populations[19,20]. Despite differences between countries in treatment guidelines, a recent study found small variations in hypertension treatment rates, with somewhat higher rates in Italy and lower rates in Finland and England[18]. On average, only 8% of hypertensive individuals had their condition controlled in Europe[18]. Furthermore, a higher prevalence of poor hypertension treatment has been observed among low socioeconomic groups[20]. These findings suggest that educational differences in hypertension prevalence and treatment may partly explain the association between educational level and stroke mortality observed in our study.

Relatively high smoking prevalence rates have been observed among men in Denmark, Spain and Italy[12]. However, socioeconomic differences in smoking prevalence have only been observed in Northern States, whereas small or no disparities have been reported in Southern European countries[12]. Dietary factors such as salt and fat intake are also important risk factors for stroke. Socioeconomic differences in dietary patterns have been reported in Nordic countries[21,22], the UK[13], Austria[23] and Switzerland[24]. However, no socioeconomic differences in diet have been observed in Southern Europe[13]. Although a higher prevalence of obesity has been reported in Italy and Spain as compared to other countries[25], consistent socioeconomic differences in obesity prevalence have been observed among women across Europe[13,19]. This may have contributed to educational differences in stroke mortality among women, although this pattern is less consistent among men[13,19]. In summary, these classical risk factors may have contributed to educational differences in stroke mortality in several countries.

However, research indicates that classical risk factors explain less than half of socioeconomic differences in stroke[6,26]. This suggests that other factors such as access to healthcare may have played a role. Socioeconomic differences in healthcare utilization among stroke patients have been observed even in countries with universal healthcare systems such as Finland[4] and Sweden[8]. A recent study found similar socioeconomic disparities in access to specialist care in most European countries[9], including Italy, Spain, Belgium, the UK and Denmark. Inequity in the utilization of both general practice and specialist care has been observed in Finland[10] and Austria[9]. Thus, socioeconomic differences in healthcare access existed in most countries during the 1990s, which possibly contributed to educational differences in stroke mortality across Europe.

Finally, research indicates that childhood socioeconomic status is related to stroke[2,5]. Education is typically completed early in life and can therefore be considered as a marker of childhood socioeconomic conditions[14,15,27]. Thus, early life circumstances may have contributed to educational differences in stroke mortality during adulthood across Europe. However, the extent to which this applies to all populations remains uncertain.

Implications

This study supports previous research and provides further evidence of higher stroke mortality rates among individuals with a low level of education. Improving the unfavourable risk profile among these groups can therefore lead to an overall reduction in stroke mortality. However, the contribution of factors such as smoking and diet may differ across populations and therefore different interventions may be required for each country. Furthermore, policies that tackle inequity in healthcare access and hypertension treatment may also be necessary to reduce stroke mortality differences between education groups.

Such a reduction could have an important public health impact by diminishing educational disparities in life expectancy in Europe.

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Chapter 3

Trends in socioeconomic disparities in stroke mortality in six European countries between 1981-1985 and 1991-1995

Avendano M, Kunst AE, van Lenthe F, Bos V, Costa G, Valkonen T, Cardano M, Harding S, Borgan JK, Glickman M, Reid A, Mackenbach JP. Trends in socioeconomic disparities in stroke mortality in six European countries between 1981-1985 and 1991-1995. *Am J Epidemiol*. 2005;161:52-61
(http://aje.oxfordjournals.org/cgi/content/full/161/1/52)

Abstract

Background and objectives: This study assesses whether stroke mortality trends have been less favourable among lower than among higher socioeconomic groups.

Methods: Longitudinal data on mortality by socioeconomic status were obtained for Finland, Norway, Denmark, Sweden, England/Wales and Turin (Italy). Data covered the entire population or a representative sample. Stroke mortality rates were calculated for the period 1981-95. Changes in stroke mortality rate ratios (RR) were analysed using Poisson regression and compared with RRs in ischaemic heat disease (IHD) mortality.

Results: Trends in stroke mortality were generally as favourable among lower as among higher socioeconomic groups, such that socioeconomic disparities in stroke mortality persisted and remained of a similar magnitude in the 1990s as in the 1980s. In Norway, however, occupational disparities in stroke mortality significantly widened, and a non-significant increase was observed in some countries. In contrast, disparities in IHD mortality widened throughout this period in most populations.

Conclusions: Improvements in hypertension prevalence and treatment may have contributed to similar stroke mortality declines in all socioeconomic groups in most countries. Socioeconomic disparities in stroke mortality generally persisted and may have widened in some populations, which underlines the need to improve preventive and secondary care for stroke among the lower socioeconomic groups.

3.1 Introduction

Higher stroke mortality rates have been observed among lower as compared to higher socioeconomic groups across Europe[1,2]. However, no study has explored how these disparities developed or examined trends in socioeconomic differences in stroke mortality. A less favourable relative decline in cardiovascular disease (CVD) mortality has been observed among lower than among higher socioeconomic groups[3-10]. However, trends in the two main cardiovascular diseases, stroke and ischaemic heart disease (IHD), differ substantially within and between populations[9,11,12], as well as their association with socioeconomic status[1,3,13,14].

During recent decades, European countries have experienced changes in the prevalence of classical cardiovascular risk factors such as smoking and hypertension[15,16]. Variations between countries exist in these trends[17,18], and socioeconomic differences in some of these factors have recently widened [19,20]. Similarly, changes in healthcare policies for stroke have occurred across Europe[21,22]. International studies on trends may point at specific policies and risk factors that may have had an impact on socioeconomic differences in stroke mortality. This may elucidate ways through which socioeconomic disparities can be reduced in order to sustain the stroke mortality decline in European countries.

The aim of this paper is to assess whether there is a common tendency among lower socioeconomic groups to experience less favourable trends in stroke mortality than higher socioeconomic groups in European countries. This is the first longitudinal study of trends in stroke mortality according to socioeconomic status across Europe. Previous research has mainly been focused on specific countries, middle-aged men, and based on cross-sectional study designs[4,5,23,24]. We analysed trends among men and women in six populations, using two complementary indicators of socioeconomic status: educational level and occupational class. It has been argued that stroke and IHD mortality share a number of risk factors. Therefore, we assessed whether trends in socioeconomic differences in these two cardiovascular diseases showed a similar pattern, which would suggest that changes over time might be related to common determinants.

3.2 Materials and methods

Data and Subjects

Within the framework of the European Union Health Monitoring Project, longitudinal data on mortality by 5-year age group, socioeconomic status and sex were obtained for six European populations in three separate periods: 1981-85, 1986-90 & 1991-95. Data were obtained from mortality registries and linked to data on socioeconomic status from population censuses carried out in 1981, 1986 (Finland only) or 1991 for each period. Participants were enumerated during each census and followed-up for different periods (table 3.1). Data from Finland, Norway, Denmark and Sweden covered the entire national population. Data from England and Wales corresponded to 1 percent representative sample of the population, whereas data from Italy were restricted to the city of Turin. Details of these data have been described elsewhere[25,26]. Table 3.1 shows the number of person-years and deaths observed in each population.

Socioeconomic status was defined on the basis of educational level and occupational class, as these are the most commonly used indicators of socioeconomic status[27,28]. Educational level can be applied equally to both men and women and is considered the most reliable indicator of socioeconomic status among the elderly, as it includes both the economically active and inactive population[28]. On the other hand, occupational class has also an independent association with mortality and is sensitive to changes over the life-course[27,28]. Thus, educational level and occupational class may represent different aspects of social standing and were both used as complementary measures of socioeconomic status[27,28].

Table 3.1. Follow-up period, number of person-years at risk, and number of deaths in six European populations, 1981–1996

	Period	ICD Code	Education*						Occupation†		
			Men			Women			Men		
			p-years (no.)‡	Stroke deaths (no.)	IHD§ deaths (no.)	p-years (no.)	Stroke deaths (no.)	IHD deaths (no.)	p-years (no.)	Stroke deaths (no.)	IHD deaths (no.)
Fin	81-85	9	5,584	6,620	30,631	6,325	7,000	14,577	4,491	1,891	11,165
	86-90	9	6,039	6,301	27,130	6,633	6,299	13,419	4,882	1,852	9,082
	91-95	9	6,438	5,807	23,163	6,906	5,256	10,415	5,144	1,622	6,658
Nor	81-85	8	4,709	4,916	22,553	4,927	4,308	8,339	3,278	707	5,550
	85-90	9	4,837	4,671	21,297	5,038	3,928	8,287	3,355	606	4,697
	91-95	9	5,076	3,943	16,175	5,228	3,238	6,370	3,699	379	2,858
Se	81-85	8	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	7,199	1,167	8,550
	86-90	8/9	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	5,827	1,076	6,911
	91-95	9	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	8,045	1,221	6,121
Den†	81-85	8	4,042	922	6,152	4,048	693	1,397	4,360	808	5,849
	86-90	8	4,248	913	5,074	4,249	731	1,228	4,457	763	4,536
	91-95	8/10	4,553	871	3,894	4,549	705	996	4,589	710	3,317
E/W	81-85	9	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	458	144	894
	86-90	9	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	381	100	748
	91-95	9	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	497	98	599
Tur	82-86	9	1,322	1,641	2,562	1,511	1,321	1,002	1,041	317	1,004
(It)	86-91	9	1,136	1,712	2,431	1,348	1,728	1,248	805	237	683
	92-96	9	1,206	912	1,772	1,363	741	677	886	191	491

* Ages 30-74 years

† Ages 30-59 years

‡ Number of person-years at risk per 1,000

§ IHD indicates ischemic heart disease

NA indicates not available; Fin indicates Finland; Nor indicates Norway; Se indicates Sweden; E/W indicates England & Wales; Tur indicates Turin; It indicates Italy

Data on educational level were available for both men and women in Finland, Denmark, Norway and Turin. Data covered the ages 30 to 74 years (age specified at the start of follow-up), except in Denmark where data on education were not available for those aged 60 years and older. Education was first coded according to national classification schemes, based on the educational level completed by participants. Following this, education was reclassified into three comparable categories based on the ISCED (International Standard Classification of Education) [29]: levels 0-2 (pre-primary, primary and lower secondary education), 3 (upper secondary education) and 4-6 (post-secondary education). The two upper levels were combined in order to obtain more precise estimates, given the small size of these education groups. In each country, the proportion of the population in the high education group was higher among men than women and increased over time. No detailed census data on educational level were available for Sweden, while educational data for England/Wales were not comparable to those collected in other countries. Therefore, no analyses on educational level were conducted for these two countries.

Data on occupational class were available for men in Finland, Sweden, Norway, Denmark, England/Wales and Turin. Data covered the ages 30 to 59 years (age specified at the start of follow-up). Men aged 60 years and older were excluded from the analysis because of lack of detailed occupational information among economically inactive men. Women were also excluded from the analysis, since it was not possible to apply an occupational classification that was both valid and comparable over time. Participants were classified into four broad occupational classes using the Erikson-Goldthorpe-Portocarero (EGP) scheme[30] as a reference: non-manual workers, manual workers, farmers and self-employed men. For summary purposes, we report only on mortality differences between 'non-manual' and 'manual' classes, excluding workers in the agricultural sector and self-employed men. The non-manual and manual classes comprised approximately 80-90 percent of the population in all countries. The share of the manual classes decreased slightly over time, whereas the share of the non-manual classes slightly increased.

Occupational class was determined based on occupation reported at the time of census. For some men, however, no information on occupation was available. This mostly corresponded to economically inactive men such as the disabled and retired. When possible, occupational class was assigned to these individuals based on a previously held occupation, by linkage to a previous census. This was possible for part of the population in Finland and England & Wales only. Men for whom no occupation could be assigned were excluded from the analysis. Their exclusion is likely to lead to an underestimation of mortality differences between occupational classes, because economically inactive men have high mortality rates and predominantly originate from lower occupational classes[1,28,31]. Therefore, in all countries, we applied a procedure that corrects for this underestimation and has been shown to perform well in a large number of tests[31]. This procedure calculates correction factors as a function of the population share and the mortality of men excluded from the analysis[1,31]. Correction factors were calculated separately for stroke and IHD, for each country and age group.

In Finland, England/Wales and Turin, the ICD-9 (9th revision of the International Classification of Diseases) was used in all periods. Stroke (cerebrovascular disease) was defined as codes 430-438 and IHD as codes 410-414. The ICD-9 was also used in Norway, except in the first period where the ICD-8 was used. In Sweden, the ICD-8 was used in the first period, both the ICD-8 and ICD-9 in the second period, and the ICD-9 in the last period. In Denmark, the ICD-8 was used in the first two periods, and both the ICD-8 and ICD-10 in the last period. From the ICD-8, codes 430-438 (stroke) and 410-414 (IHD) were used. From the ICD-10, codes G45, G46, I60-I69 (stroke) and I20-I25 (IHD) were used.

Methods of analyses

Age-standardized mortality rates were calculated by sex, educational level and occupational class strata. Rates were standardized by five-year age groups using the direct method with the European population of 1987 as the standard[32]. This procedure controlled for differences in the age distribution between men and women, socioeconomic groups, countries and periods. In order to assess socioeconomic differences in trends in stroke mortality, slope estimates that corresponded to the percentage change between the first and the last period were calculated for each socioeconomic group in each country. Age-adjusted slope estimates and corresponding 95 percent confidence intervals were calculated using Poisson regression.

Differences in mortality rates according to socioeconomic status were estimated for each period. For this purpose, age-adjusted rate ratios (RR) and corresponding 95 percent confidence intervals were calculated using Poisson regression. For educational level, this summary index compared the mortality rate of the low education group with the combined rate of the middle/high education group, using the latter as the reference category. For occupational class, RRs compared the mortality rate of manual and non-manual classes, using the latter as the reference category.

Finally, estimates of change in RRs between the first and the last period were calculated in order to assess differences between stroke and IHD mortality trends in each country. 95 percent confidence intervals for these estimates were calculated by pooling standard errors from period-specific RRs for each country. Analyses were performed using SAS, version 6.12.

3.3 Results

The age-standardized stroke mortality rate declined steadily among both men and women in most countries throughout the periods 1981-85, 1986-90 and 1991-95. A similar stroke mortality decline occurred among lower and higher socioeconomic groups in most countries, in both relative and absolute terms (tables 3.2 & 3.3). This pattern was consistent for educational level in all countries (Table 3.2). In contrast, relative declines in stroke mortality tended to be slightly larger among non-manual than among manual classes in Norway, Finland, Denmark and England/Wales (Table 3.3). Nevertheless, the only significant differential (relative) decline by occupational class was observed for Norway. Absolute stroke mortality declines were larger among lower than among higher socioeconomic groups in several populations, but these differences were not statistically significant.

Table 3.2. Stroke mortality rates and change in the periods 1981–1985, 1986–1990, and 1991–1995 by educational level among men and women aged 30–74 years in four European populations

Country	Sex	Level of Education	Stroke mortality rate			Change between 1981-85 and 1991-95		
			1981-85	1986-90	1991-95	Absolute change	% of change	95% CI†
Finland	M	Mid/high	92.2	80.2	76.7	-15.5	-17.2	-23.4, -10.6
		Low	116.6	107.3	96.7	-19.9	-17.4	-20.6, -14.0
	F	Mid/high	51.7	48.5	41.6	-10.1	-20.4	-27.3, -12.7
		Low	74.5	68.4	58.6	-15.9	-21.2	-24.3, -18.1
Norway	M	Mid/high	65.3	62.4	51.8	-13.5	-20.3	-25.2, -15.0
		Low	79.6	80.1	69.3	-10.3	-14.7	-19.3, -9.7
	F	Mid/high	40.3	36.4	31.8	-8.5	-21.3	-27.5, -14.5
		Low	57.5	51.9	44.5	-13.0	-23.3	-27.4, -18.9
Denmark*	M	Mid/high	15.2	16.8	16.3	1.1	5.1	-10.9, 24.1
		Low	21.6	21.5	18.9	-2.7	-12.2	-21.7, -1.5
	F	Mid/high	11.9	11.8	12.1	0.2	4.3	-12.8, 24.8
		Low	16.1	17.3	15.3	-0.8	-7.2	-18.8, 6.1
Turin (Italy)	M	Mid/high	100.7	96.7	56.2	-44.5	-43.3	-50.1, -.35.4
		Low	122.1	106.7	71.5	-50.6	-41.6	-47.4, -35.0
	F	Mid/high	45.9	49.0	33.1	-12.8	-26.7	-38.4, -12.7
		Low	68.2	62.4	40.5	-27.7	-41.7	-47.6, -35.1

* Data available for ages 30-59 years only
† 95% confidence interval of percentage change

Rate ratios (RRs) for stroke and IHD mortality of low compared with middle/high socioeconomic groups in the first (1981-85) and last (1991-95) study periods are presented in figure 3.1 (educational level) and figure 3.2 (occupational class). Overall, both indicators of socioeconomic status showed a similar pattern. Men and women with a low socioeconomic status had significantly higher stroke mortality rates as compared to those with a middle/high socioeconomic status throughout both periods in all populations.

However, confidence intervals were wide for Turin and England & Wales. Educational disparities in stroke mortality persisted and remained of a similar magnitude in the 1990s as in the 1980s among both men and women (figures 3.1). Occupational differences in stroke mortality showed a slight tendency to widen in Norway, Finland, Denmark and England/Wales (figure 3.2). However, this increase was only significant in Norway, whereas changes in other populations were not significant.

Socioeconomic differences in IHD mortality were observed in all populations but Turin during both periods among men and women (figures 3.1 & 3.2). In contrast to stroke, socioeconomic differentials in IHD mortality significantly widened during the study period in most countries among men (figures 3.1 & 3.2). However, occupational disparities in IHD mortality remained of a similar magnitude in Turin, and confidence intervals for occupational class overlapped in Denmark and England & Wales (figure 3.2). Among women, educational differences in IHD mortality significantly increased in Finland and Norway, whereas they remained relatively stable in Denmark and Turin (figure 3.1). Despite these variations, socioeconomic differences in IHD mortality showed a general tendency to increase in most countries.

Table 3.3. Stroke mortality rates and change in the periods 1981-85, 1986-1990 & 1991-95 by occupational class among men aged 30-59 years in six European populations

Country	Occupational class	Stroke mortality rate			Change between 1981-85 and 1991-95		
		1981-85	1986-90	1991-95	Absolute change	Percentage change	95% CI†
Finland	Non-manual	29.4	22.6	21.3	-8.1	-28.8	-38.3, -17.9
	Manual	44.3	41.8	37.3	-7.0	-15.6	-22.6, -8.0
Norway	Non-manual	16.6	15.0	8.4	-8.2	-49.2	-59.4, -36.5
	Manual	21.1	19.2	20.1	-1.0	-8.4	-23.0, 9.0
Sweden	Non-manual	14.7	17.3*	12.3	-2.4	-16.3	-26.7, -4.5
	Manual	22.2	22.3*	18.4	-3.8	-17.7	-26.8, -7.6
Denmark	Non-manual	17.1	15.7	14.9	-2.2	-16.3	-29.4, -0.8
	Manual	23.4	26.2	22.0	-1.4	-5.9	-19.7, 10.3
Eng/Wal	Non-manual	23.5	14.6*	13.9	-9.6	-38.8	-62.6, 0.1
	Manual	32.9	30.0*	22.0	-10.9	-35.4	-54.2, -9.0
Turin	Non-manual	23.1	21.4*	16.4	-6.7	-26.3	-46.7, 1.9
(Italy)	Manual	30.7	28.6*	20.3	-10.4	-35.8	-50.0, -17.7

* Data cover the age group 35-59 years only
† 95% confidence interval of percentage change

In order to assess whether trends in socioeconomic disparities in stroke and IHD mortality were significantly different, estimates of change in RRs for these two causes of death were formally compared. Whereas RR change estimates generally indicated a significant increase in socioeconomic disparities in IHD mortality, no significant change was observed in RRs for stroke mortality in most countries (figures 3.1 & 3.2). 95 percent confidence intervals of RR change estimates for stroke and IHD mortality overlapped in most populations (results not shown). However, differences in RR change estimates between these two causes of death were generally of borderline significance.

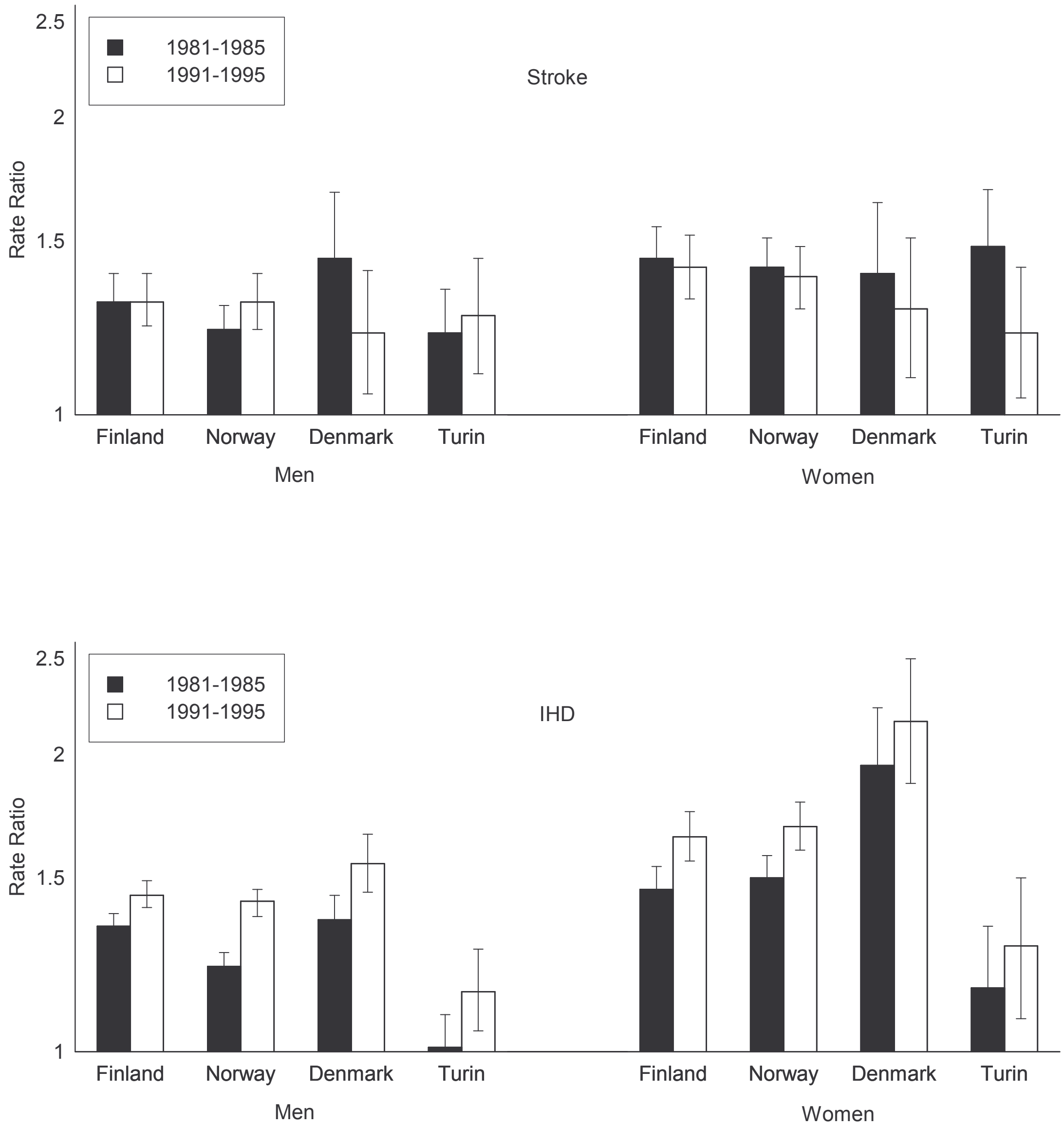

Figure 3.1. Rate Ratio (RR) between low and middle/high educational levels for stroke and ischaemic heart disease (IHD) mortality in the periods 1981-1985 & 1991-1995 among men and women in Finland, Norway, Turin (ages 30-74 years) and Denmark (ages 30-59 years)

95% Confidence Interval of estimate of change in RR does not include zero for Finland, Norway, Denmark and Turin among men (IHD), and for Finland and Norway among women (IHD)

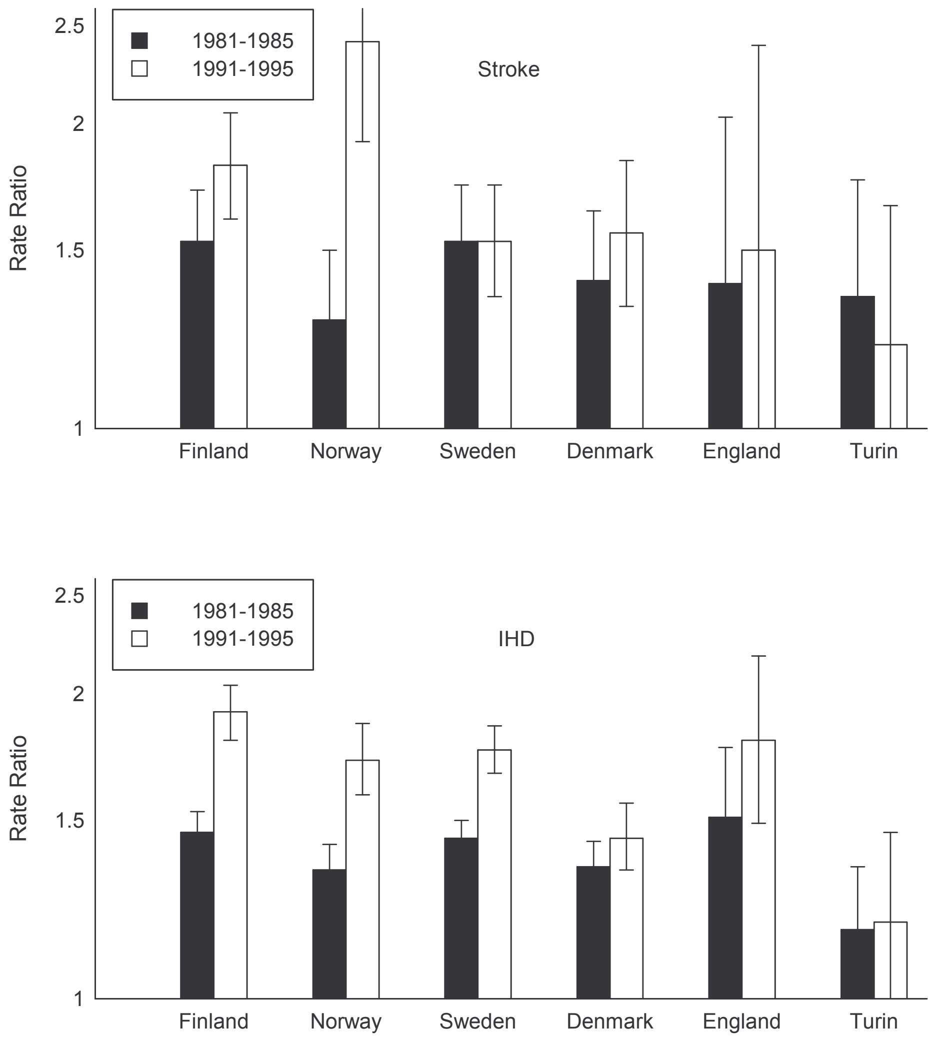

Figure 3.2. Rate Ratio (RR) between manual and non-manual occupational classes for stroke and Ischaemic heart disease (IHD) mortality in the periods 1981-1985 & 1991-1995 among men in Finland, Norway, Sweden, Denmark, England/Wales and Turin (ages 30-59 years)

95% Confidence Interval of estimate of change in RR does not include zero for Norway (stroke), and for Finland, Norway and Sweden (IHD)

3.4 Discussion

Stroke mortality has generally declined in all socioeconomic groups among both men and women. Declines in stroke mortality were generally similar among lower and higher socioeconomic groups, such that socioeconomic disparities in stroke mortality persisted and were of a similar magnitude in the 1990s as in the 1980s. For some Northern European countries, occupational differences in stroke mortality showed a slight tendency to widen. However, this increase was only significant in Norway, whereas increases observed in other populations were not significant. In contrast, socioeconomic differences in IHD mortality showed a general tendency to widen in most countries during the same period.

Evaluation of Data

International comparisons may be biased by differences between countries in the accuracy of death registrations and socioeconomic classifications. However, we did not strictly compare countries but analysed changes over time within each population.

Changes in the classification of causes of death may influence trends analyses. However, in most countries, the 9th version of the ICD code was used in all periods. It is unlikely that the late adoption of the 9th ICD revision in some countries influenced death rates, because the overall stroke category is essentially the same in the 8th and 9th ICD revisions[33]. Furthermore, our results would only be biased if deaths from stroke were classified differently by socioeconomic status. There is no evidence suggesting that this has occurred and, any bias due to this problem is likely to be small.

The classification of education and occupation used in our study remained unchanged. However, although changes in the occupational class distribution were small, the proportion of the population in the low educational category decreased considerably over time. This decline may have influenced our results, by either obscuring or inflating changes in socioeconomic differences in stroke mortality. In order to assess the impact of these changes, trends using the Relative Index of Inequality (RII)[34] were analysed (results not shown). This measure assesses differences in mortality adjusting for changes in the distribution of education in the population over time and taking into account mortality differences between the three educational levels. The pattern observed based on the RII corresponded with that based on the RR: educational differences in stroke mortality persisted and remained relatively stable over time in most countries, whereas educational disparities in IHD mortality widened in most populations. Furthermore, results based on the RII indicate that educational disparities in stroke mortality have significantly widened in Norway among men. This is consistent with the pattern observed for occupational class and suggests that socioeconomic disparities in stroke mortality have increased in this population.

Data for educational level comprised individuals aged 30-74 years, whereas occupational data covered the age range 30-59 years only. Thus, results for these two socioeconomic indicators may not be fully comparable. However, separate analyses for educational level were performed for those aged 30-59 years and 60-74 years (results not shown). The overall patterns for these two groups were identical and were therefore combined in the analysis.

Comparison with previous studies

Previous studies reported a faster proportional decline in cardiovascular disease mortality among the higher socioeconomic groups in European countries, resulting in widening socioeconomic differences in cardiovascular mortality [10,35,36]. Our results suggest that this pattern generally occurred in IHD mortality in most populations. However, we did not observe the same pattern for stroke mortality. This supports previous evidence suggesting that differences exist between trends in stroke and IHD mortality[11,37]. Similarly, socioeconomic disparities in stroke and IHD mortality have shown a different international pattern across Europe[1,14].

This is the first study to report more favourable trends in stroke mortality among higher than among lower socioeconomic groups among men in Norway. The pattern for this population may resemble that for countries such as the United States[9,23] and some parts of Australia[4], where a larger relative decline in stroke mortality has been observed among higher than among lower socioeconomic groups. A previous study in Finland reported a similar absolute decline in stroke mortality by occupational class, but a larger relative decline among non-manual than among manual classes[5]. Although this resembles the pattern that we have observed, socioeconomic differences in the relative decline in stroke mortality in Finland were not significant.

Noteworthy is the pattern for Turin (Italy), where educational disparities in stroke mortality remained of a similar magnitude and educational disparities in IHD mortality showed an increase. This is consistent with the pattern that has been observed in other Mediterranean countries such as Spain[3]. Similarly, a previous study in France reported similar stroke mortality declines across socioeconomic groups, accompanied by diverging trends in mortality from IHD[37].

Overall, similar results were observed for occupational class and educational level. However, a sharper widening of disparities in stroke mortality generally occurred for occupational class than for educational level in some populations. This discrepancy suggests that differences may exist in the effect of these two indicators of socioeconomic status on mortality [27,28]. Educational level might reflect gradual changes in factors such as health behaviour and access to health information, which may influence mortality differentials over a long period. Instead, trends in occupational disparities may reflect changes in factors such as the physical and psychosocial dimensions of work[27]. Despite these discrepancies, results from this study indicate that, overall, similar trends have occurred for educational level and occupational class in most populations.

Explanation of Results

Hypertension is involved in nearly 70 percent of strokes[38]. Recent evidence shows that hypertension prevalence and blood pressure levels have generally declined in all socioeconomic groups in Finland[19], Denmark[20], Sweden[39] and Italy[40]. However, it remains still unclear to what extent these changes are due to improvements in hypertension treatment or diet. Significant improvements in the awareness, treatment and control of hypertension have occurred in countries such as Finland[41] and Spain[16]. Within the United Kingdom, significant improvements in hypertension management across all socioeconomic groups have been observed in Scotland[42]. Hypertension management among diabetic patients has also improved significantly in many European populations[43]. Thus, improvements in access to hypertension treatment –detection and management- have probably contributed to similar stroke mortality declines in all socioeconomic groups. Furthermore, improvements in dietary salt and fat intake have been observed in all socioeconomic groups in several European countries [44-46]. Population-based strategies such as policies and legislation on salt concentrations in processed food introduced in countries such as Finland may have contributed to this pattern[47,48]. Additionally, similar declines in cholesterol level across social classes have been observed in Finland[19,49], Denmark[20] Sweden[39] and Italy[40]. These factors may have contributed to stroke mortality declines of a similar magnitude across socioeconomic groups in Europe.

Stroke and IHD share several risk factors. However, socioeconomic differences in stroke mortality remained relatively stable, whereas disparities in IHD mortality widened over time in most countries. Recent trends in risk factors such as smoking and overweight may have substantially contributed to the pattern observed for IHD. Most Nordic countries and the United Kingdom have generally experienced declining trends in smoking prevalence among the higher classes, accompanied by increasing trends in the lower socioeconomic groups[15,19,20,39,49,50]. Similarly, the prevalence of overweight and obesity has shown more favourable trends among higher than among lower socioeconomic groups[19,51]. These trends may partly explain the widening of socioeconomic differences in IHD mortality across Europe. On the other hand, trends in socioeconomic differences in stroke mortality may have been more influenced by factors such as hypertension.

As shown in previous studies[14], we observed smaller socioeconomic disparities in IHD mortality in Turin than in Northern European countries. Nevertheless, trends in inequalities in stroke and IHD mortality in Turin were similar to trends in other populations: educational disparities in stroke mortality remained of a similar magnitude, whereas educational disparities in IHD mortality tended to increase. Widening smoking inequalities in Italy may have contributed to the pattern for IHD mortality, whereas factors such as diet and hypertension may have contributed to the pattern for stroke mortality[40,52].

Finally, research indicates that declines in case-fatality rates have also contributed to declines in stroke mortality[53], which underlines the role of improvements in medical care. Socioeconomic disparities in stroke mortality persisted from the 1980s to the 1990s in all populations, which may indicate that socioeconomic disparities in healthcare utilization remain. This is supported by recent evidence of socioeconomic differences in specialist care and diagnostic procedures even in countries with universal healthcare systems such Finland[13,54] and Sweden[55]. Furthermore, the higher socioeconomic groups may have had access to some surgical procedures earlier that the lower socioeconomic groups[54,56]. This may have contributed to widening socioeconomic differences in IHD and stroke mortality in some countries. Similarly, despite favourable hypertension trends overall, socioeconomic disparities in blood pressure levels and hypertension care still remain [57,58]. These factors may have contributed to persisting or widening socioeconomic inequalities in stroke mortality in Europe.

Implications

Results from this study suggest that stroke mortality trends in all socioeconomic groups have been responsive to favourable changes in important risk factors such as hypertension. However, the persistence of socioeconomic inequalities in stroke mortality indicates that recent changes in policies and risk factors have not been sufficient to reduce these disparities. Improvements in the quality of preventive and hospital care for stroke may substantially improve survival among individuals with a low socioeconomic status[13,52]. Our results indicate that focusing on these groups may contribute to sustain the stroke mortality decline in European countries.

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Chapter 4

Socioeconomic status and ischaemic heart disease mortality in 10 western European populations during the 1990s: A comparison with stroke and lung cancer

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Abstract

Objective: To assess the association between socioeconomic status and ischaemic heart disease (IHD) mortality in 10 western European populations during the 1990s.

Design: Longitudinal study.

Setting: 10 European populations (95,009,822 person years).

Methods: Longitudinal data on IHD mortality by educational level were obtained from registries in Finland, Norway, Denmark, England/Wales, Belgium, Switzerland, Austria, Turin (Italy), Barcelona (Spain), and Madrid (Spain). Age standardised rates and rate ratios (RRs) of IHD mortality by educational level were calculated by using Poisson regression.

Results: IHD mortality was higher in those with a lower socioeconomic status than in those with a higher socioeconomic status among men aged 30–59 (RR 1.55, 95% confidence interval (CI) 1.51 to 1.60) and 60 years and over (RR 1.22, 95% CI 1.21 to 1.24), and among women aged 30–59 (RR 2.13, 95% CI 1.98 to 2.29) and 60 years and over (RR 1.36, 95% CI 1.33 to 1.38). Socioeconomic disparities in IHD mortality were larger in the Scandinavian countries and England/Wales, of moderate size in Belgium, Switzerland, and Austria, and smaller in southern European populations among men and younger women ($p < 0.0001$). For elderly women the north–south gradient was smaller and there was less variation between populations. No socioeconomic disparities in IHD mortality existed among elderly men in southern Europe.

Conclusions: Socioeconomic disparities in IHD mortality were larger in northern than in southern European populations during the 1990s. This partly reflects the pattern of socioeconomic disparities in cardiovascular risk factors in Europe. Population wide strategies to reduce risk factor prevalence combined with interventions targeted at the lower socioeconomic groups can contribute to reduce IHD mortality in Europe.

4.1 Introduction

Ischaemic heart disease (IHD) accounts for about 2.7 million deaths every year in the developed world[1]. A lower socioeconomic status is associated with a higher risk of dying of IHD[2,3,4,5,6], so that around a quarter of all IHD deaths can be attributed to a lower socioeconomic status[5]. IHD is the largest contributor to socioeconomic differences in life expectancy and mortality in Europe[6]. Thus, examining IHD disparities is essential to understand recent cardiovascular mortality trends.

During the 1980s, large social class disparities in IHD mortality were reported in northern European populations among middle aged men. In contrast, no social class disparities in IHD mortality existed in southern and Mediterranean countries[2]. This north–south gradient suggests that specific risk factors such as the Mediterranean diet may have protected the entire southern European population from higher IHD mortality[7]. Furthermore, southern European countries may be lagging behind in the epidemiological transition earlier experienced by northern Europe and the USA[2,8]. Consequently, no social class differences in risk factors such as smoking would have yet emerged in southern populations[8]. Only through international comparisons is it possible to elucidate the impact of country specific risk factors and health care practices on socioeconomic disparities in IHD mortality.

Previous studies have compared socioeconomic disparities in IHD mortality only among middle aged men based on cross sectional data for some countries[2]. Within a large European collaboration, we collated longitudinal data on mortality disparities for a more recent period. This study assessed differences in IHD mortality between socioeconomic groups during the 1990s in 10 western European populations. It is the first study of IHD disparities during this period for both men and women, which also compares middle aged and elderly populations. This is the largest study of socioeconomic differences in IHD mortality ever, comprising more than 95 million person years and around 263 000 deaths. This yielded robust estimates of the association between socioeconomic status and IHD mortality.

4.2 Methods

Data and Subjects

Longitudinal data on mortality by educational level, sex, and age were obtained for 10 European populations. Subjects were enumerated during a census in the early 1990s and followed up for different periods (appendix). For each person, information on cause of death was obtained from national statistics registries and linked to census data on educational level. Most studies covered the entire national population, except for Madrid (regional), Barcelona and Turin (urban), Switzerland (population living in German speaking areas), and England/Wales (1% representative sample of the population). Populations were selected to represent different geographical regions (for example, northern or southern) in Western Europe. Longitudinal data were not available or linkage between census and mortality registry data was not possible for other western European countries. People aged 30 years and over (age specified at the start of follow up) were studied, except in Denmark, where data on education were not available for people aged 70 years or more.

Educational level was used as an indicator of socioeconomic status and assessed at baseline for each person. As opposed to occupational class, educational level can be applied equally to both men and women, it is more comparable between age groups, and it comprises both economically active and inactive populations[9]. It is also more comparable across countries than other indicators such as income[9]. Education was first coded according to national schemes and subsequently reclassified into three equivalent categories so that the size of the low educational level group was similar across countries. Data on the distribution of education by country have been reported elsewhere[10]. These groups corresponded roughly to levels 0–2 (pre-primary, primary, and lower secondary education), 3 (upper secondary education), and 4–6 (postsecondary education) of the UNESCO standard classification scheme. In most countries, about 65–80% of the population had a low educational level, 15–30% had a middle educational level, and about 10–15% had a high educational level.

Causes of death were coded according to the *International classification of diseases* (ICD), ninth revision (ICD-9), in most countries. IHD was defined as code numbers 410–414, stroke as code numbers 430–438, and lung cancer as code numbers 162, 163, and 165. The only exceptions were Denmark and Switzerland, where codes 410–414 (IHD), 430–438 (stroke), and 162–163 (lung cancer) from the ICD-8 and codes I20–I25 (IHD), I60–I69 (stroke), and C33, C34, and C39 (lung cancer) from the ICD-10 were used.

Methods of analyses

Age standardized mortality rates were calculated for sex and educational level strata distinguishing two age groups: 30–59; and 60 years and over. Data were analysed separately for these two age groups because IHD mortality increases sharply from age about 60 years upwards, particularly for men. Nevertheless, analyses were replicated for age groups 30–65 and 65 years and over, yielding similar results. Rates were standardised by five year age groups by the direct method and the European Union population of 1995 as the standard[11]. Each population separately and a pooled dataset of all countries weighted on the size of each cohort were analysed.

Age adjusted rate ratios (RRs) were calculated by Poisson regression. RRs compared the mortality of low and middle/high combined educational level groups, with the combined middle/high group serving as the reference category. Owing to their small size, middle and high levels were combined to obtain more precise estimates. Tables and figures present results organised according to countries' approximate geographical latitude in western Europe.

Comparable RR estimates of mortality according to educational level were calculated for stroke and lung cancer, which share some determinants with IHD such as smoking and hypertension. The international pattern for IHD and these causes of death were compared, which can shed light on shared determinants that may contribute to socioeconomic differences in IHD mortality in Europe. Data were analysed with SAS, version 8.2 (SAS Institute, Cary, North Carolina, USA).

4.3 Results

In 44 673 469 person years, 146 043 men died of IHD. Table 4.1 shows that, among middle aged men (30–59 years), IHD mortality was higher among lower than among higher educational level groups in all populations. Among elderly men (60 years and over), IHD mortality differed by educational level in all but southern European populations (table 4.1). Among both middle aged and elderly men, socioeconomic differences in IHD mortality were generally larger in Scandinavian countries and England/Wales, of moderate size in Belgium, Austria, and Switzerland, and smaller in Turin, Barcelona, and Madrid (test for interaction between education and country, $p < 0.0001$). This north–south gradient was consistent both for relative and absolute differences in IHD mortality.

Table 4.1. Age-standardized IHD mortality rates (per 100 000 person-years) by educational level and rate ratio of low vs. middle/high education groups among men aged ≥ 30 years

Age	**Population**	**IHD standardized mortality rates**				**Rate Ratio**
		Low	Middle	High	Total	(95% CI)
30-59 years						
	Finland	174.3	126.3	66.6	146.5	1.59 (1.51 – 1.68)
	Norway	119.1	77.1	50.1	107.3	1.94 (1.76 – 2.14)
	Denmark	109.4	78.2	52.7	95.1	1.66 (1.54 – 1.79)
	England/Wales	148.6	79.9	68.9	131.8	2.08 (1.67 – 2.61)
	Belgium	71.4	58.7	42.6	64.5	1.41 (1.33 – 1.49)
	Austria	74.9	57.2	43.1	69.5	1.49 (1.26 – 1.76)
	Switzerland	79.0	60.6	45.4	59.8	1.40 (1.27 – 1.55)
	Turin	54.8	49.2	34.9	51.5	1.23 (1.00 – 1.51)
	Barcelona	53.2	38.6	40.6	47.9	1.35 (1.14 – 1.59)
	Madrid	29.3	29.3	24.4	28.4	1.10 (0.89 – 1.36)
	All populations	90.2	67.3	45.1	78.5	1.55 (1.51 – 1.60)
≥ 60 years						
	Finland	2478.7	2131.3	1767.8	2375.3	1.31 (1.27 – 1.35)
	Norway	1807.4	1450.7	1271.1	1757.5	1.43 (1.36 – 1.49)
	Denmark*	814.9	661.6	496.9	756.6	1.38 (1.30 – 1.47)
	England/Wales	1917.8	1639.0	1244.3	1854.0	1.33 (1.20 – 1.48)
	Belgium	863.1	823.2	684.2	843.8	1.19 (1.15 – 1.23)
	Austria	1341.3	1225.4	1008.7	1294.6	1.19 (1.12 – 1.27)
	Switzerland	1263.4	1161.3	995.2	1167.8	1.14 (1.10 – 1.18)
	Turin	721.4	865.8	769.8	738.8	0.94 (0.85 – 1.04)
	Barcelona	544.2	462.3	565.9	538.8	1.05 (0.97 – 1.13)
	Madrid	434.5	475.8	412.4	435.2	0.98 (0.87 – 1.09)
	All populations	3081.7	2880.5	2261.5	2973.9	1.22 (1.21 – 1.24)

*Ages 60-69 years

Among women, 117 802 died of IHD over 50 336 353 person years. Table 4.2 shows that IHD mortality was higher among lower educated women in all populations. Despite wide confidence intervals (CIs), RRs were generally larger in northern than in southern European populations for middle aged women (test for interaction between education and country, $p < 0.0001$). Among elderly women, however, this north–south gradient was smaller: although there were no socioeconomic disparities in IHD mortality in Madrid and Turin, disparities were large in Barcelona and RRs in other populations were generally close to the European average (RR 1.36, 95% CI 1.33 to 1.38). Absolute rate differences between educational groups were larger in northern than in southern populations among women in both age groups (tables 4.1 and 4.2). RRs were larger for women than for men in most populations, whereas absolute rate differences were generally larger for men than for women.

Table 4.2. Age-standardized IHD mortality rates (per 100 000 person-years) by educational level and rate ratio of low vs. middle/high education groups among women aged ≥ 30 years

Age	Population	IHD standardized mortality rates				Rate Ratio
		Low	Middle	High	Total	(95% CI)
30-59 years						
	Finland	27.5	14.2	5.9	21.3	2.25 (1.94 – 2.61)
	Norway	24.8	8.0	7.1	22.3	3.65 (2.57 – 5.17)
	Denmark	30.1	14.1	8.8	24.2	2.57 (2.16 – 3.05)
	England/Wales	33.6	13.9	2.0	30.3	2.89 (1.52 – 5.48)
	Belgium	17.1	10.6	7.5	15.0	1.84 (1.59 – 2.12)
	Austria	16.0	10.8	4.2	14.3	1.92 (1.28 – 2.86)
	Switzerland	14.8	8.4	6.2	10.6	1.79 (1.48 – 2.16)
	Turin	11.2	10.7	7.2	10.4	1.22 (0.74 – 2.02)
	Barcelona	7.9	5.9	3.8	7.2	1.62 (0.98 – 2.67)
	Madrid	4.6	6.1	1.3	4.5	1.22 (0.67 – 2.21)
	All populations	18.3	10.4	5.4	15.6	2.13 (1.98 – 2.29)
≥ 60 years						
	Finland	1466.7	1145.0	980.4	1407.3	1.37 (1.33 – 1.42)
	Norway	933.1	692.6	584.2	919.0	1.43 (1.33 – 1.54)
	Denmark*	309.6	176.4	171.9	278.8	1.77 (1.59 – 1.97)
	England/Wales	1095.2	850.2	592.7	1069.8	1.47 (1.26 – 1.71)
	Belgium	481.2	337.6	330.0	466.4	1.52 (1.44 – 1.60)
	Austria	804.3	595.3	568.9	772.9	1.36 (1.26 – 1.46)
	Switzerland	675.0	555.2	467.6	628.2	1.24 (1.20 – 1.29)
	Turin	384.8	390.0	344.2	384.3	1.06 (0.90 – 1.23)
	Barcelona	303.1	176.1	240.9	294.6	1.47 (1.28 – 1.68)
	Madrid	204.8	208.8	175.3	203.4	1.09 (0.90 – 1.31)
	All populations	1849.2	1652.0	1266.1	1810.9	1.36 (1.33 – 1.38)

*Ages 60-69 years

Figure 4.1 shows a pronounced north–south gradient in educational differences in IHD mortality among men aged 30 years and over. This north–south pattern existed also among women, with the exception of Barcelona, which had a relatively large RR for IHD (figure 4.2). Despite wide CIs, RRs for lung cancer mortality were larger in northern populations and smaller in southern populations in comparison to the European average for men (RR 1.62, 95% CI 1.59 to 1.66) and women (RR 1.17, 95% CI 1.12 to 1.23). In contrast, educational disparities in stroke mortality were of a similar magnitude in most populations and were all close to the European average among men (RR 1.27, 95% CI 1.24 to 1.30) and women (RR 1.29, 95% CI 1.27 to 1.32).

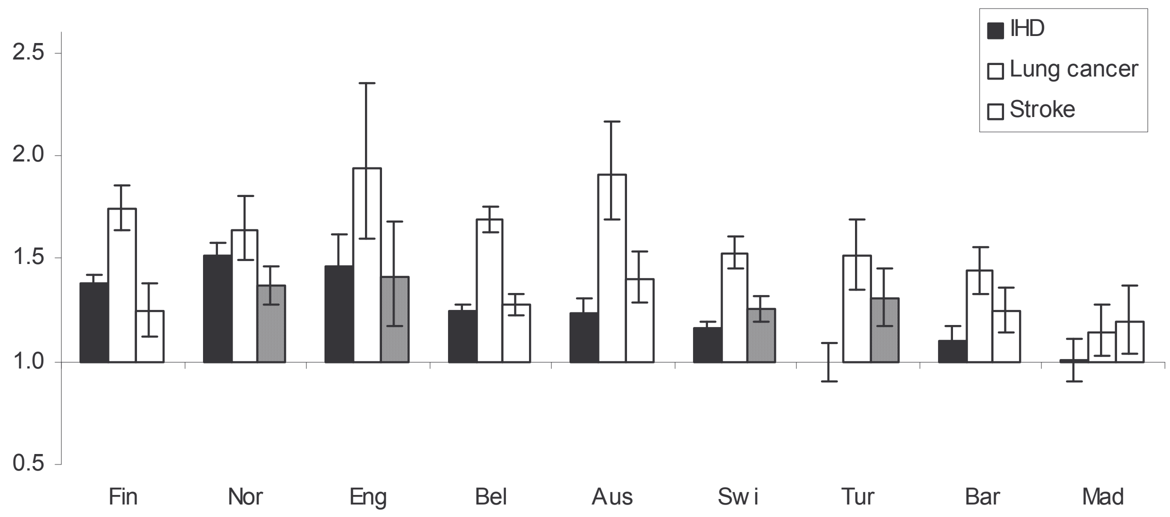

Figure 4.1. Rate ratios of ischaemic heart disease (IHD), lung cancer, and stroke mortality according to educational level for men aged 30 years and over in Western Europe. *Ages 30–69 years

Fin indicates Finland; Nor, Norway; Den, Denmark; Eng, England and Wales; Bel, Belgium; Aus, Austria; Swi, Switzerland; Tur, Turin; Bar, Barcelona; Mad, Madrid

*Ages 30-69 years

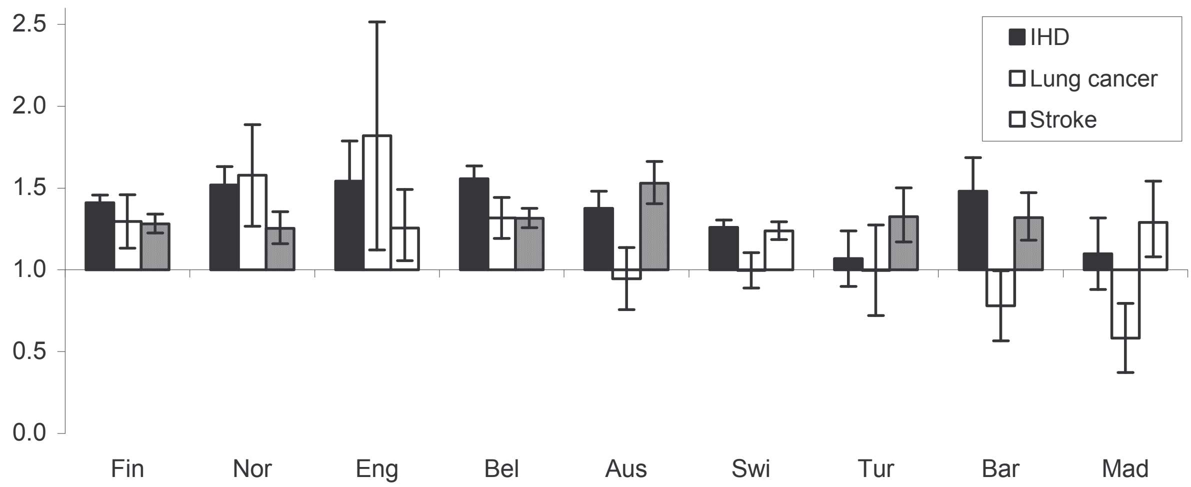

Figure 4.2. Rate ratio of IHD, lung cancer, and stroke mortality according to educational level for women aged 30 years and over in Western Europe. *Ages 30–69 years

Fin indicates Finland; Nor, Norway; Den, Denmark; Eng, England and Wales; Bel, Belgium; Aus, Austria; Swi, Switzerland; Tur, Turin; Bar, Barcelona; Mad, Madrid

*Ages 30-69 years

4.4 Discussion

Previous studies have shown that IHD mortality is low in southern and Mediterranean populations and high in the north of Europe[12]. We have shown that socioeconomic differences in IHD mortality during the 1990s were larger in Scandinavian countries and England/Wales, of a moderate size in Belgium, Austria, and Switzerland, and smaller in Turin, Barcelona, and Madrid. This north–south gradient was smaller among elderly women, with less variation between populations. These findings suggest that the association between socioeconomic status and IHD not only changes over time[3,4] but also varies considerably between countries.

Evaluation of data and study limitations

We used the most recent data on IHD disparities in Europe. Nevertheless, some limitations in this study should be considered. Firstly, IHD deaths may be wrongly coded as other causes of death[12]. This would bias our results if a greater proportion of southern populations and more lower than higher educated people were misclassified. To assess the impact of this problem, we assessed the pattern of educational disparities for a combined category of IHD and other heart diseases (ICD-9 codes 416 and 420–429). Although north–south gradients in IHD disparities were somewhat smaller for women and middle aged men, the north–south gradient for elderly men remained strong. Furthermore, our findings are consistent with studies showing a north–south gradient in cardiovascular risk factors in Europe[14,15,16]. Thus, there is no clear evidence that our results can be explained by misclassification.

Despite our efforts at standardisation, differences remained between countries in measurements and data collection. Data for Madrid and Austria comprised a shorter follow up period. However, research indicates that mortality differentials by educational level are unrelated to follow up time[17]. Thus, any bias caused by this problem is likely to be small. Furthermore, we used a different revision of the ICD code for Switzerland and Denmark, which may influence overall mortality. However, this is unlikely to affect RRs that compare mortality between educational level groups.

Although census data were collected by standard procedures, differences between populations may remain in the precision with which educational level was measured. However, if measurement precision differed systematically between northern and southern countries, a north–south gradient would have also been observed for other causes of death. Instead, we did not observe a north–south gradient for disparities in most other causes, including stroke and all cause mortality[6,10,18]. Furthermore, we reclassified national levels into broad categories[10], thus minimising the impact of misclassification across country specific educational levels. Thus, misclassification of educational attainment is unlikely to explain our findings.

Except in Switzerland, where the proportion of highly educated people was larger, the distribution of educational level was comparable between countries[10]. Thus, our study compared the effect of relative—as opposed to absolute—socioeconomic position on IHD mortality between populations. However, reclassified categories corresponded roughly with the UNESCO standard classification[10]. Furthermore, sensitivity analyses based in the relative index of inequality (an effect measure that is based on all educational levels and simultaneously adjusts for differences in the educational distribution)[19] showed an identical pattern (results not shown). Thus, results are likely to be comparable when assessing the effect of absolute educational level. Nevertheless, we do not know whether findings would be similar when dividing the lower educated group into more specific levels.

Data for Switzerland can only be generalised to the German speaking population. However, this corresponds to about 72% of the entire Swiss population. The dataset for most countries comprised the national population or a representative sample of the total population, whereas only regional or urban data were available for southern Europe. However, previous studies of national data have also reported smaller IHD disparities in southern countries such as Spain and Portugal[2]. Furthermore, urban areas are often in a more advanced stage of the epidemiological transition, so that socioeconomic differences in mortality are generally larger within cities than at the national level[20]. Thus, by including national estimates for Italy and Spain, the north–south contrast in educational disparities in IHD mortality is likely to be greater than that observed in our study.

Comparison with previous studies

Previous research reported a north–south gradient in social class differences in IHD mortality among middle aged men during the 1980s[2]. Our findings suggest that this north–south gradient also existed during the 1990s, for middle aged men and women and for elderly men. These findings are interesting in the context of previous research showing that overall IHD mortality is also lower in southern European countries and France than in northern countries such as Finland[12]. Our data also show a north–south gradient in overall IHD mortality, for both the higher and the lower socioeconomic groups separately (tables 4.1 and 4.2). However, this north–south gradient was greater among the lower socioeconomic classes. This pattern resulted in both lower IHD mortality and smaller socioeconomic differences in IHD mortality in southern than in northern European populations.

Austria, Belgium, and Switzerland generally occupied an intermediate position in the size of educational differences in IHD mortality. This further highlights the persistence of the north–south gradient throughout western Europe. Previous studies reported that the pattern for Switzerland resembled that for Mediterranean populations[2]. However, previous research relied on cross sectional and occupational data for this country and may have been biased by excluding economically inactive people[9,17].

Previous studies suggested that socioeconomic differences in IHD mortality started to emerge in southern populations during the 1990s[3,4]. Although our data are not fully comparable with data from previous studies[2,3], our results suggest that socioeconomic disparities in IHD mortality may have indeed recently emerged in younger cohorts in Italy and Spain, particularly among men. In contrast, no disparities existed among elderly men. Nevertheless, socioeconomic differences in IHD mortality were still smaller in southern than in other European populations.

Explanation of results

Our results raise questions about risk factors for IHD that may explain the north–south gradient in IHD disparities, among which smoking is an interesting candidate. Research indicates that smoking diffuses within societies as an epidemic[8]. It is first adopted by the higher socioeconomic classes; subsequently, smoking declines among the higher classes and spreads rapidly among the lower socioeconomic groups[8]. Whereas northern European countries and the USA have already experienced this transition, the smoking epidemic is far less advanced in Spain and Italy[8,14,21,22]. These findings are in line with the pattern we observed for lung cancer mortality, which partly reflects smoking prevalence during previous decades[8,22]. Our study shows that socioeconomic disparities in lung cancer mortality tended to be larger in northern than in southern European populations. Accordingly, a striking north–south gradient in socioeconomic disparities in smoking has been reported in Europe[14]. This lag in the progression of the smoking epidemic in southern as compared with northern populations may partly explain why socioeconomic differences in IHD mortality are smaller in the south than in the north of Europe.

Other risk factors, however, have traditionally protected southern European populations from higher IHD rates, which may have benefited all social classes equally. Adherence to the Mediterranean diet can reduce the risk of dying of IHD as much as 40%[7]. Previous research has shown that a healthy diet based on vegetables, fruits, and olive oil is generally available to all in southern Europe but only to the higher socioeconomic groups in northern populations[15,16]. The Mediterranean diet may thus contribute not only to low IHD mortality but also to small socioeconomic differences in IHD mortality in southern Europe. Similarly, larger socioeconomic disparities in excessive alcohol consumption exist among men in Scandinavian countries and the UK[15,16,23], whereas alcohol disparities are small in most southern countries[15]. Lastly, socioeconomic disparities in overweight and obesity among men are smaller in southern than in northern European populations[15,24]. These factors may have protected the entire southern European population from higher IHD mortality.

Cross country variation was smaller in socioeconomic disparities in IHD mortality among elderly women. Owing to the low prevalence of smoking in this group[14], relatively few IHD deaths might be attributable to this risk factor in older women. Thus, other factors may have had a more prominent role. Obesity, an important predictor of cardiovascular risk among women, is a plausible candidate. The consistency of socioeconomic disparities in IHD mortality among elderly women may result from lasting socioeconomic disparities in obesity. Since the 1960s, a higher prevalence of obesity in lower than in higher socioeconomic groups has been observed among women in Europe[25]. These disparities are larger and have existed for a longer period among women than among men[15,24,25]. Thus, the obesity epidemic may have preceded the smoking epidemic that occurred decades later[8,14,21] and influenced the pattern of IHD disparities only for younger women. Obesity may have also partly contributed to larger socioeconomic disparities in IHD mortality among women than among men in Europe.

The north–south gradient in socioeconomic disparities in IHD mortality was not observed for stroke[18]. This raises questions about other risk factors that may explain the similarities in the size of stroke disparities in Europe. A possible candidate is hypertension, a major risk factor for stroke. There are socioeconomic differences in the prevalence and treatment of hypertension in Europe[26,27], which may have a role in the consistency of stroke disparities. However, a different pattern may exist for the two broadest categories of stroke: trends in IHD and cerebral infarct have had a similar pattern, whereas trends in cerebral haemorrhage mortality are very different[28]. Thus, the pattern of socioeconomic disparities in cerebral infarction may resemble that for IHD mortality, whereas other determinants such as adverse childhood circumstances may contribute to similar socioeconomic disparities in cerebral haemorrhage in European populations[29]. Further research should compare socioeconomic disparities in stroke subtypes and IHD mortality in Europe.

Absolute differences in IHD mortality were largest among those aged 60 years and over. However, the strength of the relative association between socioeconomic status and IHD mortality declined with age. This may be partly explained by the differential effect of selective survival. People with a lower socioeconomic status may have died earlier and only the healthiest may have survived into old age. Consequently, socioeconomic differences in IHD mortality diminished at older ages. However, previous research indicates that selective survival cannot fully explain this age pattern[30]. Further research is warranted to assess the impact of this mechanism.

Lastly, inequity in health care access may have also contributed to socioeconomic disparities in IHD mortality. Inequity in access to procedures such as coronary artery bypass surgery and angiography has been reported both in northern[31] and in southern populations[32]. Similarly, inequity in specialist care persists in most European countries[33]. Nevertheless, countries with more egalitarian policies such as the Scandinavian populations had larger socioeconomic disparities in IHD mortality than southern populations. Thus, it is uncertain to what extent health care disparities contribute to cross country variations in socioeconomic disparities in IHD mortality in Europe.

Clinical implications

We observed smaller socioeconomic disparities in IHD mortality in southern European populations, where overall IHD mortality is low[12]. A strategy to reduce IHD disparities may comprise two complementary approaches. Firstly, population wide strategies to decrease the overall prevalence of risk factors such as diet and obesity may provide great benefits to reduce both overall IHD mortality and IHD disparities[5]. Secondly, interventions to reduce the prevalence of risk factors such as smoking[14,34] targeted at the lower socioeconomic groups can boost the impact of interventions in this high risk population. Furthermore, clinicians are confronted with a large number of low socioeconomic status patients[33]. Therefore, clinicians can contribute to improved survival after the first occurrence of heart disease by assuring equal access to secondary prevention and care for patients from the lower socioeconomic groups[31,32]. Cross country variations suggest that specific interventions and policies may be required for each country. In conclusion, population wide strategies to reduce the prevalence of risk factors such as diet combined with prevention of risk factors such as smoking targeted at the lower socioeconomic groups are likely to contribute to reduced IHD mortality in Europe.

Appendix

Table. Follow-up period, number of person-years at risk and IHD deaths among men and women aged ≥ 30 years in 10 Western European populations

Population	Follow-up period	Number of person-years		Number of IHD deaths	
		Men	Women	Men	Women
Finland	1991-1995	6 758 254	7 690 004	35 805	33 285
Norway	1990-1995	5 473 624	5 973 625	28 892	21 178
Denmark*	1991-1995	5 434 935	5 542 294	10 534	3 781
England/Wales	1991-1996	796 618	894 517	4 312	3 576
Belgium	1991-1995	13 047 398	14 587 998	31 164	25 076
Switzerland	1991-1995	5 586 898	6 580 829	18 249	15 319
Austria	1991-1992	2 092 643	2 459 619	7 335	7 914
Turin	1991-1996	1 276 242	1 532 676	2 827	2 153
Barcelona	1992-1996	2 229 996	2 753 341	4 608	3 844
Madrid	1996-1997	1 976 860	2 321 451	2 317	1 676
All populations		44 673 469	50 336 353	146 043	117 802

* Data available for ages 30-69 years only

Fin indicates Finland; Nor, Norway; Den, Denmark; Eng, England and Wales; Bel, Belgium; Aus, Austria; Swi, Switzerland; Tur, Turin; Bar, Barcelona; Mad, Madrid

*Ages 30-69 years

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Chapter 5

Wealth, income and education disparities in stroke incidence in older Americans: Results from The HRS study

Avendano, M., Glymour, M. Socioeconomic disparities in stroke incidence in older Americans: Results from the HRS study. *Submitted 2006.*

Abstract

Background and objectives: This study examines the independent effect of wealth, income and education on stroke throughout middle and old age and the contribution of risk factors to these disparities.

Methods: Stroke-free participants in the Health and Retirement Study (n=19,565) were followed for an average of 8.5 years. Total wealth, income and education assessed at baseline were used in Cox proportional hazards models to predict time to stroke. Separate models were estimated for three age-strata (50-64, 65-74 and $\geq$75), and incorporating risk factor measures (smoking, physical activity, BMI, hypertension, diabetes, and heart disease).

Results: 1,536 subjects developed incident stroke. Higher education predicted reduced stroke risk at ages 50-64, but not after adjustment for wealth and income. Wealth and income were independent risk factors for stroke at ages 50-64. Adjusted hazard ratios comparing the lowest decile with the 75^{th}-90^{th} percentiles were 2.4 (95%CI 1.6, 3.5) for wealth and 1.7 (95%CI 1.2, 2.4) for income. Risk factor adjustment attenuated these effects by 30-50%, but coefficients for both wealth (HR=1.7, 95%CI 1.2, 2.6) and income (HR=1.5, 95%CI 1.1, 2.1) remained significant. Wealth, income and education did not consistently predict stroke beyond age 65.

Conclusions: Wealth and income are independent predictors of stroke at ages 50-64, but do not predict stroke among the elderly. This age patterning might reflect buffering of the negative effect of social deprivation by improved access to social and health care programs at old ages, but may also be an artefact of selective survival.

5.1 Introduction

Stroke is the second leading cause of death and a major cause of disability worldwide[1]. Large socioeconomic disparities in stroke prevail in most developed countries[2-4]. Although 89% of strokes occur after age 65[5], little research has examined socioeconomic disparities in stroke risk among the elderly. As opposed to conventional socioeconomic status (SES) measures such as education and income, wealth reflects both lifelong earnings and intergenerational transfers; wealth increases access to medical care and other material and psychosocial resources[6-8]. Thus, wealth might be a more appropriate indicator of SES among the elderly[2,3,6,8].

Research on SES disparities in stroke in old age has yielded mixed results, perhaps partially due to the limited SES measures available, and, in the US studies, the use of small, geographically localized samples[2]. In Europe, educational disparities in stroke diminish but persist among the oldest-old[3]. In contrast, stroke disparities across education and income in the US seem to reverse at age 74, resulting in excess stroke among those with high education or income[2] . This age-attenuation might result from diminishing SES effects on health due to old-age entitlement programs such as Medicare. However, it may also be an artefact of selective survival[6,8,9], or reflect the inadequacy of income and education as SES measures in the very old. Wealth remains associated with several health outcomes through late life[6], but it is not known whether this is the case for stroke.

Based on follow-up data from the Health and Retirement Study (HRS), we examined the independent effects of wealth, income and education on incidence of first stroke across age strata. Additionally, we assessed the role of cardiovascular risk factors in explaining stroke disparities in US adults. We hypothesized that wealth predicts stroke incidence independently of income and education, and that this effect of wealth persists even among the oldest old. To our knowledge, this is the first study assessing the age patterning of wealth, income and education disparities in stroke.

5.2 Methods

Study population

HRS is a longitudinal survey of a national sample of U.S. adults aged 50 or older and their spouses. Details of the study are provided elsewhere[10]. Enrolment was staggered by birth cohort with enrolments in 1992, 1993 and 1998 (figure 5.1). Biennial interviews (or proxy interviews for decedent participants) were conducted through 2004. We included all HRS participants born 1900-1947 who were aged 50-plus and stroke-free at baseline interview.

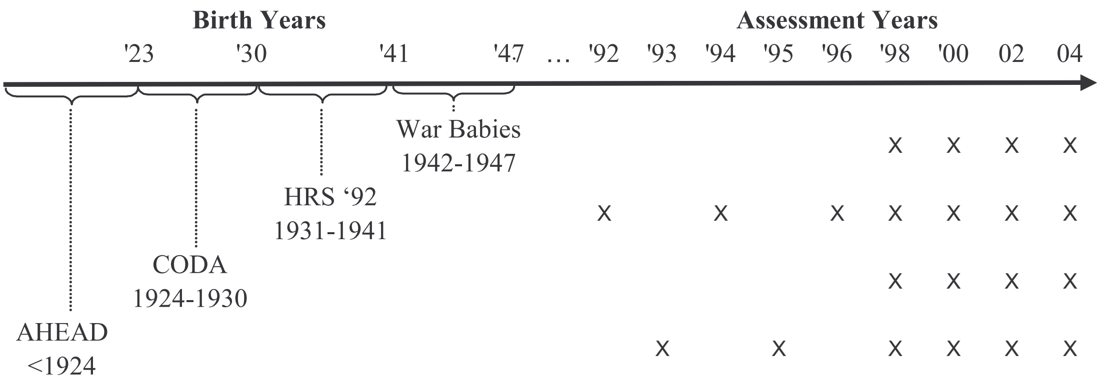

Figure 5.1. Enrolment and assessment schedule for Health and Retirement Study birth cohorts

From 24,579 age-eligible respondents interviewed at least once, we excluded 2,229 (9.1%) due to unknown stroke status at enrolment; 1,073 (4.4%) due to reporting prevalent stroke at enrolment; 292 (1.2%) due to unknown failure date (unknown last interview or implausible stroke date reported); and 1,420 (5.8%) cases due to missing values on adult risk factors.

Socioeconomic status

Household wealth, household income and education were used as indicators of SES. Household net worth comprised the sum of all financial and real assets minus liabilities. Household income comprised information on income by all household members. To ensure comparability with other HRS studies, data coding by the RAND Institute, with missing values hot-decked, were used for household income and wealth data[11]. To account for differences in household size, income and net worth were divided by the square root of the number of household members[12] and then collapsed into percentile categories (<10th, 10-24th, 25-49th, 50-74th, 75-89th, and ≥90th). The top and bottom deciles were considered separate categories to explore non-linearity at the extremes of the distribution. The 75-89th percentile group was treated as the reference category in all analyses. In supplementary models, we used the natural log of income and wealth as continuous variables. Education was coded as continuous years of schooling completed (up to 17).

Confounders and intermediary variables

All models were adjusted for potential confounders temporally prior to the exposure of interest, including: Hispanic ethnicity, black race, age at first interview (linear and quadratic terms), sex, region of birth (South, Northeast, Midwest, West, non-US, missing), mother's education (<8 years, >=8 years, missing), father's education (<8 years, >=8 years, missing), father's occupation (0-3, military, farming, missing), and retrospective report of childhood health (5 point scale from poor to excellent, missing).

Potential mediators of the association between SES and stroke included first available report of: current smoking status, body mass index (BMI), vigorous physical activity (dichotomised at 3+ times a week), and self-reported baseline diagnoses of hypertension, diabetes and heart disease.

Stroke outcomes

Incident events were defined as first non-fatal or fatal strokes, based on self- or proxy-report of a doctor's diagnosis. Reports of temporary ischaemic attacks were not coded as strokes. For deceased participants, interviews were conducted with proxy informants, predominantly spouses. At each assessment, respondents were asked the month and year of stroke, except for 1994 interviews, when only year was recorded. For these events, December was assigned for strokes in 1992, April for 1993 strokes, and January for strokes in 1994. Stroke events with unknown date (n=302) were assigned the median stroke date for events reported by other participants in the same interview wave. Sensitivity analyses assigning interview dates as stroke dates did not change our findings.

Methods of analysis

Cox proportional hazard models were fitted using wealth, income and education to predict incident stroke, after confounder adjustment. Survival was defined as time from baseline interview to date of first stroke, date of proxy report of death due to other causes, or last interview date. Initial analyses used the entire sample (ages 50+). Analyses were then stratified into three age groups representing critical life-course stages: 50-64, 65-74 and

≥75. Income, wealth and education were first modelled separately and then simultaneously incorporated into combined SES models to estimate their independent effects. Finally, cardiovascular risk factors were added to the combined models to assess their contribution to stroke disparities. Analyses were conducted using SAS 9.1.

5.3 Results

Participant characteristics are summarised in Table 5.1. During an average of 8.5 person-years, 1,536 subjects developed stroke. Education, wealth, and income tended to be lower among sample members with stroke events, who were also more likely to report hypertension, diabetes, and heart disease at baseline. Participants in the youngest group (50-64) reported 460 events per 100,000 person-years of follow-up; the rate more than doubled to 1,245 in those aged 65-74 and 2,161 in those aged 75 or older.

In the entire sample aged 50 and older, each additional year of completed education was associated with a 2% reduction in incident stroke risk (HR=0.98, 95% CI 0.96-0.99). This association disappeared in models simultaneously adjusted for income and wealth (HR=1.00, 95% CI 0.98-1.02). A steep gradient in stroke risk is evident across quintiles of income and wealth (figure 5.2). Individuals in the lowest income decile had nearly twice the risk of stroke (95% CI 1.6-2.5) of those in the 75-90th percentile, and individuals in the lowest wealth decile had 1.7 times the hazard of stroke (95% CI 1.4, 2.0). Income and wealth remained significant predictors of stroke risk in models simultaneously adjusted for all three dimensions of SES. After adjustment for cardiovascular risk factors, only income remained associated with excess stroke (HR for the lowest decile=1.5, 95% CI 1.2-1.9).

The estimated hazard ratios for wealth, income and education differed across age-strata (Table 5.2). At ages 50-64, higher education predicted lower risk of stroke (HR=0.94, 95% CI .92-.97), but the education coefficient was non-significant after adjustment for income and wealth. In this young age-group, wealth was strongly associated with increased stroke incidence. Those in the lowest 10% of net worth had a three-fold higher risk than those in the 75-<90th percentile (HR=3.1, 95%CI 2.2, 4.5). This effect was modestly attenuated and remained significant after adjustment for other SES indicators (HR=2.4 95%CI 1.6, 3.5). A similar pattern was observed for income in the basic models. However, after adjustment for wealth and education, the estimated coefficient for income was strongly attenuated and only the lowest decile remained significant (HR=1.7, 95%CI 1.2, 2.4).

Above age 65, wealth was no longer significantly associated with stroke risk. This pattern remained unchanged after adjustment for education and income (Table 5.2). A decline in the effect of income on stroke was also observed at older ages. After adjustment for education and wealth, the risk associated with low income was only significant for the 10-<25th income percentile group at ages 75 or over (HR=1.6, 95%CI 1.0, 2.6) (Table 5.2). Education was not a significant predictor of stroke beyond age 65. To test whether the apparent age-attenuation was statistically significant, we tested for interactions between age and (continuous) log income, log wealth, and education; in all cases the interaction terms were statistically significant (p<0.01) and indicated that the risk associated with low SES declined with age.

Table 5.1. Characteristics of HRS participants aged ≥50 years and stroke-free at baseline interview

	Eligible Sample		Sample Members With Events	
	n / mean	% / (std)	n / mean	% / (std)
n	19,565	100	1,536	100
Mean years of follow-up (std)	8.5	(3.4)	5.6	(3.1)
Mean years of education (std)	11.9	(3.3)	11.2	(3.4)
Median wealth (interquartile range)*	69,765	(143,621)	50,000	(114,185)
Median income (interquartile range)*	20,145	(25,014)	14,495	(17,411)
Age at enrolment				
50-64	11,536	59	492	32
65-74	4,519	23	402	26
75+	2,852	15	463	30
Male	8,585	44	664	43
Black	2,828	14	270	18
Hispanic ethnicity	1,450	7	107	7
Birth Regions				
Northeast	3,510	18	261	17
West	1,980	10	171	11
Midwest	5,023	26	358	23
South	6,878	35	655	43
Not US	891	5	39	3
Unknown	1,283	7	52	3
Mother's Education				
< 8 Years	8,062	41	882	57
8+ Years	9,460	48	444	29
Unknown	2,043	10	210	14
Father's Education				
< 8 Years	8,515	44	922	60
8+ Years	8,327	43	370	24
Unknown	2,723	14	244	16
Hypertension	8,286	42	896	58
Diabetes	2,217	11	322	21
Heart disease	3,469	18	464	30
Current smoker	4,033	21	337	22
Vigorous activity	5,163	26	329	21
Mean BMI (std)	26.8	(5.0)	27.0	(5.4)

Sample members were all stroke-free at baseline
* Income and wealth values are standardized by dividing by the square root of household size

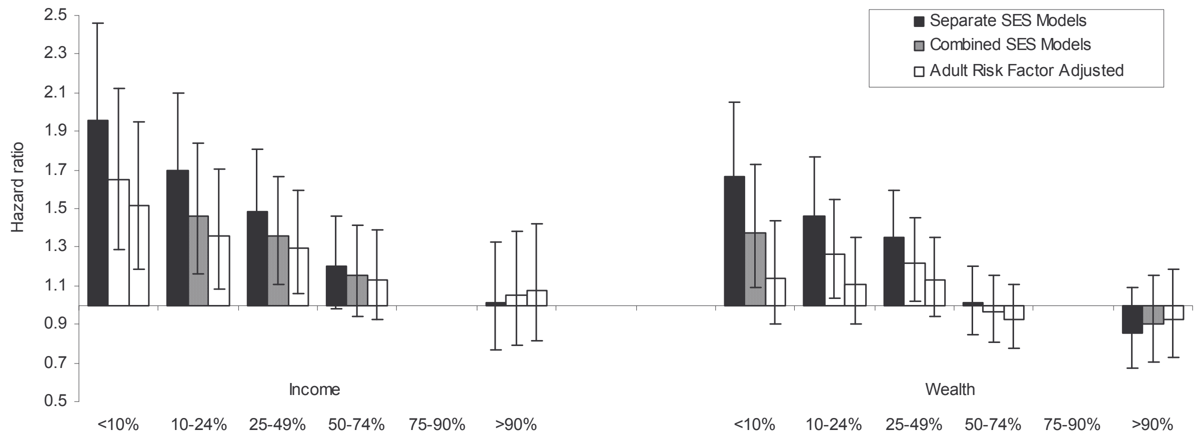

Figure 5.2. The association of wealth and income (%tile) with stroke risk among HRS participants aged >50 and stroke-free at baseline interview

Reference category is 75th-90th percentile

At ages 50-64, cardiovascular risk factor adjustment attenuated wealth and income disparities in stroke by 30-50% (Table 5.3). However, a significantly increased stroke risk remained for all categories of wealth below the median and for the lowest income decile (HR=1.5, 95%CI 1.1, 2.1). The coefficient for education was not statistically significant after adjustment for wealth and income and the hazard ratio was unchanged after adjustment for cardiovascular risk factors. Overall, similar results were observed when using the natural log of wealth and income as continuous variables. Among 50-64 year olds, the estimated coefficients were 0.96 (0.94-0.99) for log wealth, 0.97 (0.92-1.02) for log income, and 0.98 (0.95, 1.01) for education, in models adjusted for all three SES measures and cardiovascular risk factors. At age 75+, these coefficients were all 1.00. Similar results were found for men and women in sex-stratified models (results not shown).

Table 5.2. The association of wealth, income and education with stroke incidence among HRS participants aged ≥50 years and stroke-free at baseline interview, by age-strata

	Separate SES Models*						**Combined SES Models^**					
	50-64		65-74		75+		50-64		65-74		75+	
	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)
Wealth												
Lowest 10%	3.1	(2.2,4.5)	1.2	(0.8,1.9)	1.0	(0.7, 1.5)	2.4	(1.6,3.5)	0.9	(0.6,1.5)	0.9	(0.6, 1.4)
10-<25%ile	2.3	(1.6,3.2)	1.2	(0.9,1.8)	1.2	(0.8, 1.7)	2.0	(1.4,2.8)	1.0	(0.7,1.5)	1.1	(0.8, 1.6)
25-<50%ile	2.1	(1.5,3.0)	1.0	(0.8,1.4)	1.1	(0.8, 1.5)	2.0	(1.4,2.7)	0.9	(0.7,1.3)	1.0	(0.7, 1.4)
50-<75%ile	1.0	(0.7,1.5)	1.1	(0.8,1.4)	1.0	(0.7, 1.4)	1.0	(0.7,1.4)	1.0	(0.7,1.3)	1.0	(0.7, 1.3)
75-<90%ile			*reference*						*reference*			
Top 10%	1.0	(0.7,1.6)	0.8	(0.5,1.2)	0.9	(0.6, 1.3)	1.1	(0.7,1.7)	0.8	(0.5,1.1)	0.9	(0.6, 1.5)
Income												
Lowest 10%	2.6	(1.9,3.5)	1.9	(1.2,3.1)	1.2	(0.7, 2.1)	1.7	(1.2,2.4)	1.7	(1.0,3.0)	1.2	(0.7, 2.1)
10-<25%ile	1.7	(1.2,2.4)	1.4	(0.9,2.2)	1.6	(1.0, 2.6)	1.2	(0.9,1.7)	1.3	(0.8,2.1)	1.6	(1.0, 2.6)
25-<50%ile	1.5	(1.1,2.0)	1.5	(1.0,2.1)	1.3	(0.9, 2.1)	1.1	(0.8,1.5)	1.4	(0.9,2.0)	1.3	(0.8, 2.1)
50-<75%ile	1.3	(0.9,1.7)	1.0	(0.7,1.5)	1.3	(0.8, 2.1)	1.1	(0.8,1.4)	1.0	(0.6,1.5)	1.3	(0.8, 2.1)
75-<90%ile			*reference*						*reference*			
Top 10%	0.8	(0.6,1.2)	1.4	(0.9,2.3)	1.0	(0.5, 2.0)	0.9	(0.6,1.4)	1.5	(0.9,2.5)	1.0	(0.5, 2.0)
Years of education	0.94	(0.92,0.97)	0.97	(0.94,1.01)	0.99	(0.96, 1.02)	0.99	(0.96,1.02)	0.99	(0.95,1.03)	1.00	(0.97, 1.04)

*Separate SES models are adjusted for: age, age-squared, male, black, Hispanic, birth regions (northeast, west, Midwest, south, not US, unknown), father's occupation (graded from 0-3, with indicators for farming, military, or unknown), mother's education (<8 years, 8+ years, unknown), father's education (<8 years, 8+ years, unknown), and self-reported childhood health. Each of the three models includes measures for only a single dimension of SES

^Combined SES models are adjusted for the above confounders and include education, income categories, and wealth categories in the same model

Table 5.3. The association of wealth, income and education with stroke incidence after adjustment for cardiovascular risk factors among HRS participants aged >50 years and stroke-free at baseline interview

	50-64		65-74		75+	
	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)
Wealth						
Lowest 10%	1.7	(1.2,2.6)	0.8	(0.5,1.3)	0.9	(0.6,1.3)
10-<25%ile	1.6	(1.1,2.3)	0.9	(0.6,1.3)	1.0	(0.7,1.5)
25-<50%ile	1.8	(1.3,2.5)	0.9	(0.6,1.2)	1.0	(0.7,1.4)
50-<75%ile	0.9	(0.7,1.4)	1.0	(0.7,1.3)	0.9	(0.7,1.3)
75-<90%ile			*reference*			
Top 10%	1.2	(0.7,1.8)	0.8	(0.5,1.2)	0.9	(0.6,1.5)
Income						
Lowest 10%	1.5	(1.1,2.1)	1.6	(0.9,2.7)	1.2	(0.7,2.1)
10-<25%ile	1.1	(0.8,1.6)	1.2	(0.8,1.9)	1.5	(0.9,2.5)
25-<50%ile	1.1	(0.8,1.5)	1.3	(0.9,2.0)	1.3	(0.8,2.1)
50-<75%ile	1.1	(0.8,1.4)	1.0	(0.6,1.4)	1.3	(0.8,2.1)
75-<90%ile			*reference*			
Top 10%	0.9	(0.6,1.4)	1.5	(0.9,2.5)	1.0	(0.5,2.1)
Years of education	0.99	(0.96,1.03)	0.99	(0.95,1.03)	1.01	(0.97,1.04)

Models are adjusted for: education, income categories, wealth categories, age, age-squared, male, black, Hispanic, birth regions (northeast, west, Midwest, south, not US, unknown), father's occupation (graded from 0-3, with indicators for farming, military, or unknown), mother's education (<8 years, 8+ years, unknown), father's education (<8 years, 8+ years, unknown), and self-reported childhood health, self-reported diagnosis of hypertension, current smoking, diabetes, heart disease at baseline, level of vigorous activity at baseline, and BMI at baseline.

5.4 Discussion

Among men and women aged 50 and older, lower wealth, income and education were associated with higher stroke incidence rates. This association was mainly attributable to large effects in those aged 50-64 at baseline. In this age stratum, wealth was the strongest independent predictor of stroke net of other SES indicators. The effect of all SES indicators decreased sharply beyond age 65, resulting in no consistent effect of wealth, income or education among the elderly. Adjustment for risk factors attenuated income and wealth disparities in stroke at ages 50-64 by 30-50%. Results suggest that wealth and income are independent predictors of stroke at ages 50-64, whereas disparities decrease considerably beyond age 65.

Study limitations

Despite the unique strengths in the HRS data, some limitations should be considered. Medical record verification of strokes was not possible, and self-reported stroke data may be inaccurate. However, incidence rates in our sample were similar to those reported in other US studies. For comparison, the Greater Cincinnati/Northern Kentucky stroke study reported first stroke rates in the 50-64 year age stratum of 273/100,000 for whites and

637/100,000 for blacks[13]. Nevertheless, incomplete stroke ascertainment might have occurred differentially by SES, potentially biasing our results.

Misreporting of SES is possible, but HRS has some of the best available wealth data on US adults, and extensive efforts at verification have been conducted. By using percentiles, the impact of moderate inaccuracies in income and wealth reports was substantially reduced. Analyses using substantial amounts of imputed data tend to provide conservative estimates[11,14]. Measures of cardiovascular risk factors were also vulnerable to misreporting, which may have led to underestimation of their contribution to stroke disparities[15].

We did not have data on stroke sub-types. Although previous research indicates that lower SES is associated with similar increases in risk of ischaemic and hemorrhagic stroke[4,16,17], future studies should assess whether wealth effects differ across stroke sub-types.

Adjusting regression models for covariates influenced by the exposure of interest estimates direct effects only under strict assumptions[18]. For basic models, we therefore considered only covariates that temporally preceded SES. We also presented results simultaneously adjusting for income, wealth, and education. Education influences income and wealth, which might downwardly bias education coefficients. A similar caveat applies to models including cardiovascular risk factors. Nevertheless, this underestimation is unlikely to fully account for the overall age-pattern we observed.

Comparisons with previous studies

Socioeconomic disparities in stroke have been reported in Europe and the US[2-4,16,17,19,20]. We found large socioeconomic disparities in stroke at ages 50-64, but these were substantially attenuated or null after age 65. A previous study in 10 European populations reported that educational disparities in stroke mortality diminish but persist into old age[3]. In contrast, results from the US-based EPESE study found large disparities in stroke incidence at ages 65-74, but a crossover at age 75[2]. Although we observed a similar effect of income on stroke incidence at ages 65-74, this effect was largely attenuated after adjustment for education and wealth. Furthermore, although a crossover was not observed in HRS, our results suggest that lower SES does not predict excess risk in individuals older than 75.

To our knowledge, this is the first study reporting that lower wealth predicts increased stroke incidence independently of income and education. Consistent with our findings, previous studies indicate that wealth is an important predictor of major health outcomes such as all-cause mortality[6] and symptom burden[21]. Over and above income and education, wealth seems to be the strongest predictor of stroke at ages 50-64. Previous reports indicate wealth is associated with health throughout adulthood and becomes a more important health determinant than education or income at older ages[6,8]. Our results suggest this pattern does not apply to stroke.

Previous studies suggest that risk factors such as smoking and hypertension explain about half of stroke disparities[19]. We found that adjustment for smoking, hypertension, diabetes, heart disease, physical activity, and BMI attenuated but did not eliminate wealth and income disparities in stroke.

Interpretation of findings

SES may affect stroke through access to medical care or via behavioural, material, or psychosocial pathways. Lower SES is associated with higher prevalence of conventional risk factors such as smoking[22], obesity[23], diabetes[24] and alcohol consumption[25], which contribute to socioeconomic disparities in stroke[19]. Psychosocial risk factors such as depression and social isolation also appear to contribute to socioeconomic disparities in stroke incidence in US elderly[2]. Psychosocial risks may be mediated by cardiovascular risk factors, and through central nervous system activation of autonomic, neuroendocrine and immunological responses[26].

Over and above income and education, wealth was the strongest and most consistent predictor of stroke at ages 50 to 64. In the US, wealth inequalities are more extreme than income inequalities, and racial inequalities in wealth are especially stark[27]. Research characterizing socioeconomic risk exclusively in terms of education and income may substantially underestimate the excess stroke burden potentially attributable to SES. Wealth is a special form of capital that represents material resources better than income[6,27]. It is also a much more permanent stock that reflects lifelong asset accumulation. Lifetime income, costly health and economic shocks, and intergenerational transfers of material resources all affect wealth[6,27]. Due to its intergenerational and cumulative nature[6,27], wealth may be closely related to childhood socioeconomic position, a strong determinant of adult stroke risk[28]. Possessing assets may also enhance access to healthcare and other health-related material resources. Wealth may increase individuals' sense of control over their lives, thus reducing stress levels[26] and stroke risk[29]. Overall, wealth more comprehensively reflects the traditional notion of economic well-being[6,27] and encompasses multiple dimensions of SES that influence stroke risk.

The majority of strokes occur after age 65[5]. However, beyond this age, socioeconomic gradients in stroke incidence were substantially attenuated across all SES dimensions. The extent of attenuation in the wealth coefficients was unexpected, because wealth seems especially relevant for the elderly[6]. Age-attenuation of SES and race disparities has been found for mortality and several health outcomes[6,8]. Several mechanisms have been suggested to explain this pattern in other contexts[30]. Age-attenuation can arise when relative risk measures, instead of absolute risk contrasts, are used. This is not an adequate explanation for our findings, because SES coefficients declined with age even in absolute terms. Advocates of selective survival explanations note that low-SES individuals die earlier from multiple causes. As a consequence, low-SES survivors at older ages are a selection of the fittest and therefore no longer comparable to high-SES survivors[8]. Thus, selective survival could artificially attenuate the association between SES and stroke. Finally, entitlement programs such as Medicare may buffer negative effects of social deprivation on stroke in the oldest old. However, the age-attenuation in socioeconomic disparities in stroke is less marked in European populations with more generous welfare policies and universal access to care. Thus, these mechanisms are unlikely to account for our results.

Implications

Our results identify economic insecurity as an important risk factor for stroke and highlight the importance of life-course perspectives for understanding socioeconomic inequalities in stroke. Although wealth is a major determinant of stroke, many US residents reach middle age with few assets. Policies improving economically disadvantaged groups' access to medical care and other basic resources before reaching old age might reduce stroke rates as these cohorts age. Alternatively, enhancing opportunities for low-SES individuals to accumulate assets throughout life might help reduce stroke rates and ameliorate SES disparities in stroke. The age-attenuation of socioeconomic disparities in stroke likely reflects selective survival, a consequence of the cumulative disadvantage faced by individuals throughout the life-course. Disentangling substantive from artefactual explanations will be crucial for interpreting and predicting population trends in stroke and prioritising prevention strategies.

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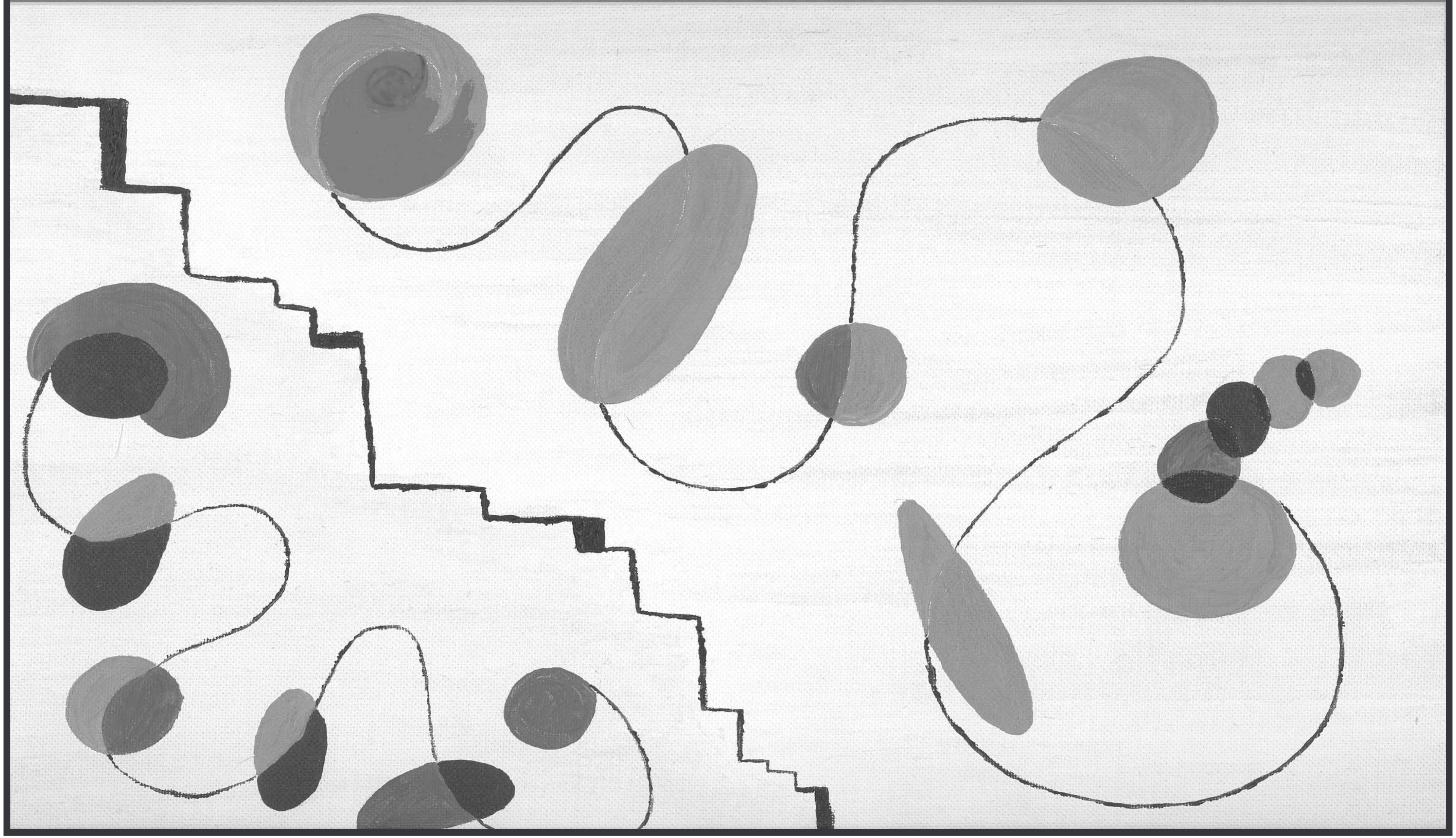
Part III

Explaining socioeconomic disparities in stroke



Chapter 6

Socioeconomic status and stroke: The impact of risk factors on absolute and relative disparities

Avendano M, Lenthe FV, Boshuizen HC, Van Den Bos GAM, Mackenbach JP. The potential impact of risk factor modification on socioeconomic disparities in stroke: The Globe study. *Submitted 2006.*

Abstract

Background and objectives: Conventional risk factors explain less than half of relative stroke disparities. Their contribution to absolute disparities and the role of psychosocial factors has not yet been examined. This study estimates the impact of conventional and psychosocial risk factors to both relative and absolute stroke disparities.

Methods: Data came from 3,339 participants of the Globe study aged 40-74 years. Information on biomedical, behavioural and psychosocial factors was obtained through interview, and 12-year stroke incidence was ascertained through linkage with the national hospital diagnosis registry. Using Poisson regression, we developed a counterfactual approach to estimate predicted rate ratios and rate differences under a hypothetical scenario, whereby population exposure to risk factors would be reduced to the theoretical minimum.

Results: Lower socioeconomic status was associated with higher stroke incidence ($RR_{education}$=2.23, 95%CI 1.04, 4.81; RR_{income}=2.81, 95%CI 1.41, 5.60). Adjustment for biomedical/behavioural risk factors alone attenuated rate ratios by 15-40%, but after incorporating locus of control and emotional support relative disparities were attenuated by 50-70%. Reducing biomedical/behavioural (blood pressure, smoking, excessive alcohol consumption and heart disease) and psychosocial factors (locus of control and emotional support) to the theoretical minimum would reduce absolute stroke disparities by 74-84%, both risk factor groups contributing to a similar extent.

Conclusions: About half of stroke relative disparities not explained by behavioural/biomedical factors can be attributed to psychosocial factors, whereas both risk factor groups contribute equally to absolute stroke disparities. Interventions to eliminate population exposure to both conventional and psychosocial factors can substantially reduce socioeconomic disparities in stroke.

6.1 Introduction

Stroke is the second leading cause of death worldwide and the first cause of disability in the developed world[1]. Lower socioeconomic status is associated with higher stroke rates[2-7]. Risk factors such as blood pressure and smoking are major stroke determinants, but explain less than half of socioeconomic disparities in stroke[8-10]. Psychosocial risk factors such as depression and social networks are also risk factors for stroke[11, 12]. However, little research has examined their contribution to stroke disparities, and the mechanisms behind this association are not yet fully understood.

Conventional risk factors such as hypertension explain a small part of relative disparities in heart disease, but contribute considerably to absolute disparities[13]. Research on stroke has only focused on assessing the impact of risk factors on relative disparities[8, 9, 14]. Absolute estimates can be more informative by illustrating the reduction that would occur in stroke disparities if a given risk factor would be reduced to the theoretical minimum. This counterfactual may lead to a larger contribution of risk factors to stroke disparities, as it additionally assesses the full impact of risk factor modification in the entire population[13].

This study examines the role of biomedical, behavioural and psychosocial risk factors in explaining socioeconomic disparities in stroke incidence. Adopting a counterfactual analysis perspective[15, 16], we developed a novel approach to estimate the potential reduction that would be achieved in absolute and relative stroke differentials, under a hypothetical scenario of optimal theoretical minimum population distribution of risk factors (e.g., zero-prevalence of smoking)[15, 16]. This is the first study to assess the contribution of biomedical, behavioural and psychosocial risk factors to relative and absolute stroke differentials.

6.2 Materials and methods

Study population

Data came from Globe[17], a longitudinal study conducted in the Netherlands. In 1991, a postal survey was conducted among 27,070 non-institutionalised individuals aged 15 to 74 years. The response rate was 70.1% (n=18,973) and did not differ by age, sex, marital status, level of urbanization or social class[17]. Additional structured interviews were conducted in two sub-samples: In one sub-sample, individuals with major chronic diseases were oversampled. The response rate was 72.3% (n=2,865). The second sub-group was a random respondent sample, with a response rate of 79.4% (n=2,802). The present study is based on these sub-samples with detailed risk factor information (n=5,667). We excluded participants aged less than 40 years (n=1,369). Individuals who reported a stroke at baseline or moved outside the coverage area were also excluded (n=148), as were those with missing values for basic confounders or risk factors (n=774). This yielded a final sample of 3,376 participants. Data on education were missing for 63 individuals (1.9%) and data on income for 440 participants (13.0%). The final sample comprised 3,313 individuals for education and 2,936 individuals for income.

Socioeconomic status

Educational level and income were used as complementary indicators of socioeconomic status[18, 19]. Four levels of education were distinguished: Higher vocational school or University (level 1), intermediate vocational or intermediate/higher secondary school (level 2), lower vocational or lower secondary school (level 3) and primary education only (level 4). Household income was defined as the sum of all income sources in the household. It was divided by the square root of the number of household members[20, 21] and classified into quartiles.

Biomedical and behavioural risk factors

Data were obtained on: (1) *High blood pressure* was measured by asking participants whether they had been diagnosed with high blood pressure by a doctor. (2) *Body mass index (BMI)* was based on self-reported height and weight, and was calculating by dividing weight (kg) by the square of height (m). (3) *Diabetes* and *heart disease* were measured by asking participants whether they had suffered from any of these conditions in the last five years. (4) *Smoking* was based on current status and number of cigarettes currently smoked daily (never smoker, former smoker, pipe/cigar smoker, current smoker consuming 20 cigarettes or less, or more than 20 cigarettes per day). (5) *Alcohol intake* was classified into total abstinence, light (> 6 glasses one day/week, 4-5 glasses < two days/week, 2-3 glasses < 3 days/week, or one glass < 7 days/week), moderate (> 6 glasses 2 days/week, 4-5 glasses 3-4 days/week, or 2-3 glasses > 4 days/week) and excessive (> 6 glasses 3-4 days/week, or 4-5 glasses > 5 days/week). (6) *Physical activity* was based on the number of hours spent per week on sport activities, and on gardening, cycling and walking. It was classified into inactivity, low, moderate or high physical activity.

Psychosocial factors

Data were collected on: (1) *Difficult life events* was defined as the number of difficult events (i.e., divorce, death of partner) during previous year (no events, 1, 2, or ≥ 3 events). (2) *Locus of control* refers to individuals' belief over their control on own life. It was measured by an adapted 11-item version of the Rotter's scale and reclassified into quintiles[22, 23]. (3) *Social support* was measured using an adapted version of a Dutch validated scale[24] and divided into two dimensions: *Emotional support* and *instrumental support*. A good internal consistency was observed for both the emotional (Cronbach's =0.60) and instrumental (Chronbach's=0.67) support sub-scales. (4) *Coping styles* were measured by the Utrecht Coping style questionnaire[25]. Two sub-scales were included: *Depressive reaction pattern* (being overwhelmed by problems) and *social support seeking* (seeking comfort and understanding from others).

Study Follow-up and stroke outcomes

Data were linked with the national hospital diagnosis registry to ascertain stroke occurrence. Five hospitals that covered almost the entire study population were selected. Coverage area was defined as the area comprising municipalities where at least 90% of the population attended one of the five hospitals in case of admission. Linkage was based on 6-digit area postcode, sex and birth date. Linkage was complete for almost the entire sample (>99%). Stroke was defined as codes 430-434 and 436-438 from the 9th revision of the international classification of disease code.

An incident event was defined as first hospital diagnosis of stroke after baseline. Survival was defined as time from baseline to date of: (a) first stroke diagnosis; (b) death, (c) emigration outside the coverage area; or (d) censoring. Participants alive and free of stroke were censored at the latest date of complete follow-up (22 December 2003), or latest date of complete basic demographic information available for linkage with the hospital registry.

Methods of analysis

As there were no significant interactions by gender, we pooled data for men and women. Age and sex standardized incidence stroke rates by educational level and income were calculated. In order to assess the contribution of risk factors to socioeconomic differences in stroke, a step-wise approach was followed:

(a) A counterfactual population representing the theoretical minimum exposure distribution was constructed[15, 16]. For biomedical/behavioural risk factors, the minimum exposure distribution comprised: Zero-prevalence of hypertension, smoking, diabetes and heart disease; BMI > 18.5 and < 25; light or moderate alcohol consumption; and moderate or high physical activity. The minimum exposure distribution for psychosocial factors comprised: Lowest three quintiles of locus of control (internal); lowest two tertiles of depressive reaction pattern coping style; highest two tertiles of social support seeking coping style; highest two tertiles of social and instrumental support; and less than three difficult life events. A more extreme optimal exposure for these factors yielded almost identical results.

(b) Poisson regression was used to model the effect of socioeconomic status on stroke. RRs (Rate ratios) compared stroke incidence by education and income, taking the highest level as reference category. Basic model RRs (age and sex adjusted) were then compared with adjusted RRs, whereby the entire sample would experience the same counterfactual risk factor distribution. Risk factors were first added to the basic model individually, and subsequently all risk factors were entered simultaneously.

(c) Based on the models above, we predicted what the rates of stroke in each socioeconomic status group would be, if everyone had experienced the counterfactual distribution of risk factors defined as the theoretical minimum. The predicted counterfactual RD (rate difference) was then compared to the basic model RD (adjusted only for age and sex).

(d) The attenuation of the effect -expressed as a percentage- was interpreted as the reduction that would be expected in RRs and RDs, if the entire population had experienced the theoretical minimum risk factor distribution.

Unless otherwise indicated, analyses were weighted in order to account for the sampling design (including oversampling of participants with chronic conditions) and non-response. Analyses were conducted in SAS version 8.2 using the GENMOD procedure.

6.3 Results

During 36,496.1 person-years, 114 individuals developed incident stroke (table 6.1). Lower socioeconomic status was associated with higher stroke incidence for both education (RR= 2.23, 95% confidence interval (CI): 1.04, 4.81) and income (RR=2.81, 95% CI: 1.41, 5.60). Individuals with the lowest socioeconomic status had an excess of 156-209 strokes per 100,000 person-years as compared to those in the highest socioeconomic categories.

Table 6.1. Stroke incidence (per 100,000 person-years) by educational level and income in men and women aged 40 to 74 years

	No. Strokes*	Subjects*	P-years*	Incidence rate†	Rate ratio†	95%CI	Rate difference†	Trend
Education‡								
1 (high)	13	549	5922.0	126.4	1.00		Reference	p =0.05
2	20	596	6473.2	230.4	1.82	0.81, 4.12	104.0	
3	35	1366	15088.6	192.4	1.52	0.72, 3.23	66.0	
4 (low)	41	802	8326.5	282.5	2.23	1.04, 4.81	156.1	
Income‡								
1 (high)	20	779	8432.7	115.3	1.00		Reference	p <0.05
2	19	758	8328.1	164.0	1.42	0.68, 2.99	48.7	
3	32	744	8066.3	254.7	2.21	1.12, 4.35	139.4	
4 (low)	27	655	6840.3	324.2	2.81	1.41, 5.60	208.9	

*Unweighted

†Adjusted for age and sex

‡Education: 1=higher vocational school or University; 2=intermediate vocational or intermediate/higher secondary school; 3=lower vocational or lower secondary; 4=primary education only; Income is divided into quartiles

Rate ratios marginally decreased after adjustment for smoking, alcohol consumption and previous heart disease, whereas adjustment for high blood pressure, BMI, diabetes and physical activity did not attenuate rate ratios (tables 6.2 and 6.3). Adjustment for locus of control and emotional support moderately attenuated RRs, whereas other psychosocial risk factors did not change estimates for education or income. Overall, RRs for income were more attenuated after adjustment for psychosocial ($RR_{lowest/highest}$=1.94, 95% CI: 0.94, 4.00) than for biomedical/behavioural risk factors ($RR_{lowest/highest}$=2.56, 95% CI: 1.25, 5.23). Furthermore, on a model already adjusted for biomedical/behavioural factors, additional adjustment for psychosocial factors further decreased RRs (tables 6.2 and 6.3). Adjustment for all risk factors attenuated the effect of education by about 70% ($RR_{lowest/highest}$=1.33, 95% CI: 0.58, 3.05) and income by about 50% ($RR_{lowest/highest}$=1.88: 95% CI, 0.89, 3.97).

Table 6.2. Rate ratio of stroke incidence by educational level after adjustment for risk factors: Men and women aged 40 to 74 years

Educational level*	1 (high)	2		3		4 (low)	
	RR	RR	95%CI	RR	95%CI	RR	95%CI
Basic model[†]	1.00	1.82	0.81,4.12	1.52	0.72, 3.23	2.23	1.04, 4.81
Behavioural/biomedical							
+ High blood pressure	1.00	1.82	0.80, 4.11	1.49	0.70, 3.16	2.21	1.03, 4.74
+ Body mass index	1.00	1.82	0.80, 4.11	1.57	0.74, 3.33	2.35	1.09, 5.07
+ Diabetes	1.00	1.80	0.79, 4.07	1.50	0.71, 3.18	2.17	1.00, 4.67
+ Smoking	1.00	1.68	0.74, 3.81	1.38	0.65, 2.93	2.00	0.93, 4.31
+ Alcohol intake	1.00	1.79	0.79, 4.05	1.43	0.67, 3.06	1.97	0.90, 4.29
+ Physical activity	1.00	1.82	0.80, 4.13	1.51	0.71, 3.22	2.24	1.04, 4.85
+ Previous heart disease	1.00	1.78	0.79, 4.04	1.50	0.71, 3.19	2.15	1.00, 4.62
+ All behavioural/biomedical	1.00	1.57	0.69, 3.57	1.29	0.60, 2.77	1.75	0.80, 3.86
Attenuation[‡]		30.4%		44.0%		39.0%	
Psychosocial							
+ Locus of control	1.00	1.67	0.73, 3.81	1.27	0.58, 2.77	1.84	0.82, 4.11
+ Depressive mood	1.00	1.84	0.81, 4.16	1.54	0.72, 3.26	2.24	1.04, 4.83
+ Social support seeking	1.00	1.81	0.80, 4.10	1.50	0.70, 3.19	2.22	1.03, 4.77
+Emotional support	1.00	1.76	0.78, 3.98	1.51	0.71, 3.20	2.02	0.94, 4.35
+Instrumental support	1.00	1.80	0.79, 4.07	1.53	0.72, 3.26	2.16	1.01, 4.65
+Difficult life events	1.00	1.82	0.80, 4.12	1.55	0.73, 3.29	2.18	1.02, 4.69
+ All psychosocial	1.00	1.69	0.74, 3.88	1.34	0.62, 2.93	1.62	0.72, 3.62
Attenuation		16.2%		34.9%		49.9%	
All risk factors	1.00	1.50	0.65, 3.43	1.14	0.52, 2.51	1.33	0.58, 3.05
Attenuation		39.6%		73.2%		73.3%	

*Education: 1=higher vocational school or University; 2=intermediate vocational or intermediate/higher secondary school; 3=lower vocational or lower secondary; 4=primary education only

[†]Rate ratios adjusted for age and gender

[‡]Attenuation of basic model rate ratio by education after adjustment for risk factors

Tables 6.4 and 6.5 show predicted RDs if the entire population experienced the theoretical minimum risk factor distribution. Modification of high blood pressure, smoking, excessive alcohol consumption and heart disease, as well as locus of control, emotional and instrumental support would each reduce RDs. Other risk factors did not alter RDs. Modification of all risk factors would decrease rate differentials by about 84% for education ($RD_{lowest/highest}$=24.2 per 100,000), and 74% for income ($RD_{lowest/highest}$=54.6 per 100,000).

Table 6.3. Rate ratio of stroke incidence by income after adjustment for risk factors: Men and women aged 40 to 74 years

Income quartile	1 (high)	2		3		4 (low)	
	RR	RR	95%CI	RR	95%CI	RR	95%CI
Basic model*	1.00	1.42	0.68, 2.99	2.21	1.12, 4.35	2.81	1.41, 5.60
Behavioural/biomedical factors							
+ High blood pressure	1.00	1.38	0.66, 2.90	2.16	1.09, 4.25	2.73	1.37, 5.44
+ Body mass index	1.00	1.43	0.68, 3.01	2.29	1.16, 4.51	2.96	1.49, 5.90
+ Diabetes	1.00	1.40	0.67, 2.95	2.18	1.11, 4.30	2.75	1.38, 5.49
+ Smoking	1.00	1.44	0.69, 3.04	2.16	1.10, 4.26	2.70	1.36, 5.37
+ Alcohol intake	1.00	1.36	0.65, 2.87	2.16	1.08, 4.31	2.68	1.33, 5.40
+ Physical activity	1.00	1.43	0.68, 3.01	2.25	1.14, 4.44	2.87	1.43, 5.75
+ Previous heart disease	1.00	1.41	0.67, 2.96	2.21	1.12, 4.36	2.67	1.34, 5.33
+ All Biomedical factors	1.00	1.37	0.65, 2.91	2.23	1.11, 4.47	2.56	1.25,5.23
Attenuation†		11.8%		0%		14.1%	
Psychosocial factors							
+ Locus of control	1.00	1.30	0.61, 2.77	1.97	0.99, 3.95	2.48	1.22, 5.06
+ Depressive mood	1.00	1.43	0.68, 3.00	2.23	1.13, 4.40	2.84	1.42, 5.67
+ Social support seeking	1.00	1.45	0.69, 3.04	2.20	1.12, 4.34	2.83	1.42, 5.63
+Emotional support	1.00	1.39	0.66, 2.92	2.12	1.07, 4.18	2.48	1.24, 4.95
+Instrumental support	1.00	1.41	0.67, 2.96	2.12	1.07, 4.18	2.71	1.36, 5.39
+Difficult life events	1.00	1.41	0.67, 2.95	2.17	1.10, 4.28	2.58	1.29, 5.16
+ All psychosocial factors	1.00	1.26	0.59, 2.69	1.79	0.89, 3.60	1.94	0.94, 4.00
Attenuation		37.5%		34.7%		48.1%	
All risk factors	1.00	1.26	0.59, 2.72	1.92	0.94, 3.94	1.88	0.89, 3.97
Attenuation		38.2%		23.7%		51.2%	

* Rate ratios adjusted for age and sex

†Attenuation of basic model rate ratio by income quartile after adjustment for risk factors

Overall, the impact of risk factors on stroke differentials was larger for rate differences than for rate ratios (tables 6.2-6.5). This pattern was more marked for income: Whereas adjustment for biomedical/biomedical risk factors did not attenuate RRs, these factors attenuated income RDs by almost half. Psychosocial risk factors seemed to contribute more than biomedical/behavioural risk factors to relative disparities (tables 6.2 and 6.3). However, both groups of factors contributed to a similar extent to absolute disparities in stroke (tables 6.4 and 6.5).

Table 6.4. Absolute rate differences (per 100,000) in stroke incidence by educational level before and after adjustment for risk factors: Men and women aged 40 to 74 years

Educational level*	1 (high)	2	3	4 (low)
Basic model†	Reference	104.0	66.0	156.1
Biomedical/biomedical factors				
+ High blood pressure		85.2	51.0	125.8
+ Body mass index		110.7	76.9	182.6
+ Diabetes		100.3	62.7	146.4
+ Smoking		77.6	43.4	114.7
+ Alcohol intake		89.7	49.0	110.3
+ Physical activity		104.4	65.2	157.7
+ Previous heart disease		93.5	60.0	136.7
+ All biomedical factors	Reference	52.4	26.7	68.9
Attenuation‡		49.7%	49.5%	55.9%
Psychosocial factors				
+ Locus of control		82.4	33.6	102.9
+ Depressive mood		105.9	67.8	157.5
+ Social support seeking		105.0	64.7	157.6
+Emotional support		72.4	48.4	97.3
+Instrumental support		85.0	57.0	123.9
+Difficult life events		96.4	64.7	139.4
+ All psychosocial factors	Reference	65.2	32.4	58.0
Attenuation		37.4%	51.0%	62.8%
All risk factors	Reference	36.4	10.3	24.2
Attenuation		65.0%	84.5%	84.5%

*Education: 1=higher vocational school or University; 2=intermediate vocational or intermediate/higher secondary school; 3=lower vocational or lower secondary; 4=primary education only

†Rate differences adjusted for age and sex

‡Attenuation of basic model rate difference by education after adjustment for risk factors

Table 6.5. Absolute rate differences (per 100,000) in stroke incidence by income before and after adjustment for risk factors: Men and women aged 40 to 74 years

Income quartile	1 (high)	2	3	4 (low)
Basic model*	Reference	48.7	139.4	208.9
Biomedical/biomedical factors				
+ High blood pressure		36.8	112.1	167.4
+ Body mass index		54.4	160.9	245.5
+ Diabetes		45.9	134.8	199.5
+ Smoking		43.0	111.9	163.9
+ Alcohol intake		36.7	117.7	170.0
+ Physical activity		50.1	144.3	216.2
+ Previous heart disease		44.2	131.1	180.7
+ All biomedical factors	Reference	28.3	93.4	118.0
Attenuation†		42.0%	33.0%	43.5%
Psychosocial factors				
+ Locus of control		32.7	104.7	159.4
+ Depressive mood		50.1	144.6	215.9
+ Social support seeking		52.1	140.4	213.2
+Emotional support		34.2	98.5	130.3
+Instrumental support		40.6	111.1	169.2
+Difficult life events		45.3	130.6	176.1
+ All psychosocial factors	Reference	23.5	70.3	83.7
Attenuation		51.8%	49.6%	59.9%
All risk factors	Reference	16.1	56.9	54.6
Attenuation		66.9%	59.2%	73.9%

*Rate differences adjusted for age and sex

†Attenuation of basic model rate difference by income quartile after adjustment for risk factors

6.4 Discussion

Lower education and income were associated with higher stroke incidence. Biomedical and behavioural risk factors alone explained 15-40% of relative disparities, but after incorporating locus of control and emotional support relative disparities were attenuated by 50-70%. Interestingly, elimination of risk factors would reduce absolute stroke disparities by 74-84%, with both behavioural/biomedical (blood pressure, smoking, alcohol consumption and heart disease) and psychosocial factors (locus of control and emotional support) contributing to a similar extent. Findings suggest that both biomedical/behavioural and psychosocial risk factors play a role in the explanation of socioeconomic disparities in stroke.

Study limitations

Some methodological limitations should be considered in this study. Firstly, stroke was ascertained through linkage with the hospital diagnosis registry. We were unable to include cases that did not reach the hospital or died before admission. Due to higher stroke mortality levels in the lower classes[5], we may have underestimated stroke disparities. However, due to national healthcare coverage in the Netherlands, most stroke cases are likely to be admitted to the hospital. Thus, any bias due to this problem is likely to be small.

Due to the limited number of cases, we were unable to analyse data for specific sub-types of stroke. Studies have shown different trend patterns for cerebral infarct and hemorrhage[26], which may reflect differences in determinants. However, evidence indicates that socioeconomic status is similarly associated with different stroke sub-types[3, 4, 6]. Furthermore, stroke sub-types share most risk factors included in our study[27]. Nevertheless, we do not know whether differences may exist in the impact of specific risk factors on socioeconomic disparities in stroke sub-types.

Risk factor data were based on self-report. As there seemed to be no differential misclassification by socioeconomic status[17], bias on the contribution of risk factors to relative disparities is likely to be small. However, we may have underestimated the contribution of some risk factors to absolute disparities due to misreporting. Future studies should replicate results using more precise measurements of factors such as blood pressure.

Comparison with previous studies

Psychosocial risk factors such as social networks are risk factors for stroke[12]. In accordance with previous studies[14], our results indicate that psychosocial factors such as locus of control and emotional support contribute to stroke disparities, both in absolute and relative terms. This is consistent with previous studies indicating that conventional factors explain only part of stroke disparities[8, 9], and highlight the role of psychosocial factors in stroke disparities[14].

Previous research has only assessed the contribution of risk factors to relative disparities in stroke[8-10]. In accordance with previous studies[14], we found that hypertension did not contribute to relative stroke disparities. However, due to its strong association with stroke, removing hypertension in the population would reduce stroke disparities by about 20%. This is consistent with recent research on coronary heart disease, showing that conventional risk factors have a larger impact on absolute than relative disparities[13]. In our study, both conventional and psychosocial risk factors had a larger contribution to absolute than relative disparities.

In contrast to previous research[14, 28], We found that a depressive reaction pattern was not associated with stroke and did not contribute to stroke disparities. Whereas previous studies measured depressive symptoms[14], our study only comprised data on depressive coping style. Alternatively, depression might be an important determinant of stroke at older ages[14], whereas it may play a less important role in relatively young cohorts.

Explanation of results

Behavioural and biomedical factors contributed to stroke disparities, but their contribution was largest in absolute terms. Hypertension is the most important risk factor, accounting for about 40% of strokes[29]. Smoking is a risk factor for both ischaemic and hemorrhagic stroke, accounting four about 12% of cases[27]. Consumption of more than 100-299 g/week of alcohol can lead to hemorrhagic stroke and accounts for around 21% of events[30]. Hypertension and alcohol consumption were weakly associated with socioeconomic status, and therefore did not consistently contribute to relative disparities. However, as a large fraction of strokes is attributable to these factors, reducing their prevalence to the theoretical minimum would reduce absolute stroke disparities by about 44-55%.

BMI, diabetes and physical activity did not seem to contribute to either relative or absolute stroke disparities. BMI was strongly associated with education and income but was weakly associated with stroke. The latter may be due to the fact that we did not measure BMI changes over the life-course[10, 31], which may explain its limited contribution to both absolute and relative stroke disparities. Diabetes and physical activity were associated with both socioeconomic status and stroke. However, associations were only significant beyond age 70 (results not shown), at which age they may play a more important role[14].

Psychosocial factors contributed to both absolute and relative socioeconomic disparities in stroke. An external locus of control was 5 to 10 times more common in those with low education and income, and was associated with increased stroke risk. An external locus of control might increase stroke risk through decreasing adherence to healthy behaviours. However, compared with a model already adjusted for biomedical/biomedical risk factors ($HR_{education}$=1.75, 95% CI: 0.79, 3.86), additional adjustment for locus of control further decreased rate ratios ($HR_{education}$=1.50, 95% CI: 0.66, 3.41). Nevertheless, locus of control can influence other health behaviours not included in our study such as salt and fat consumption[32]. Locus of control and social support may also influence stroke risk via psychobiological pathways. Psychosocial factors can stimulate biological systems through central nervous system activation[33]. Studies have found increased cardiovascular and blood pressure stress reactivity in lower socioeconomic groups[34, 35], which is associated with higher stroke rates[35]. Control at work may influence cardiovascular risk partly through provoking greater fibrinogen stress responses[36, 37], which are associated with lower socioeconomic status[37]. Thus, psychosocial factors may contribute to stroke disparities through a combination of behavioural and psychobiological pathways.

The impact of risk factors was generally larger for absolute than for relative disparities. Most importantly, biomedical/behavioural risk factors explained about half of absolute but almost none of relative income disparities in stroke. This reflects the selection of a different counterfactual: Attenuation of relative disparities after adjustment reflects the impact of eliminating disparities in a risk factor, given that all individuals adopted the population average risk factor distribution. Thus, only risk factors that are socially patterned will have an impact on relative stroke disparities. In contrast, attenuation of absolute estimates illustrates the reduction in stroke disparities if risk factor prevalence would be reduced to the theoretical minimum in the population. This estimation attributes weight to factors such as hypertension, which are not socially patterned but are strong population determinants of stroke. Estimates of the role of risk factors in stroke disparities should not only be based on reductions in relative risks[13]. Absolute measures can illustrate the potential public health gains of population risk factor modification[16], and should be considered as complementary measures[13].

Implications

Socially disadvantaged populations face a larger burden of stroke. Population wide strategies to modify conventional cardiovascular risk factors such as smoking, alcohol consumption and blood pressure can contribute to reduce socioeconomic disparities in stroke, particularly in absolute terms. Additionally, interventions to increase the level of control and social support among the lower socioeconomic groups are necessary to reduce both absolute and relative stroke disparities. Psychosocial disadvantage occurs as a result of long-term experiences across life. Thus, interventions need to focus on different stages over the life course[10, 31]. Overall, combined interventions to reduce population exposure to both conventional and psychosocial factors can contribute to reduce socioeconomic disparities in stroke.

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Chapter 7

Socioeconomic status and stroke incidence in the US elderly: The role of risk factors in the EPESE study

Avendano M, Kawachi I, Van Lenthe F, Boshuizen HC, Mackenbach JP, Van den Bos GA, Fay ME, Berkman LF. Socioeconomic Status and Stroke Incidence in the US Elderly: The Role of Risk Factors in the EPESE Study. *Stroke*. 2006;37:1368-73.
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Abstract

Background and objectives: This study assesses the effect of socioeconomic status on stroke incidence in the elderly, and the contribution of risk factors to stroke disparities.

Methods: Data comprised a sample of 2,812 men and women aged 65 years and over from the New Haven cohort of the Established Populations for the Epidemiologic Studies of the Elderly. Individuals provided baseline information on demographics, functioning, cardiovascular and psychosocial risk factors in 1982 and were followed for 12 years. Proportional hazard models were used to model survival from initial interview to first fatal or non-fatal stroke.

Results: 270 subjects developed incident stroke. At ages 65 to 74, lower socioeconomic status was associated with higher stroke incidence for both education ($HR_{lowest/highest}$=2.07, 95%CI 1.04-4.13) and income ($HR_{lowest/highest}$=2.08, 95%CI 1.01-4.27). Adjustment for race, diabetes, depression, social networks and functioning attenuated hazard ratios to a non-significant level, whereas other risk factors did not change associations significantly. Beyond age 75, however, stroke rates were higher among those with the highest education ($HR_{lowest/highest}$=0.42, 95%CI 0.22-0.79) and income ($HR_{lowest/highest}$=0.43, 95%CI 0.22-0.86), which remained largely unchanged after adjustment for risk factors.

Conclusions: We observed substantial socioeconomic disparities in stroke at ages 65 to 74, whereas a crossover of the association occurred beyond age 75. Policies to improve social and economic resources at early old age, and interventions to improve diabetes management, depression, social networks and functioning in the disadvantaged elderly can contribute to reduce stroke disparities.

7.1 Introduction

Disparities in cardiovascular health are a major public health problem. Eliminating these disparities is one of the major goals of the Healthy people 2010 public agenda, which calls for further research to understand the causes of these disparities[1]. Lower socioeconomic status is associated with higher stroke incidence in European countries[2-6]. However, little research has examined this association in the US and how it varies across age-groups. It is also not well established which risk factors mediate this association. Previous research in the UK suggests that conventional risk factors such as hypertension and smoking explain about half of these disparities[3]. However, these studies were focused on those aged less than 65[3]. Around 89% of strokes occur after age 65[7], whereby factors such as depression and functioning are also major risk factors for stroke[8,9].

We assessed the effect of socioeconomic status on stroke incidence in the US elderly, and the role of risk factors in explaining stroke disparities. Furthermore, we examined the role of race. We used data from a representative sample of the elderly in New Haven followed for 12 years. As relative disparities decrease or disappear at old age[10,11], we assessed whether this age-pattern applies to stroke. To our knowledge, this is the first study to assess the contribution of biomedical, psychosocial and functioning risk factors to stroke disparities in the elderly, and how this pattern varies for the old and oldest old.

7.2 Materials and methods

Study population

Data came from the New Haven (Connecticut) sample of the EPESE (Established Populations for the Epidemiologic Studies of the Elderly) study, a prospective investigation aimed at identifying predictors of mortality and disability in the elderly. Details of this study have been described elsewhere[12]. The sample was stratified by type of residence: (1) Public elderly housing, (2) private elderly housing and (3) general community housing. Due to the preponderance of women, men were oversampled in community and private housing[12]. The response rate was 82%, yielding a baseline sample of 2,812 participants. Respondents with a history of stroke at baseline (n=208) or missing basic demographics were excluded. Education data were missing for 73 individuals (2.8%) and income data for 347 participants (13.4%). The final sample comprised 2,524 individuals for education and 2,250 individuals for income.

Data collection and measurements

Interviews were conducted in 1982 by trained interviewers and included information on:

Socioeconomic status and Demographics

Education and income were used as indicators of socioeconomic status. Education was measured as years of schooling completed (0-7, 8-9, 10-12, or $\geq$13), and income as household income in the year before baseline (0-4,999, 5,000-9,999, 10,000-14,999, or $\geq$15,000 US dollars). Race was classified into white non-Hispanic, black non-Hispanic and other. Age was based on self-report and used as a continuous variable.

Conventional risk factors

(a) Blood pressure was measured according to the Hypertension Detection and Follow-up Program protocol[13]. A hypertension diagnosis was based on blood pressure measurements or use of hypertension medication. Categories comprised normotensive, controlled, isolated systolic, and diastolic (with our without systolic) hypertension. (b)

Smoking was classified into never smoked, ex-smoker, and currently smoking daily less than 14, 15-24, and $\geq$25 cigarettes. (c) Diabetes mellitus was ascertained through self-report at baseline. (d) Body mass index was based on self-reported weight and height (weight(kg)/height(m^2)). (e) Physical activity was measured by self-reported walks, garden work and active sports (scale: often, sometimes and never), and defined as number of items with response category 'often'[14]. (f) Alcohol consumption was based on self-reported use in the preceding month and categorized into: non-drinkers, moderate (0.1-20 oz/month) or heavy ($\geq$21 ounces/month) drinkers.

Physical/cognitive functioning

Three complementary measures of physical functioning were used: (a) A modified version of the Katz Activities of Daily Living scale[15] assessed the ability to perform basic activities without assistance (none vs. $\geq$1 limitations). (b) The Rosow-Breslau Functional Health Scale[16] assessed the number of limitations in activities of gross mobility. (c) The Nagi scale measured the number of limitations in physical performance activities (e.g., difficulty in stooping, crouching and kneeling)[17].

Cognitive function was measured using a 10-item version of the SPMSQ (Short Portable Mental Status Questionnaire)[18] and scored by the number of errors ($\leq$1, 2-3, and $\geq$4)[19].

Psychosocial risk factors

(a) Depressive symptoms were measured using the Center for Epidemiologic Studies Depression scale[20]. A score of 21 or more indicates depressive symptomatology in the elderly[21]. (b) The Social networks index measured social ties with children, relatives, friends and a confidant, and social participation[22]. (c) Stressful life events were the summed score of 8 items on stressful events (e.g., death of a close relative) during the past year (none, 1, 2, or $\geq$3)[23].

Stroke outcomes

An Incident event was defined as first non-fatal or fatal stroke. Non-fatal strokes were ascertained through yearly interviews from 1983 through 1990/1991, and in 1994. Education/income information was ascertained at baseline only. Independently, participants were asked in subsequent waves whether they had been diagnosed with stroke since last interviewed. Only 99 survivors (3.9%) did not have complete interviews until 1994, and were censored at last interview date.

Fatal strokes were ascertained through daily review of obituaries, hospital admission records and annual interviews with participant or next of kin. Records were matched to the National Death index and death certificates obtained. Data on mortality and cause of death were successfully obtained for almost all participants ($\geq$99%).

Methods of analysis

As results did not differ by sex, men and women were combined to obtain more precise estimates. Firstly, standardized stroke rates were calculated by education and income, using the entire population as the standard. Cox Proportional hazard models were then used to quantify the impact of socioeconomic indicators on stroke. Survival was defined as time from baseline to date of first fatal or non-fatal stroke, death from other causes, or last interview. Initial models were adjusted for age, sex and race. Subsequently, conventional, functioning and psychosocial factors were added. Psychosocial factors and functioning measures were correlated. However, correlations were generally modest, so that there was no collinearity in the models. Final models were adjusted for all factors. HRs (Hazard ratios) for the reference model (adjusted for age, sex and race) were compared with HRs additionally adjusted for risk factors, using the following formula: (100X[$HR_{reference}$-$HR_{adjusted}$]/[$HR_{reference}$-1]). Analyses were weighted using SUDAAN (version 9.01). Weights permitted the sample characteristics to be inflated to the total New Haven older population, thus assuring the validity of generalizations. We applied housing unit weights, weights to account for male oversampling, and post-stratification weights[12].

7.3 Results

During 20,315 person-years, 270 subjects developed incident stroke. Among individuals aged 65 to 74 years, lower socioeconomic status was associated with a higher stroke incidence (Table 7.1). The standardized stroke incidence rates in those with low education or income were twice as high than in those with high education (HR=2.07, 95%CI 1.04-4.13) or income (HR=2.08, 95%CI 1.01-4.27). A reverse pattern occurred at ages 75 and over, so that stroke incidence rates were higher in the highest education (HR=0.42, 95%CI 0.22-0.79) and income (HR=0.43, 95%CI 0.22-0.86) groups (Table 7.1).

Table 7.1. Stroke incidence (per 100,000 person-years) by socioeconomic status among men and women aged ≥65

Age	Socioeconomic status	No. Strokes*	Subjects*	P-years*	Incidence rate†	Hazard ratio† (95%CI)	Trend
65-74							
	Education(years)						p=0.06
	Highest (≥13)	17	216	1,985.7	641.2	1.00	
	High (10-12)	42	443	3,925.2	1104.6	1.74(0.90-3.38)	
	Middle (8-9)	43	402	3,458.5	1089.5	1.67(0.83-3.34)	
	Low (0-7)	38	366	3,228.8	1277.2	2.07(1.04-4.13)	
	Income(dollars)						p<0.05
	≥15,000	12	157	1,596.6	667.3	1.00	
	10,000-14,999	16	164	1,404.2	844.8	1.30(0.56-3.06)	
	5,000-9,999	45	503	4,287.3	897.1	1.40(0.69-2.81)	
	0-4,999	49	468	4,087.8	1239.4	2.08(1.01-4.27)	
≥75							
	Education(years)						p<0.05
	Highest (≥13)	21	119	811.2	2740.5	1.00	
	High (10-12)	30	264	1,741.9	1729.8	0.45(0.23-0.87)	
	Middle (8-9)	33	325	2,236.8	1467.9	0.43(0.23-0.80)	
	Low (0-7)	36	389	2,540.4	1346.7	0.42(0.22-0.79)	
	Income(dollars)						
	≥15,000	13	60	428.1	3555.7	1.00	p<0.05
	10,000-14,999	12	86	570.9	2002.1	071(0.30-1.66)	
	5,000-9,999	33	374	2,393.5	1105.3	0.30(0.14-0.63)	
	0-4,999	46	438	2,968.0	1529.5	0.43(0.22-0.86)	

*Unweighted

†Age and sex adjusted

Adjustment for race attenuated hazard ratios between the highest and lowest socioeconomic groups by about one third (Tables 7.2 and 7.3), and confidence intervals became wide and overlapped with the null value. Hazard ratios remained largely unchanged after adjustment for hypertension, smoking and alcohol consumption, and adjustment for physical activity and BMI slightly decreased hazard ratios for education but not for income. Hazard ratios for both education and income were attenuated after adjustment for diabetes. Accordingly, although most risk factors predicted stroke incidence, only diabetes was clearly associated with socioeconomic status (Appendix Table). Adjustment for all conventional risk factors attenuated the effect of education by 22% and income by 43%, which was almost entirely due to diabetes.

Table 7.2. Hazard ratios of stroke incidence by educational level among men and women aged 65 to 74

Education (years)	Highest (≥13)	High (10-12)	Middle (8-10)	Low (0-7)
Basic model*	1.00	1.74(0.90-3.38)	1.64(0.83-3.34)	2.07(1.04-4.13)
+Race	1.00	1.68(0.86-3.25)	1.75(0.78-1.36)	1.74(0.84-3.58)
Conventional factors†				
+Hypertension	1.00	1.71(0.88-3.31)	1.57(0.78-3.14)	1.73(0.85-3.56)
+Smoking	1.00	1.74(0.90-3.38)	1.59(0.78-3.21)	1.78(0.86-3.70)
+Diabetes mellitus	1.00	1.53(0.78-3.00)	1.39(0.68-2.85)	1.62(0.79-3.36)
+Alcohol	1.00	1.69(0.88-3.24)	1.55(0.78-3.07)	1.74(0.85-3.55)
+BMI	1.00	1.64(0.84-3.17)	1.47(0.72-2.95)	1.62(0.78-3.36)
+Physical activity	1.00	1.57(0.81-3.07)	1.45(0.71-2.95)	1.63(0.79-3.36)
+All conventional factors	1.00	1.55(0.79-3.04)	1.35(0.68-2.67)	1.58(0.77-3.26)
Psychosocial factors†				
+Depression (cut-off 21)	1.00	1.55(0.79-3.04)	1.46(0.72-2.95)	1.52(0.73-3.15)
+Social networks	1.00	1.57(0.81-3.05)	1.43(0.71-2.91)	1.54(0.75-3.15)
+Difficult life events	1.00	1.63(0.83-3.20)	1.55(0.77-3.12)	1.73(0.85-3.54)
+All psychosocial factors	1.00	1.46(0.74-2.88)	1.37(0.67-2.79)	1.37(0.66-2.83)
Functioning†				
+Physical functioning	1.00	1.68(0.85-3.34)	1.61(0.79-3.25)	1.62(0.78-3.37)
+Cognitive functioning	1.00	1.68(0.86-3.26)	1.52(0.75-3.08)	1.63(0.79-3.37)
+All functioning factors	1.00	1.65(0.83-3.28)	1.57(0.78-3.16)	1.55(0.74-3.25)
Full model	1.00	1.45(0.72-2.91)	1.31(0.65-2.65)	1.28(0.60-2.75)

*Basic model=age+sex

†Adjusted for age, sex, race and indicated risk factors

Adjustment for depressive symptoms and social networks attenuated hazard ratios considerably for both education and income, whereas life events did not change hazard ratios. Altogether, psychosocial factors reduced hazard ratios by about 50%. This reflected the consistent association of depression and social networks with education, income and stroke (appendix Table). Adjustment for physical and cognitive functioning reduced hazard ratios by about one quarter (Tables7.2 and 7.3). After adjusting for all factors, hazard ratios were no longer significant and decrease by about 60% for education and almost 90% for income.

Table 7.3. Hazard ratios of stroke incidence by income among men and women aged 65 to 74

Income (dollars)	High ($\geq$15,000)	10,0000-14,999	5,000-9,999	Low (0-4,999)
Basic model*	1.00	1.30(0.56-3.06)	1.40(0.69-2.81)	2.08(1.01-4.27)
+ Race	1.00	1.23(0.52-2.88)	1.33(0.66-2.68)	1.79(0.87-3.67)
Conventional risk factors†				
+Hypertension	1.00	1.22(0.52-2.89)	1.33(0.65-2.71)	1.76(0.85-3.64)
+Smoking	1.00	1.19(0.50-2.80)	1.30(0.64-2.66)	1.80(0.87-3.75)
+Diabetes	1.00	1.17(0.50-2.75)	1.16(0.57-2.36)	1.56(0.76-3.21)
+Alcohol	1.00	1.27(0.54-2.97)	1.35(0.68-2.67)	1.80(0.89-3.64)
+BMI	1.00	1.20(0.51-2.80)	1.26(0.62-2.57)	1.73(0.84-3.55)
+Physical activity	1.00	1.10(0.47-2.61)	1.26(0.61-2.59)	1.72(0.84-3.53)
+All conventional factors	1.00	1.03(0.43-2.48)	1.07(0.52-2.21)	1.45(0.70-3.01)
Psychosocial factors†				
+Depression (cut-off 21)	1.00	1.27(0.54-2.98)	1.28(0.63-2.58)	1.61(0.78-3.32)
+Social networks	1.00	1.12(0.47-2.70)	1.18(0.58-2.39)	1.50(0.72-3.12)
+Difficult life events	1.00	1.22(0.52-2.87)	1.35(0.67-2.72)	1.78(0.87-3.64)
+All psychosocial factors	1.00	1.19(0.50-2.85)	1.17(0.58-2.36)	1.45(0.70-3.02)
Functioning†				
+Physical functioning	1.00	1.37(0.57-3.29)	1.34(0.64-2.80)	1.59(0.78-3.24)
+Cognitive functioning	1.00	1.20(0.51-2.82)	1.30(0.64-2.62)	1.75(0.85-3.58)
+All functioning factors	1.00	1.35(0.56-3.22)	1.32(0.63-2.74)	1.57(0.77-3.20)
Full model	1.00	1.03(0.42-2.55)	0.96(0.46-2.00)	1.10(0.52-2.31)

*Basic model=age+sex

†Adjusted for age, sex, race and indicated risk factors

At ages 75 and over, major risk factors such as hypertension and BMI did not consistently predict stroke (appendix Table). Thus, entering risk factors did not change hazard ratios for education or income, which remained well below 1 after adjustment (Table 7.4).

Table 7.4. Hazard ratios of stroke incidence by education and income among men and women aged ≥75

Socioeconomic status	Risk factor	Highest	High	Middle	Low
Education					
	Basic model*	1.00	0.45(0.23-0.87)	0.43(0.23-0.80)	0.42(0.22-0.79)
	+Race	1.00	0.45(0.23-0.89)	0.42(0.22-0.80)	0.44(0.23-0.83)
	+Conventional†	1.00	0.44(0.21-0.95)	0.40(0.20-0.78)	0.45(0.22-0.92)
	+Psychosocial †	1.00	0.49(0.25-0.95)	0.43(0.23-0.82)	0.45(0.24-0.85)
	+Functioning†	1.00	0.42(0.22-0.82)	0.38(0.21-0.71)	0.39(0.21-0.73)
	Full model	1.00	0.52(0.25-1.07)	0.41(0.21-0.81)	0.47(0.23-0.94)
Income					
	Basic model*	1.00	0.71(0.30-1.66)	0.30(0.14-0.63)	0.43(0.22-0.86)
	+Race	1.00	0.71(0.30-1.68)	0.31(0.15-0.64)	0.46(0.23-0.94)
	+Conventional†	1.00	0.71(0.31-1.66)	0.30(0.14-0.65)	0.44(0.22-0.90)
	+Psychosocial †	1.00	0.71(0.30-1.61)	0.30(0.14-0.63)	0.46(0.23-0.92)
	+Functioning†	1.00	0.77(0.33-1.81)	0.31(0.15-0.67)	0.44(0.21-0.93)
	Full model	1.00	0.82(0.34-1.93)	0.31(0.14-0.70)	0.50(0.24-1.08)

*Basic model=age+sex

†Adjusted for age, sex, race and indicated risk factor group:

Conventional (hypertension, smoking, diabetes, alcohol consumption, BMI and physical activity); psychosocial (depressive symptoms, social networks and difficult life events); and functioning (physical and cognitive)

7.4 Discussion

At ages 65 to 74 years, lower education and income were associated with higher stroke incidence. Adjustment for race, diabetes, depressive symptomatology, social networks, and cognitive/physical functioning reduced these associations considerably, whereas other conventional risk factors did not alter associations. Beyond age 75, higher socioeconomic status was associated with higher stroke rates, even after adjustment for risk factors. This suggests a crossover of the association beyond age 75.

Study limitations

Strength of our study was the long and virtually complete follow-up. However, some limitations should be considered. Mortality was accurately ascertained throughout follow-up. However, non-fatal strokes were ascertained through yearly interviews, which may have resulted in underestimation of stroke incidence. Nevertheless, we found no evidence that underestimation occurred differentially by socioeconomic status. Furthermore, a data audit in the period 1982-1988 showed high correspondence between cases detected through interview and hospital records inspection[24]. Thus, any bias caused by this problem is likely to be small.

A majority of the EPESE cohort was retired, with some participants living in elderly housing. Thus, although we asked participants to report income from all household sources, income may not fully reflect all resources available to participants. Thus, we do not know whether a different pattern might be observed for factors such as wealth, which reflect assets accumulation through life[25].

Data on stroke sub-types were not available in our study. However, previous research indicates that the effect of socioeconomic status is similar for both ischemic and hemorrhagic stroke[5,6]. Nevertheless, future studies should assess whether the role of risk factors in explaining stroke disparities may vary by stroke sub-type.

Comparison with previous studies

Previous research suggests that conventional risk factors such as smoking explain about half of stroke disparities before age 65[3]. However, we found that these factors play a less important role, with only diabetes and less conventional factors contributing to stroke disparities. Accordingly, a previous study indicated that conventional risk factors do not fully explain stroke disparities among elderly women[4].

Previous research indicates that stroke is associated with depression[9] and low social networks[9], which highlights their potential role in explaining stroke disparities. Previous studies have also shown that physical functioning limitations predict stroke[8]. These factors contributed to stroke disparities in our study. Alternatively, their contribution may also reflect a reverse effect of these factors (e.g., physical functioning) on income. However, reverse causality cannot explain results for educational level, which is largely determined early in life[2].

Socioeconomic disparities in stroke at ages 65 to 74 partly reflect the higher stroke rates among African-americans than Whites[26]. African-americans have on average less education and income, and are more likely to develop stroke than their white counterparts[26] (appendix table). This is partly explained by a higher burden of risk factors among African-Americans, and may also reflect genetic susceptibility[26]. However, despite wide confidence intervals, an elevated risk remained after adjustment or stratification by race. Thus, despite large racial stroke disparities, the effect of socioeconomic status on stroke appears to be independent from race.

Prior research reported that stroke disparities diminish but remain beyond age 75[2]. However, our study comprised a longer follow-up and included both first fatal and non-fatal strokes. Studies indicate that the effect of socioeconomic status on all-cause mortality disappear or even reverses at approximately age 75[11]. Our findings suggest that this crossover[10] might be even stronger for stroke.

Interpretation of findings

Conventional risk factors such as smoking were strong predictors of stroke at ages 65 to 74, but did not explain stroke disparities. This may be due to their weak association with socioeconomic status. Accordingly, in earlier birth cohorts, the prevalence of risk factors did not vary as much by socioeconomic status, and only in more recent cohorts do disparities in risk factors such as smoking begin to emerge[27]. Their role in explaining stroke disparities may thus be limited at ages 65 to 74, whereas they may play a more important role in more recent birth cohorts[3].

On the other hand, socioeconomic disparities in other risk factors played a more important role. Diabetes disparities may originate from differentials in obesity throughout life[28]. Depression is associated with an increased risk of artherosclerosis[29], through which it may contribute to stroke disparities. Lower social networks are associated with higher functional limitations[19], which might lead to less physical activity and thus higher stroke rates. However, physical limitations may also be a marker for other health problems, which might mediate the association of socioeconomic status on stroke.

Beyond age 75, higher socioeconomic status was associated with higher stroke rates. Due to their weak association with stroke and socioeconomic status, adjustment for risk factors did not explain this crossover. Failure of education and income to represent the true socioeconomic resources of the oldest old may explain this pattern. Nevertheless, a similar race crossover has also been previously reported, whereby Black mortality rates can become lower than White rates after approximately age 75[10]. Selective survival and competing causes of death may explain this pattern. Individuals with a lower socioeconomic status may die earlier from other causes, so that only the healthiest survive into old age. Simultaneously, better survival might lead to postponement of death towards older ages among higher socioeconomic groups[10,11]. Thus, higher socioeconomic groups might be more likely to live 'long enough' to develop stroke at very old ages. Nevertheless, previous research indicates that selective survival cannot fully account for age-variations in mortality differentials[11]. Further studies should attempt to replicate these findings and explore possible explanations.

Implications

Social and economic circumstances of the elderly shape a wide array of conditions such as stroke. Men and women with a low socioeconomic status face a disproportionate share of social and health disadvantage. Thus, policies aimed at providing both economic and social resources may improve their profile. This can be supplemented with interventions to improve diabetes and depression management, and to maintain social networks and functioning in the lower socioeconomic groups[19,24]. As world populations age, the toll of social and economic disadvantage is likely to increase, along with the societal impact of stroke. Thus, it is incumbent on us to develop effective interventions at middle and early old age, and thus diminish the higher burden of stroke among disadvantaged populations.

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Appendix

Table. Prevalence of risk factors by educational level and income and their association with stroke incidence among men and women aged ≥65

Age	Risk factor	Education (years)				Income (US dollars)*				Stroke†
		≥13	10-12	8-10	0-7	≥15	10-14	5-9.9	0-4.9	
65-74										
	Race (black)	5.2	10.7	12.1	37.3	4.3	9.8	13.6	31.0	1.74 (1.05–2.87)
	Conventional factors									
	Hypertension††	19.3	17.6	21.5	22.4	16.9	27.1	19.5	20.8	1.74 (1.00-3.04)
	Current smoking	18.4	22.2	24.0	21.9	14.6	23.0	25.0	20.6	1.73 (1.03-2.90)
	Diabetes	9.3	15.0	16.0	15.2	6.2	14.2	16.6	16.5	2.91 (1.78-4.74)
	Alcohol (≥21oz/month)	10.7	9.5	11.3	4.7	11.1	14.9	7.5	5.8	1.25 (0.60-2.60)
	BMI (mean)	25.4	25.5	26.9	27.3	25.6	26.2	26.4	26.4	1.04 (1.00-1.08)
	Low physical activity	38.2	42.4	44.7	36.6	40.2	47.9	35.9	40.7	4.37 (1.81-10.54)
	Psychosocial factors									
	Depressive symptoms	3.1	5.8	6.8	11.8	3.4	1.8	7.9	8.8	3.05 (1.63-5.70)
	Social networks (≤ 1)	11.3	14.3	17.6	19.5	5.3	11.2	16.1	24.2	2.03 (0.96-4.28)
	Life events (≥3)	14.0	14.7	16.8	21.0	16.0	13.3	18.4	16.9	1.37 (0.73-2.57)
	Functioning factors									
	Katz (≥1)	4.9	4.7	4.5	5.3	0.7	3.7	6.9	6.7	2.41 (1.19-4.89)
	Rosow-Breslau (≥1)	26.7	28.6	29.0	32.7	26.4	23.3	29.4	35.1	4.82 (2.54-9.17)
	Nagi (≥1)	28.4	34.6	28.2	38.2	27.8	29.6	32.9	34.8	5.90 (1.85-18.76)
	Cognitive impairment	0.0	1.86	4.6	7.7	0.0	0.0	3.6	3.1	0.87 (0.30-2.50)
75+										
	Race (black)	0.8	8.9	14.5	16.0	4.1	4.5	12.7	16.6	1.13 (0.53–2.41)
	Conventional factors									
	Hypertension††	19.2	11.2	17.2	9.2	19.8	23.0	7.0	14.2	0.86 (0.39-1.90)
	Current smoking	10.1	13.9	18.3	8.0	5.6	9.6	12.2	16.6	1.66 (0.88-3.12)
	Diabetes	10.4	13.6	12.8	14.1	15.7	5.9	13.8	13.8	1.71 (0.85-3.24)
	Alcohol (≥21oz/month)	8.7	3.5	4.9	6.9	8.6	7.8	5.2	3.9	0.56 (0.20-1.55)
	BMI (mean)	23.3	24.5	24.7	26.3	24.1	24.6	25.5	24.9	0.97 (0.91-1.03)
	Low physical activity	43.6	48.8	59.1	55.1	56.2	39.9	48.3	61.3	2.41 (0.94-6.19)
	Psychosocial factors									
	Depressive symptoms	7.8	6.5	7.8	11.1	7.5	8.5	7.4	12.2	0.95 (0.46-1.98)
	Social networks (≤ 1)	19.4	23.2	27.8	28.1	17.3	19.7	21.5	36.9	1.36 (0.48-3.81)
	Life events (≥3)	19.7	18.9	14.8	13.5	8.0	19.9	15.4	18.7	1.00 (0.48-2.08)
	Functioning									
	Katz (≥1)	11.4	11.1	16.7	16.9	22.2	11.0	11.7	19.6	1.82 (1.00-3.32)
	Rosow-Breslau (≥1)	56.1	48.7	54.7	52.4	67.8	42.3	44.1	58.6	1.34 (0.60-3.00)
	Nagi (≥1)	37.1	42.2	45.5	43.3	38.6	34.7	38.7	48.6	2.22 (0.57-8.58)
	Cognitive impairment	2.5	2.0	9.9	21.5	6.9	3.9	8.3	14.4	2.08 (1.14-3.81)

*Per 1,000 US dollars

†Models are adjusted for age, gender, race, education and income

††Uncontrolled diastolic hypertension (with or without systolic hypertension)

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Chapter 8

Socioeconomic disparities in stroke mortality in Europe: The role of biological, behavioural and dietary risk factors in the EPIC study

Avendano M et al. Socioeconomic disparities in stroke mortality in Europe: The role of biological, behavioural and dietary risk factors in the EPIC study. *Submitted to the Epic steering committee*

Abstract

Objective: Lower socioeconomic status is associated with higher stroke and IHD mortality. This study assessed the role of biological, behavioural and dietary risk factors in explaining these disparities in Europe.

Methods: Data came from the European Prospective Investigation into Cancer (EPIC) prospective cohort and comprised 507,000 men and women aged 30 to 74 years in nine European countries (Denmark, France, Germany, Greece, Italy, the Netherlands, Spain, Sweden and United Kingdom) who completed a validated diet and health questionnaire at baseline and were followed for mortality (mean 5.3 years). Cox proportional hazard models stratified by study centre, sex and baseline age were fitted. Hazard ratios (HR) and the relative index of inequality (RII) were calculated, adjusting for biological, behavioural and dietary risk factors. Analyses were conducted for the entire sample, and separately for northern and southern European populations.

Results: Increasing educational level was associated with reduced stroke (RII=0.58, 95%CI 0.38, 0.88) and IHD mortality (RII=0.48, 95%CI 0.35, 0.66), both in northern and southern Europe. Adjustment for blood pressure and hypertension, smoking, physical activity at work and fruit and vegetable consumption attenuated the effect of education on stroke by only one third (RII=0.72, 95%CI 0.47, 1.12), and that on IHD by about half (RII=0.72, 95%CI 0.54, 0.96), whereas adjustment for other factors did not attenuate estimates. Smoking contributed to cardiovascular disparities in the north but not in the south, whereas the contribution of blood pressure to stroke disparities was relatively larger in southern than northern populations. Body mass index contributed to IHD but not to stroke disparities.

Conclusion: There is a socioeconomic gradient in stroke and IHD mortality across Europe, which is partly explained by differences in risk factors. The role of risk factors such as smoking and blood pressure in explaining cardiovascular disparities seems to differ between Northern and Southern European populations, which may require specific intervention strategies for each region.

8.1 Introduction

Ischaemic heart disease (IHD) and stroke account for over 10.6 million deaths worldwide every year[1-3]. Lower socioeconomic status is associated with higher stroke and IHD mortality, so that cardiovascular diseases are the major contributor to socioeconomic differences in life expectancy and mortality in Europe[4]. Risk factors such as smoking and blood pressure explain only about half of socioeconomic differences in IHD and stroke mortality in Nordic countries and the UK[5,6]. However, the role of these risk factors in other European populations remains unexplored. Furthermore, it is not known whether disparities in nutrition and diet might contribute to socioeconomic differences in cardiovascular mortality. Overall, the mechanisms through which socioeconomic status influences cardiovascular risk remain largely unknown[7].

Socioeconomic differences in stroke mortality were of similar magnitude across Europe during the 1990s[8]. In contrast, socioeconomic differences in IHD mortality were larger in northern than in southern and Mediterranean European countries[9]. Larger socioeconomic differences in smoking prevalence have been observed in northern Europe[10]. Furthermore, the Mediterranean diet may have protected the entire southern European population from higher IHD mortality[11,12], whereas in northern Europe socioeconomic disparities in nutrition and diet might be larger[13]. Northern populations might be in a more advanced stage of the epidemiological transition, so that socioeconomic differences in risk factors such as smoking and diet tend to be larger in these countries than in the south[9]. On the other hand, socioeconomic disparities in risk factors such as hypertension might be similar in both northern and southern Europe, which could explain the uniform socioeconomic differences in stroke mortality across the region.

This study assesses socioeconomic differences in stroke and IHD mortality in Europe, and estimates the contribution of biological, behavioural and nutritional risk factors to these disparities. Furthermore, we tested the hypothesis that the contribution of risk factors to socioeconomic differences in stroke and IHD mortality is different for northern and southern European populations. This is the first study to assess the contribution of nutritional risk factors to cardiovascular socioeconomic differentials, and to compare northern and southern European populations in the contribution of risk factors to these disparities.

8.2 Methods

Study Subjects

The European Prospective Investigation into Cancer and Nutrition (EPIC) is a multicentre prospective cohort study designed to investigate the impact of diet, environmental and lifestyle factors on cancer and other chronic diseases. Details on study methodology are reported elsewhere[14]. Briefly, EPIC comprised 519,978 apparently healthy participants in 23 centres located in 10 European countries (Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden and the UK) enrolled between 1992 and 2002. Study populations were not intended to be representative samples, but were selected based on practical considerations to obtain high participation and long-term follow-up[14]. Subjects were recruited from the general population residing in a specific region or town, except the French cohort (based on members of the health insurance for school and university employees), the Utrecht (Dutch) and Florence (Italian) cohorts (women attending breast cancer screening), part of the Italian and Spanish cohort (blood donors and their spouses), and the Oxford cohort (vegetarian volunteers and healthy eaters). Subjects who agreed to participate following an invitation by mail or personal contact completed a questionnaire on their diet. A blood specimen was drawn and anthropometric measurements were taken from these subjects.

We excluded the Norwegian cohort (N=36, 460) due to short follow-up and small number of incident cases, as well as subjects who had missing information on vital status (n=727). Subjects aged 30 to 74 years from all other populations were selected for the analysis (n= 446, 577). For analyses on stroke, subjects who had reported a stroke at baseline (n=3,673) or did not know whether they had had a stroke were excluded (n=463), leaving 442,441 eligible subjects. For analyses on IHD, subjects who reported a heart disease at baseline (n=6,475) or did not know whether they had had a heart disease (n=577) were excluded, leaving 439,525 eligible participants.

Diet and lifestyle questionnaires

Information on usual individual dietary intakes over the previous 12 months was obtained using different assessment instruments developed and validated in each participating country[15-19]. Most centres used a self-administered questionnaire of 88 to 266 food items, and some centres used additionally a 7- or 14-day on meals consumed records. Most participants completed the questionnaire at home and were invited for an examination, during which anthropometrics and blood pressure (BP) were measured. For BP measurements, uniform procedures were recommended but no standard method or common type of instrument was introduced[14,20]. Blood pressure measurements were available in approximately 70% of eligible participants. For those with missing BP information, a dummy indicating a diagnosis of self-reported hypertension at baseline was introduced. BMI (Body mass index) was calculated as weight (kg) divided by height (m) squared. Lifestyle data comprised information on: Lifetime smoking (never, former, current, unknown) and number of cigarettes currently smoked per day; physical activity at work (sedentary, standing, manual, heavy manual, non-worker, or unknown occupation); leisure physical activity based on metabolic equivalent (MET) units; and self-reported prevalence of hypertension, hypercholesterolemia, heart disease, angina and diabetes. Nutritional data comprised information on: Lifetime alcohol consumption (grams per day (g/d)); fruit and vegetable consumption (g/d); fish consumption (g/d); total energy intake (kcal/d); saturated fatty acids (g); calcium intake (mg); and potassium intake (mg). Information was missing for some individuals in one or more of these variables. In order to include these participants in the analysis, dummies indicating missing values were constructed for these individuals.

Socioeconomic status

The highest educational level attained was used as indicator of socioeconomic status, as it can be applied in a comparable way to both men and women, and is more comparable across countries than other socioeconomic status indicators such as occupational class[21,22]. Educational level was classified into: (1) Only primary school or less, (2) vocational secondary education, (3) other secondary education and (4) college or university. Educational level was missing for 17,541 participants (3.9%), which were included in the analysis as a separate category.

Stroke and IHD outcomes

Data on stroke and IHD outcomes were collected from mortality registries at the regional or national level, by active follow-up and by death-record collection[14]. Stroke was defined as codes 430-434 and 436-438 of the 9th revision of the International Classification of Diseases (ICD-9), and codes I60-I69 from the ICD-10. IHD was defined as codes 410-414 of the ICD-9 and codes I20-I25 of the ICD-10. The last year of follow-up varied between centres and ranged from 1998 in France to 2004 in Cambridge (UK). Survival was defined as time from enrolment to date of death or censoring.

Statistical methods

Age and centre adjusted rates of mortality according to educational level were first calculated. As results were similar for men and women, pooled analyses were conducted for both groups. We applied Cox proportional hazard regression models using age as the time scale[23], with age at recruitment as entry-time and age of death or censoring as end-time. Cox models were stratified by centre in order to control for potential differences in data collection and methodology. Additionally, Cox models were stratified by sex and age at recruitment. Hazard ratios and corresponding 95% confidence intervals were calculated. The association between educational level and risk factors was estimated by calculating odds ratios using logistic regression for dichotomous outcomes, and mean differences using linear regression for continuous outcomes.

We hypothesised that the impact of adjusting for risk factors on hazard ratios for the effect of educational level was different for northern (UK, Sweden, Denmark, Netherlands, Germany) and southern Mediterranean (France, Italy, Spain, Greece) populations. In order to test this hypothesis, a dummy for region (north vs. south Mediterranean) was constructed, and an interaction term between RII score and region was entered into the models. Separate estimates for northern and southern populations were then obtained by parameterisation of estimates for each region.

Despite efforts to construct a comparable educational classification, differences remained between countries in the education system. Therefore, we calculated the relative index of inequality (RII)[24] using Cox regression. The RII has the advantage of adjusting for cross-country differences in the distribution of education, taking into account the relative position of each educational level group in each country. A score was constructed within each country and sex strata, corresponding to the midpoint of the cumulative proportion of individuals in a given educational level. Based on this score, the RII regresses the mortality rate on the proportion of the population that has a higher position in the educational classification[24]. The resulting estimate can be interpreted as the ratio of mortality rates of those at the bottom compared with those at the top of the educational classification[24]. Analyses were conducted using SAS, version 8.2 (SAS Institute, Cary, North Carolina, USA).

8.3 Results

During the entire follow-up period, 417 subjects died from stroke and 935 from IHD. The mean age at recruitment was 61.7 for stroke cases and 61.4 for IHD cases. Individuals who developed stroke or IHD were approximately 10 years older than those who were free of cardiovascular disease at the end of follow-up. Females accounted for 69.0% of the entire sample.

Table 8.1 summarises the effect of educational level on stroke and IHD mortality. Higher educational level was inversely associated with lower stroke mortality, with the lower risk observed in those with other secondary education (HR 0.67, 95%CI 0.47, 0.96). This association tended to be more linear among women than men, but these variations were not statistically significant. Similarly, higher education was inversely associated with IHD mortality, with the lowest risk observed in those with university or college education (HR 0.57, 95%CI 0.46, 0.71). Likewise, a higher score in the RII was associated with higher stroke (RII score HR 0.58, 95%CI 0.38, 0.88) and IHD (RII score HR 0.48, 95%CI 0.36, 0.63) mortality.

Table 8.1. The association of educational level with stroke and ischaemic heart disease (IHD) mortality in European men and women aged 30 to 74 years

Sex	Educational level	Stroke			IHD		
		Cases	Rate*	HR (95%CI)†	Cases	Rate*	HR (95%CI)†
Men	Primary	68	21.9	1.00	302	101.3	1.00
	Technical	42	24.0	0.97 (0.65-1.45)	180	103.6	0.92 (0.76-1.12)
	Secondary	8	8.9	0.40 (0.19-0.85)	68	74.3	0.77 (0.58-1.01)
	University	30	18.6	0.85 (0.53-1.35)	88	53.8	0.56 (0.44-0.72)
	RII	148	20.3	0.63 (0.33-1.21)	638	85.4	0.48 (0.35-0.66)
Women	Primary	114	18.2	1.00	123	18.9	1.00
	Technical	55	17.0	0.83 (0.59-1.17)	59	18.5	0.81 (0.59-1.12)
	Secondary	37	10.5	0.79 (0.52-1.20)	25	7.5	0.62 (0.38-0.99)
	University	30	10.7	0.64 (0.41-1.00)	25	9.5	0.63 (0.39-0.99)
	RII	236	14.1	0.54 (0.31-0.95)	232	14.0	0.48 (0.27-0.84)
All	Primary	182	19.4	1.00	425	45.7	1.00
	Technical	97	19.4	0.88 (0.68, 1.15)	239	47.8	0.89 (0.75, 1.05)
	Secondary	45	10.3	0.67 (0.47, 0.96)	93	21.0	0.72 (0.57, 0.92)
	University	60	13.6	0.73 (0.53, 1.01)	113	25.5	0.57 (0.46, 0.71)
	RII	384	16.1	0.58 (0.38, 0.88)	870	37.6	0.48 (0.36, 0.63)

*Age, sex and centre adjusted mortality rate per 100,000
†Hazard ratios are stratified by age at baseline, sex and centre

Tables 8.2 and 8.3 summarize the effect of adjusting for cardiovascular risk factors. The effect of educational level on stroke and IHD mortality was moderately attenuated after adjustment for blood pressure and hypertension, height, smoking, physical activity at work and fruit and vegetable consumption. Adjustment for BMI attenuated the effect of education on IHD but not on stroke mortality. Surprisingly, adjustment for other risk factors did not attenuate these associations. Although the association between educational level and stroke was attenuated by about one third and confidence intervals became wide, an inverse association remained after adjustment for all risk factors (HR score HR 0.72, 95%CI 0.47, 1.12). The associated between educational level and heart disease was attenuated by about half after incorporating all risk factors into the model but remained significant (HR score HR 0.72, 0.57, 0.96).

Table 8.2. The impact of cardiovascular risk factors on the association between socioeconomic status and stroke mortality among men and women aged 30 to 74 years in the EPIC population

	Model	**HR (95%CI)***			
		Technical	Secondary	University	RII (95%CI)
	Basic*	0.88 (0.68, 1.15)	0.67 (0.47, 0.96)	0.73 (0.53, 1.01)	0.58 (0.38, 0.88)
Non-dietary factors	BP or hypertension	0.91 (0.70, 1.18)	0.70 (0.49, 1.00)	0.78 (0.57, 1.08)	0.64 (0.42, 0.97)
	Height	0.89 (0.69, 1.16)	0.68 (0.48, 0.97)	0.74 (0.53, 1.03)	0.60 (0.39, 0.91)
	BMI	0.88 (0.68, 1.15)	0.67 (0.47, 0.95)	0.72 (0.52, 1.00)	0.57 (0.37, 0.87)
	Smoking status	090 (0.70, 1.18)	0.68 (0.48, 0.97)	0.77 (0.56, 1.07)	0.62 (0.41, 0.95)
	Physical activity at work	0.90 (0.69, 1.17)	0.68 (0.47, 0.97)	0.76 (0.54, 1.05)	0.61 (0.39, 0.93)
	Leisure physical activity	0.88 (0.68, 1.15)	0.67 (0.47, 0.96)	0.73 (0.53, 1.01)	0.58 (0.38, 0.88)
	Hypercholesterolemia	0.88 (0.68, 1.15)	0.67 (0.47, 0.96)	0.73 (0.52, 1.01)	0.58 (0.38, 0.88)
	Heart disease/angina	0.89 (0.68, 1.16)	0.67 (0.47, 0.96)	0.74 (0.53, 1.02)	0.59 (0.39, 0.90)
	Diabetes	0.89 (0.69, 1.16)	0.68 (0.47, 0.96)	0.74 (0.53, 1.02)	0.59 (0.39, 0.90)
	All non-dietary factors	0.94 (0.72, 1.23)	0.71 (0.49, 1.02)	0.86 (0.61, 1.20)	0.70 (0.45, 1.09)
Dietary factors	Alcohol	0.88 (0.68, 1.15)	0.67 (0.47, 0.95)	0.73 (0.53, 1.01)	0.58 (0.38, 0.88)
	Fruit & vegetables	0.89 (0.69, 1.16)	0.68 (0.48, 0.97)	0.74 (0.54, 1.03)	0.60 (0.39, 0.91)
	Fish consumption	0.89 (0.68, 1.16)	0.67 (0.47, 0.96)	0.74 (0.53, 1.02)	0.59 (0.38, 0.90)
	Total energy intake	0.88 (0.68, 1.15)	0.67 (0.47, 0.96)	0.73 (0.53, 1.01)	0.58 (0.38, 0.89)
	Saturated fatty acids	0.88 (0.68, 1.15)	0.67 (0.47, 0.96)	0.73 (0.53, 1.01)	0.58 (0.38, 0.88)
	Calcium	0.88 (0.68, 1.15)	0.67 (0.47, 0.96)	0.73 (0.53, 1.01)	0.58 (0.38, 0.88)
	Potassium	0.89 (0.68, 1.15)	0.67 (0.47, 0.96)	0.73 (0.53, 1.01)	0.58 (0.38, 0.89)
	All dietary factors	0.89 (0.69, 1.16)	0.68 (0.48, 0.98)	0.75 (0.54, 1.04)	0.61 (0.40, 0.93)
	Fully Adjusted	0.95 (0.73, 1.24)	0.72 (0.50, 1.03)	0.87 (0.62, 1.22)	0.72 (0.47, 1.12)

*Hazard ratios are stratified by centre, sex and age at baseline (basic model); risk factors are individually added to the basic model; BP indicates blood pressure; BMI indicates body mass index

Table 8.4 summarises the association between educational level and cardiovascular risk factors separately for northern and southern Mediterranean European populations. Overall, those in the lowest educational groups had a worse cardiovascular risk profile than those in the highest educational categories in both northern and southern Europe. Differences favouring the highest educated in current smoking, hypercholesterolemia, fruit and vegetable consumption, saturated fatty acids and potassium intake tended to be larger in northern than in southern countries. In contrast, educational differences in blood pressure, BMI, alcohol consumption and total energy intake tended to be larger in southern than northern European populations. Higher levels of leisure physical activity were observed in those with the lowest educational level.

Table 8.3. The impact of cardiovascular risk factors on the association between educational level and IHD (Ischaemic heart disease) mortality among European men and women aged 30 to 74 years

	Model	HR (95%CI)*			
		Technical	Secondary	University	RII (95%CI)
	Basic*	0.89 (0.75, 1.05)	0.72 (0.57, 0.92)	0.57 (0.46, 0.71)	0.48 (0.36, 0.63)
Non-dietary factors	BP or hypertension	0.90 (0.76, 1.07)	0.74 (0.58, 0.94)	0.61 (0.49, 0.76)	0.52 (0.39, 0.68)
	Height	0.91 (0.77, 1.07)	0.75 (0.59, 0.95)	0.60 (0.48, 0.75)	0.52 (0.39, 0.68)
	BMI	0.91 (0.77, 1.08)	0.75 (0.59, 0.96)	0.61 (0.49, 0.76)	0.52 (0.40, 0.69)
	Smoking status	0.92 (0.78, 1.09)	0.76 (0.60, 0.96)	0.64 (0.52, 0.80)	0.56 (0.42, 0.73)
	Physical activity at work	0.90 (0.77, 1.07)	0.74 (0.58, 0.94)	0.59 (0.47, 0.74)	0.50 (0.38, 0.67)
	Leisure physical activity	0.89 (0.75, 1.05)	0.72 (0.57, 0.92)	0.57 (0.46, 0.71)	0.48 (0.36, 0.63)
	Hypercholesterolemia	0.89 (0.76, 1.05)	0.72 (0.57, 0.92)	0.58 (0.46, 0.72)	0.48 (0.37, 0.64)
	Angina	0.89 (0.76, 1.06)	0.73 (0.57, 0.92)	0.58 (0.47, 0.72)	0.49 (0.37, 0.65)
	Diabetes	0.90 (0.76, 1.06)	0.73 (0.57, 0.92)	0.58 (0.46, 0.72)	0.49 (0.37, 0.64)
	All non-dietary factors	0.98 (0.83, 1.16)	0.83 (0.65, 1.06)	0.76 (0.60, 0.95)	0.69 (0.52, 0.92)
Dietary factors	Alcohol	0.89 (0.75, 1.05)	0.72 (0.57, 0.91)	0.57 (0.46, 0.71)	0.48 (0.36, 0.63)
	Fruit & vegetables	0.90 (0.77, 1.07)	0.74 (0.58, 0.94)	0.60 (0.48, 0.74)	0.51 (0.38, 0.67)
	Fish consumption	0.89 (0.75, 1.05)	0.72 (0.57, 0.92)	0.57 (0.46, 0.71)	0.48 (0.36, 0.63)
	Total energy intake	0.89 (0.75, 1.05)	0.72 (0.57, 0.92)	0.57 (0.46, 0.71)	0.48 (0.36, 0.63)
	Saturated fatty acids	0.89 (0.75, 1.05)	0.72 (0.57, 0.92)	0.57 (0.46, 0.71)	0.48 (0.36, 0.63)
	Calcium	0.89 (0.76, 1.05)	0.72 (0.57, 0.92)	0.58 (0.46, 0.72)	0.49 (0.37, 0.64)
	Potassium	0.90 (0.76, 1.06)	0.73 (0.57, 0.92)	0.58 (0.46, 0.72)	0.49 (0.37, 0.64)
	All dietary factors	0.90 (0.76, 1.06)	0.74 (0.58, 0.94)	0.59, 0.48, 0.74)	0.50 (0.38, 0.66)
	Fully Adjusted	0.99 (0.84, 1.17)	0.85 (0.66, 1.08)	0.77 (0.61, 0.97)	0.72 (0.54, 0.96)

*Hazard ratios are stratified by centre, sex and age at baseline (basic model); risk factors are individually added to the basic model; BP indicates blood pressure; BMI indicates body mass index

The impact of adjusting for selected risk factors on the RII for stroke and IHD is presented separately for northern and southern Mediterranean populations in Table 8.5. Overall, adjustment for blood pressure attenuated the effect of education on stroke to a relatively larger extent in southern than in northern populations. In contrast, whereas adjustment for smoking attenuated the effect of education on stroke and IHD in northern Europe, it did not attenuate the effect of education in southern countries. This pattern was particularly marked among women in southern Europe, where adjustment for smoking increased the RII for IHD (results not shown). After adjustment for all risk factors, a larger attenuation of the RII for IHD was observed in northern than southern Europe. In contrast, the RII for stroke was attenuated to a similar extent in both regions after adjusting for all risk factors, which largely reflected the impact of blood pressure in both regions and smoking in Northern populations.

Table 8.4. Mean difference and odds ratio of risk factors comparing the lowest and highest (reference) educational level among men and women aged 30 to 74 years

Risk factor	**Mean difference/Odds ratio***		
	Northern†	Southern†	Total
DBP, mmHg (MD) ††	3.6 (3.4, 3.9)	5.7 (5.3, 6.1)	4.2 (4.0, 4.4)
SBP, mmHg (MD)	1.7 (1.6, 1.9)	2.5 (2.3, 2.8)	2.0 (1.8, 2.1)
BMI (MD) ††	1.6 (1.6, 1.7)	1.9 (1.8, 2.0)	1.7 (1.7, 1.8)
Current smoking (OR) ††	1.8 (1.8, 1.9)	0.9 (0.8, 0.9)	1.4 (1.4, 1.4)
Physical activity, METS (MD)	7.5 (7.0, 8.0)	12.8 (12.1, 13.5)	10.0 (9.6, 10.5)
Hypercholesterolemia (OR)	1.3 (1.3, 1.4)	1.0 (0.9, 1.0)	1.1 (1.1, 1.2)
Angina (OR)	1.5 (1.4, 1.7)	1.4 (1.1, 1.6)	1.5 (1.3, 1.6)
Diabetes (OR)	1.6 (1.5, 1.8)	1.7 (1.5, 1.9)	1.6 (1.5, 1.7)
Alcohol (MD)	-1.0 (-1.2, -0.8)	2.9 (2.6, 3.2)	0.4 (0.2, 0.6)
Fruit & vegetables, g/d (MD)	-70.3 (-73.1, -67.6)	-60.7 (-65.6, -55.7)	-69.7 (-72.2, -67.3)
Fish consumption, g/d (MD)	-3.2 (-3.5, -2.9)	-3.0 (-3.4, -2.5)	-3.3 (-3.5, -3.1)
Total energy intake, kcal/d (MD)	-11.3 (-17.4, -5.2)	36.0 (26.5, 45.6)	-0.3 (-5.4, 4.9)
Saturated fatty acids, g (MD)	0.7 (0.6, 0.9)	-0.4 (-0.6, -0.3)	0.3 (0.2, 0.4)
Calcium, mg (MD)	-40.4 (-44.7, -36.2)	-38.5 (-45.6, -31.3)	-40.9 (-44.6, -37.3)
Potassium, mg (MD)	-69.4 (-79.6, -59.2)	-6.3 (-23.4, 10.8)	-55.5 (-64.3, -46.8)

*Mean differences and odds ratios compare the highest and lowest educational level groups and are adjusted by centre, age and sex

†Northern Europe comprises UK, Sweden, Denmark, Netherlands and Germany; southern Europe comprises France, Italy, Spain and Greece.

††MD indicates mean difference; DBP indicates diastolic blood pressure; SBP indicates systolic blood pressure; BMI indicates body mass index; OR indicates odds ratio

Table 8.5. Educational level and stroke and IHD (ischaemic heart disease) mortality: Relative index of inequality (RII) for northern and southern European countries after adjustment for selected risk factors

Model	**RII score HR (95%CI)***			
	Stroke		**IHD**	
	North (n=345)†	South (n=72)†	North (n=814)	South (n=121)
Basic	0.57 (0.36, 0.89)	0.65 (0.21, 1.99)	0.49 (0.37, 0.66)	0.37 (0.16, 0.86)
BP††	0.62 (0.39, 0.98)	0.75 (0.24, 2.34)	0.53 (0.40, 0.71)	0.40 (0.17, 0.94)
Smoking	0.62 (0.40, 0.98)	0.61 (0.20, 1.89)	0.59 (0.44, 0.79)	0.35 (0.15, 0.82)
BMI††	0.56 (0.36, 0.90)	0.64 (0.21, 1.96)	0.54 (0.40, 0.72)	0.42 (0.18, 0.99)
All non-dietary	0.70 (0.44, 1.12)	0.73 (0.23, 2.28)	0.73 (0.54, 0.98)	0.45 (0.19, 1.07)
Alcohol	0.56 (0.36, 0.89)	0.67 (0.22, 2.07)	0.49 (0.37, 0.66)	0.37 (0.16, 0.88)
Fruit & vegetables	0.59 (0.37, 0.92)	0.67 (0.22, 2.06)	0.52 (0.39, 0.70)	0.38 (0.16, 0.89)
Saturated fatty acids	0.57 (0.36, 0.90)	0.65 (0.21, 1.99)	0.49 (0.37, 0.66)	0.37 (0.16, 0.86)
All dietary	0.59 (0.37, 0.93)	0.70 (0.22, 2.16)	0.52 (0.39, 0.70)	0.37 (0.16, 0.87)
All factors	0.72 (0.45, 1.15)	0.74 (0.24, 2.34)	0.76 (0.56, 1.02)	0.44 (0.18, 1.05)

*Hazard ratios are stratified by centre, sex and age at baseline (basic model); risk factors are individually added to the basic model

†North Europe comprises UK, Sweden, Denmark, Netherlands and Germany; south Europe comprises France, Italy, Spain and Greece

††BP indicates blood pressure; BMI indicates body mass index

8.4 Discussion

In this large prospective study, lower educational level was associated with higher stroke and IHD mortality in Europe. These associations were partly attenuated after adjustment for blood pressure and hypertension, height, smoking, physical activity at work, and fruit and vegetable consumption. BMI contributed to socioeconomic differences in IHD mortality only, whereas other risk factors did not contribute to stroke or IHD socioeconomic differentials. Smoking contributed to socioeconomic differentials in cardiovascular disease in northern but not in southern populations. In contrast, blood pressure and hypertension contributed to stroke socioeconomic differentials in all countries. Apart from a modest contribution of fruit and vegetable consumption, we found no evidence of a major role of nutrition patterns in explaining socioeconomic differentials in cardiovascular mortality.

Strengths and limitations

Strengths of this multi-centre study are the prospective design, the consideration of relevant confounding and explanatory variables, and the large sample size with a long follow-up. However, some limitations should be considered. Despite efforts for standardization, differences remained between study centres in methodology and the accuracy of data collection. We pooled data for all centres, which may have concealed subtle differences in associations among countries. However, heterogeneity tests yielded no significant differences in the pattern for different centres. Furthermore, we fitted Cox proportional hazard models stratified by centre, thus taking into account potential variations among populations. We found no substantive evidence of a different pattern for different study centres. Thus, any bias due to this problem is likely to be small.

Most EPIC study populations were not intended to be representative samples, but were selected on the basis of practical considerations to ensure high participation and follow-up[14]. Subjects participating in EPIC may be more educated than the general population, which may have resulted in attenuated risk estimates due to less intra-individual variation in educational level. However, analyse restricted to those centres that closely represented a certain city or region i.e., Bilthoven, the Netherlands, yielded similar results as those observed in the entire sample. Nevertheless, results should be interpreted cautiously when trying to generalize findings to the European population.

Data on BP were available for a majority of participants. However, no measurements were recorded for about one third of the EPIC population, which may have resulted in residual confounding and underestimation of the contribution of this factor. To assess the impact of this bias, we conducted analyses restricted to individuals with data on measured BP (results not shown). In this sub-sample, Adjustment for BP attenuated the effect of education by about 20%. Thus, we may have slightly underestimated the contribution of BP. However, this attenuation was only somewhat larger than that observed for the entire sample (14%). Thus, it is unlikely that the overall pattern observed can be explained by residual confounding due to unmeasured BP in a fraction of the EPIC population.

In order to minimise the impact of mortality registration inaccuracies and increase statistical power, analyses were based on both ischaemic and haemorrhagic stroke as a single category. However, trends in both stroke major subtypes have shown a different pattern, possibly reflecting differences in their determinants[25]. Thus, we performed separate analyses of the effect of educational level on ischaemic and haemorrhagic stroke. Although confidence intervals became wide, educational level was similarly associated with both ischaemic (RII score HR 0.61, 95%CI 0.33, 1.14) and haemorrhagic stroke (RII score HR 0.59, 95%CI 0.33, 1.07), which is consistent with findings from previous studies[26-28]. Adjustment for BP attenuated these effects, but this attenuation was slightly larger for haemorrhagic stroke (RII score HR 0.67, 95%CI 0.37, 1.22). In contrast, adjustment for fruit and vegetable consumption only attenuated the effect of education on ischaemic stroke (RII score HR 0.65, 95%CI 0.35, 1.21). After adjustment for all risk factors, there was a slightly larger attenuation in the effect of education on ischaemic than on haemorrhagic stroke.

Comparison with previous studies

Previous studies showed that educational level is a strong predictor of stroke and IHD mortality in Europe[2,8,9], which is consistent with our findings. Whereas similar educational level differences in stroke have been observed across countries[8], larger socioeconomic differentials in IHD mortality have been observed in northern than southern populations, particularly among men[9,29]. We did not observed this north-south pattern, as educational level differentials in IHD mortality were similar in northern and southern countries. Previous studies focused on different southern European populations such as Madrid, where social differentials in IHD mortality might be smaller[9,29]. Furthermore, our study did not comprise populations representative of the entire southern European population, and different patterns may be evident for different sub-regions. Nevertheless, our results are consistent with previous reports suggesting that in relatively young cohorts, socioeconomic differentials in IHD mortality have emerged across northern and southern Europe during recent decades[2,9].

Previous research suggested that smoking explains part of socioeconomic differentials in stroke and IHD mortality[6,30]. However, we found that smoking only contributes to socioeconomic differences in cardiovascular mortality in northern but not in southern Europe. This is consistent with the previously reported north-south gradient in socioeconomic differences in smoking prevalence particularly among women[10,31], and highlights differences between countries in the causes of socioeconomic disparities in cardiovascular mortality. Consistent with previous studies[13], we observed large socioeconomic differences in fruit, vegetables and fish consumption both in northern and southern populations. However, this is the first study to report that fruit and vegetable consumption moderately contributes to socioeconomic differentials in cardiovascular mortality, whereas other nutritional factors did not contribute to these disparities. Our results confirm previous findings of an association between socioeconomic status and BP levels[32,33], and further suggest that this association tends to be larger in southern than northern European populations.

Explanation of results

We found that educational level differences in stroke and IHD mortality are partly explained by socioeconomic differences in smoking in northern but not in southern populations. It has been suggested that smoking spreads as an epidemic[34]: It is first adopted by those in the high socioeconomic classes; it subsequently declines in these groups, and spreads rapidly in the socially disadvantaged groups[34]. Studies indicate that countries in northern Europe have already experienced the smoking epidemic, whereas this transition is less advanced in southern countries such as Italy and Spain[10,31,34-36]. This is in line with the pattern observed in our study. In Italy, Spain, Greece and France, we observed smaller socioeconomic disparities in smoking prevalence than in northern populations. This pattern was more marked in women, where smoking was more prevalent in those with highest education. Thus, a different staging in the progression of the smoking epidemic[34,36] might explain the larger contribution of smoking to socioeconomic differentials in cardiovascular disease in northern than southern Mediterranean countries.

Educational level differences in the consumption of foods and nutrients were evident in our study. We observed large socioeconomic differences in the consumption of fruit and vegetables, which partly contributed to socioeconomic disparities in stroke and IHD mortality. Adherence to the Mediterranean diet can reduce the risk of cardiovascular disease by as much as 30%[37]. Higher levels of fruit and vegetable consumption were observed in southern than in northern European populations[38]. However, socioeconomic disparities in the consumption of these foods tended to be larger in the north, which might explain their relatively larger contribution to socioeconomic differentials in IHD mortality in northern countries. Foods such as fruits and vegetables might be seen as ‘modern’ in northern countries, where the higher socioeconomic groups might be more willing to adopt them. Instead, social disparities in fruit and vegetable consumption might be smaller in the south of Europe, where fruit and vegetables make part of the population traditional diet[38].

Hypertension is the major risk factor for stroke. Lower educational level was associated with higher BP levels both in northern and southern populations, which partly contributed to socioeconomic differentials in stroke mortality across Europe. Socioeconomic disparities in BP levels are likely to reflect differences in detection, management and control of hypertension, which raises questions about the potential role of disparities in healthcare utilization. On average, only 8% of hypertensive individuals have their condition controlled in Europe[39]. Furthermore, a lower prevalence of poor hypertension treatment has been reported in the lower socioeconomic groups[32]. We observed larger socioeconomic disparities in BP levels in northern populations, which may reflect larger socioeconomic disparities in awareness, detection and treatment in the south. Overall, reducing socioeconomic disparities in BP and hypertension, and improving overall hypertension management is likely to contribute to reduce socioeconomic differentials in stroke mortality across Europe.

BMI was a major contributor to socioeconomic differences in IHD mortality, reflecting the large socioeconomic differentials in BMI observed in our study. Larger overall levels of BMI were observed in southern countries, which might explain the relatively larger mean differences in BMI by educational level in these populations. Nevertheless, socioeconomic differentials in BMI were consistent across Europe and appear to have widened during recent decades[40,41]. Individuals in the lower socioeconomic groups might be more vulnerable to weight gain and less able to maintain weight, which has resulted in increasing socioeconomic differentials in BMI[42]. These disparities are likely to reflect less healthy nutritional habits in the lower socioeconomic groups[38], which are not compensated by their higher levels of physical activity. On the other hand, obesity did not contribute to socioeconomic differentials in stroke mortality, which might be explained by its weak association with both ischaemic and haemorrhagic stroke in our study.

Despite their important contribution, biological, behavioural and nutritional risk factors in our study explained less than half of socioeconomic differentials in cardiovascular mortality. Although measurement error in these variables might explain why they do not explain more of these differentials, these results nevertheless raise questions about other risk factors that may explain the social gradient in stroke and IHD mortality. Psychosocial risk factors have been suggested as potential pathways through which socioeconomic status increases cardiovascular risk. Individuals with a low socioeconomic status have higher depression and less social networks, which largely contribute to socioeconomic differentials in stroke incidence among the elderly[43]. Similarly, after taking into account the impact of conventional risk factors, adjustment for low control at work accounted for the unexplained social gradient in coronary heart disease among British men and women[44]. These findings highlight the role of psychosocial factors in the explanation of socioeconomic disparities in cardiovascular mortality. However, further research is necessary to elucidate the role of these factors in different European countries.

Implications

Large socioeconomic differences in stroke and IHD mortality remain in Europe, which reflect the larger share of health and social disadvantage in the low socioeconomic groups. A strategy to reduce socioeconomic differences in cardiovascular disease might require interventions to reduce smoking and to improve hypertension detection and management in the low socioeconomic groups. Furthermore, increasing fruit and vegetable consumption in the low socioeconomic groups can moderately contribute to reduce stroke and IHD socioeconomic differentials. However, different strategies are required to tackle these disparities in different regions. Whereas tackling smoking differentials is an essential target in northern countries, reducing differences in blood pressure and hypertension are more likely to have an impact in southern populations. Nevertheless, reducing differences in these risk factors might not be enough, and focus on other determinants such as depression and control at work might be required[43,44]. In conclusion, a combination of strategies to reduce the prevalence of smoking in northern Europe and to improve BP control in the lower socioeconomic groups across Europe can partly contribute to reduce socioeconomic differences in stroke and IHD mortality.

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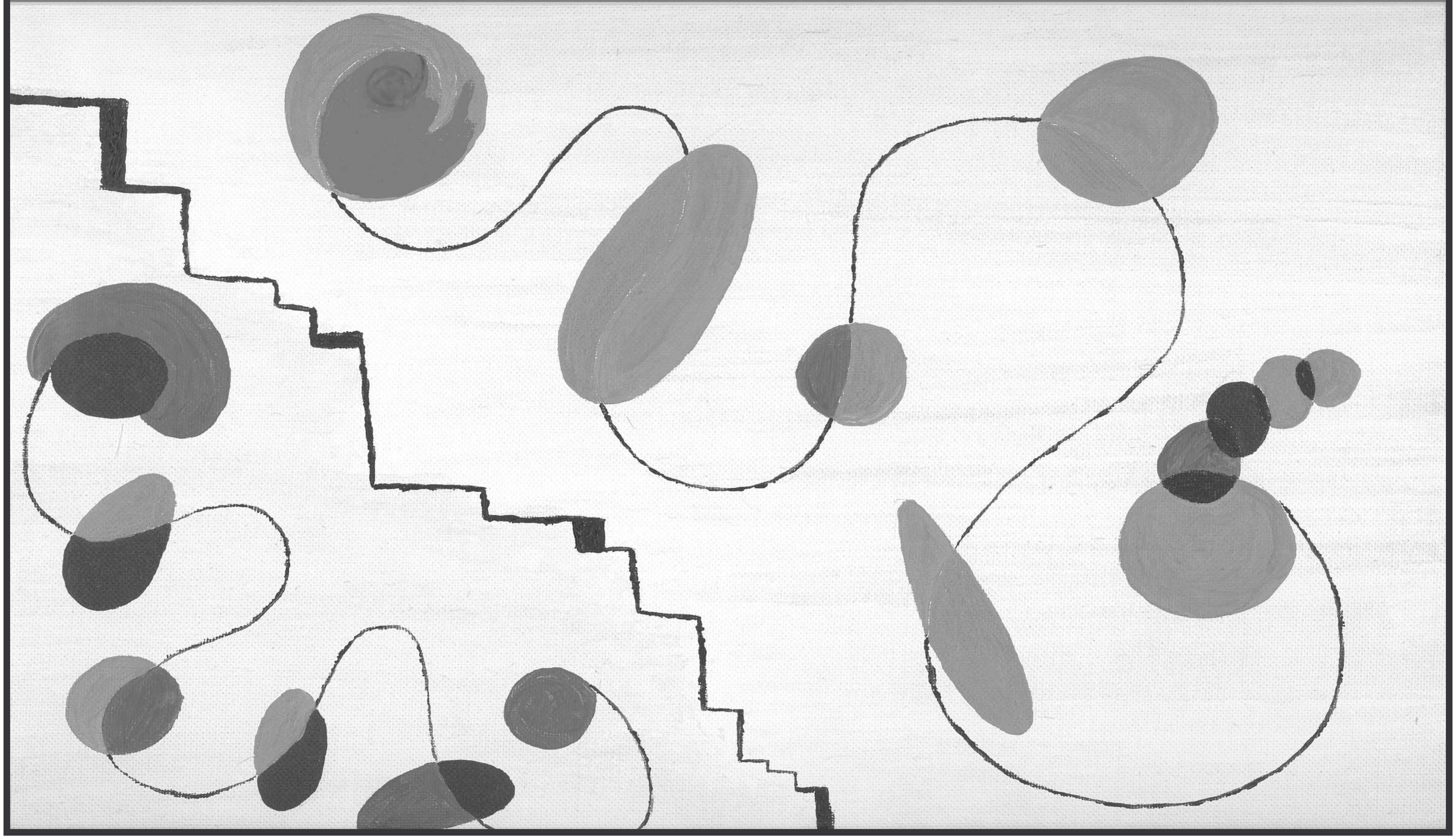
Part IV The role of preventive care



Chapter 9

Disparities in stroke preventive care in general practice did not explain socioeconomic disparities in stroke in the Netherlands

Avendano M, Boshuizen H, Schellevis F, Mackenbach JP, Lenthe FV, Van den Bos GAM. Disparities in stroke preventive care in general practice did not explain socioeconomic disparities in stroke in the Netherlands. *J Clin Epidemiol*. *In press.*
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Abstract

Objective: To assess socioeconomic disparities in stroke incidence and in the quality of preventive care for stroke in the Netherlands.

Study design and settings: 190,664 patients registered in 96 general practices were followed up for 12 months. Data were collected on diagnoses, referrals, prescriptions and diagnostic procedures. Hazard ratios (HR) were calculated to assess the association between educational level and stroke incidence. Multilevel logistic regression was used to assess socioeconomic disparities in the quality of preventive care for stroke precursors.

Results: Lower educational level was associated with higher incidence of stroke in men (HR=1.36, 95%CI 1.06-1.74) but not in women. Among both men and women, there were socioeconomic disparities in the prevalence of hypertension, hypercholesterolemia, diabetes, angina pectoris, heart failure and peripheral artery disease. Lower educated hypercholesterolemia patients under medication were less likely to be prescribed statins (OR=0.62, 95%CI 0.42-0.91). However, for other precursors of stroke, there were no major disparities in the quality of preventive care.

Conclusion: There are socioeconomic disparities in stroke incidence among men, but not among women. Disparities in factors such as hypertension and diabetes are likely to contribute to these disparities. However, GPs provide care of a similar quality to patients from different socioeconomic groups.

9.1 Introduction

Stroke is the second leading cause of death and one of the major causes of disability worldwide, accounting for 4.3 million deaths every year[1]. A lower socioeconomic status is associated with a higher risk of stroke[2-9], so that more than one third of strokes can be attributed to a lower socioeconomic status[5]. Moreover, stroke contributes considerably to socioeconomic differences in life expectancy[8]. Previous research reported that socioeconomic deprivation is associated with a poor management of cardiovascular risk factors such as hypertension[10]. This underlines a large potential for stroke prevention by improving primary care interventions in the lower socioeconomic groups.

European countries have a long tradition of universal health care coverage, so that access to care is guaranteed to the whole population. In the Netherlands, general practice care is exceptionally well organized. Almost all individuals in the Dutch population are registered with a general practice, and care is accessible to all through health insurance schemes. Thus, in principle, the quality of care should be equal for all individuals. However, socioeconomic disparities in health care utilization persist[11]. As in most European countries, individuals with a lower socioeconomic status use more general practice care, even after adjustment for health need[11,12]. Conversely, the higher socioeconomic groups use more specialist care[11,12]. It is not known whether there might also be socioeconomic differences in the quality of care. Overall, the mechanisms through which health care can contribute to health disparities remain largely unexplored[13].

Since 1989, the Dutch College of general practitioners has introduced guidelines for the management of specific diagnoses[14]. This includes guidelines to improve the quality of GPs' care for stroke precursors such as hypertension and diabetes mellitus, covering specific aspects of care such as medical prescriptions and diagnostic procedures. Guidelines can refer to general aspects for the prevention of stroke such as hypertension treatment, or specific aspects for the prevention of ischaemic or haemorrhagic stroke only, e.g., aspirin prescription for ischaemic stroke prevention. Few studies have systematically assessed socioeconomic disparities in preventive care provided by GPs. Research on these disparities may reveal specific aspects of care that would help prevent socioeconomic disparities in stroke occurrence.

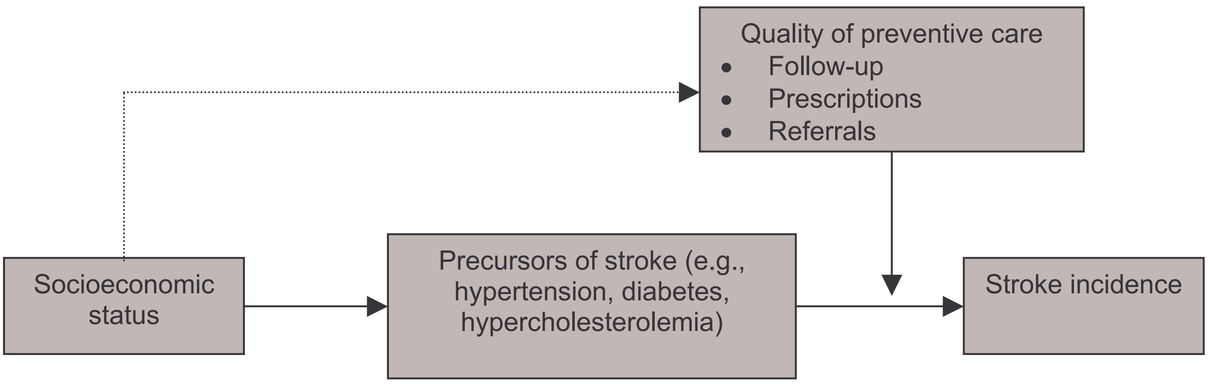

Figure 9.1. Conceptual model of the contribution of precursors of stroke and preventive care to socioeconomic differences in stroke incidence

This study assesses socioeconomic disparities in stroke incidence, and how these relate to socioeconomic disparities in the quality of preventive care for precursors of stroke (Figure 9.1). Previous studies have only focused on disparities in hospital care or have faced some methodological limitations, looking mostly at health care utilization[10,11,15]. We applied an innovative approach by developing quality indicators based on evidenced based guidelines for stroke prevention at general practice. Building upon previous research, we assessed deviations from general practice guidelines relevant for stroke prevention, and incorporated adjustment for patients' health need. We applied multilevel analyses techniques, thus taking into account general practice variations in the analyses of socioeconomic disparities in care quality. We used data from second Dutch national survey, a unique study comprising data on more than 190,000 patients registered with 96 general practices in the Netherlands and followed for a period of one year. This is the first study to use quality indicators to assess socioeconomic differences in care in general practice and to focus on preventive interventions.

9.2 Methods

Data and subjects

Within the framework of the second Dutch national survey of general practice, 104 general practices participated in a study of general practice care carried out between May 2000 and April 2002. Details of the study have been described elsewhere[16]. In order to obtain a representative sample, practices were selected on the basis of three classification criteria: region (north, central and south), level of urbanisation (five categories) and practice type (individual vs. group). GPs from these practices (n=195) were representative of the Dutch GP population in terms of age, gender, residence and level of urbanization. Similarly, patients were a representative sample of the Dutch population in terms of age, gender and type of health insurance.

In order to obtain information on demographic variables and socioeconomic status, a baseline survey was carried out among all registered patients. A response rate of 76.5% was obtained. Data on patients' contacts with the GP were collected during a follow-up period of 12 months. For each contact, GPs recorded information on diagnoses, referrals and drug prescriptions. Information was recorded electronically at the practice and subsequently integrated into a central information system. Contacts for the same diagnosis were grouped into disease episodes. Additionally, data on specific diagnostic procedures performed by the GP were recorded for a period of 6 weeks, including blood pressure and weight measurements.

Educational level was used as an indicator of socioeconomic status, because it can be applied in a comparable way for both men and women. Furthermore, as opposed to other indicators such as occupational class, educational level can be applied to both the economically active and inactive population[8,17]. Previous studies have also shown that educational level is consistently related to stroke[4,8]. Individuals were asked about the highest level of education they had completed. Reported levels were recoded into three categories: Low (no schooling or solely elementary education), middle (secondary school) and high (post-secondary education).

In order to assess the quality of preventive care, eight quality indicators were constructed on the basis of national guidelines provided by the Dutch College of general practitioners[14] (Table 9.1). Indicators 1 to 4 were developed by the Centre for Quality of Care Research (WOK) through an iterative consensus procedure, and were defined in terms of expected health outcomes and the prevention of unnecessary interventions[18,19]. Indicators 5 to 8 were constructed by the investigators on the basis of practice guidelines for blood pressure measurements, specialist referrals and diabetes control[14,20]. Each indicator comprised a numerator and a denominator[18]. Numerators denoted the number of patients that received a specific type of care according to the guidelines. Denominators denoted the target population that, according to the guidelines, should in principle receive a specific type of care. This innovative approach allows the assessment of quality of care by measuring adherence to guidelines and specifying the target group. Most quality of care indicators referred to guidelines for the prevention of all stroke subtypes (ischaemic stroke, intracerebral and subarachnoid haemorrhage). The only exceptions were indicators 2 and 3 regarding the prescription of statins and aspirin, which are directly relevant for the prevention of ischemic stroke only[20].

Table 9.1. Indicators of the quality of care for stroke prevention constructed on the basis of guidelines of the Dutch College of general practitioners

Quality of care indicators		
Indicator (numerator)		Target population (denominator)
1.	Prescription for diuretics (as first-step of second-line medication treatment)	Patients with uncomplicated hypertension under medication (diuretics, beta-blockers, ACE-inhibitors or calcium antagonists)
2.	Prescription for statins (as second-line medication treatment)	Patients with hypercholesterolemia under lipid reducing medication (relevant for preventing ischaemic stroke only)
3.	Prescription for aspirin	Patients with a diagnosis of transient ischemic attack, peripheral artery disease or angina pectoris (relevant for preventing ischaemic stroke only)
4.	Combined prescription for both diuretics and ACE-inhibitors	Heart failure patients with a prescription for ACE-inhibitors
5.	Referral to the specialist (neurologist or cardiologist)	Transient ischaemic attack, angina pectoris, peripheral artery disease and heart failure patients
6.	Weight measurement (diabetes)	Diabetes mellitus patients that visited the GP during a 6-week study period
7.	Blood pressure measurement (diabetes)	Diabetes mellitus patients that visited the GP during a 6-week study period
8.	Blood pressure measurement	Patients aged 60 years and over that visited the GP during a 6-week study period

Diagnoses by the GP were coded according to the ICPC (International Classification of Primary Care) coding system[21], using the following classification: Stroke (K90), transient ischemic attack (k89), hypertension (K86, K87), diabetes mellitus (T90), angina pectoris (K74), heart failure (K77), peripheral artery disease (K92) and hypercholesterolemia (T93). Medication prescriptions by the GP were coded according to the ATC (Anatomic, Therapeutic and Chemical) classification of pharmaceutical drugs[22], using the following classification: Diuretics (C03), beta-blockers (C02, C07), ACE inhibitors (C09), calcium antagonists (C08) and cholesterol-lowering medication agents (C10).

Methods of analysis

Eight practices were excluded from the analyses due to problems in data collection and quality. Thus, the base population at risk consisted of 385,461 individuals registered in 96 practices. For the present study, we included only individuals aged 25 years and over, and for whom data on educational level were available, resulting in a final sample of 190,665 subjects.

In order to assess the effect of educational level on stroke, age-standardised stroke incidence rates were calculated separately for men and women, using the Dutch population of 2000 as the standard[23]. Hazard ratios were calculated using the Cox Proportional Hazard model, incorporating age as the time scale[24]. No information was available on stroke occurrence before the start of the study. Therefore, we included both first and recurrent stroke events that occurred during the study period, applying a Cox proportional hazard model for multiple events and adjusting for the dependency of outcomes[25].

Significant practice variation existed in diagnoses and health care use patterns. Thus, multilevel analysis techniques were applied to assess the effect of educational level on the prevalence of stroke precursors and preventive care. Firstly, we calculated age-adjusted prevalence rates and odds ratios of stroke precursors according to educational level, using multilevel logistic regression. Secondly, compliance of GPs with practice guidelines was calculated for each quality indicator, adjusting for age. Thirdly, in order to further adjust for health need, multilevel logistic regression was applied, adjusting for age, self-perceived health, cardiovascular symptoms, specific cardiovascular diseases, diabetes and other comorbidities. Because patients may have received certain types of care from the specialist, analyses were also adjusted for specialist referrals. Given the smaller size of patient sub-samples, odds ratios compared the low educational level group with the middle/high educational level group. These two upper levels were combined in order to obtain more precise estimates.

Survival analyses were performed using the statistical package SAS version 8.2. Multilevel analyses were conducted using the statistical package MLWIN version 1.02.

9.3 Results

The mean age of registered patients at general practice was 49.5 for men and 50.7 for women. A total of 472 individuals developed stroke over 187,220 person-years. The mean age at stroke diagnosis was 70.9 for men and 76.1 for women. Table 9.2 presents the number of strokes, person-years, incidence rates and hazard ratios of stroke according to educational level. Among men, the age-standardised stroke incidence rate steadily increased as educational level decreased, yielding a clear socioeconomic gradient (p for trend < .05). The stroke incidence rate was higher among men with a low educational level than among men in the middle/high educational category (HR=1.36, 95% CI 1.06-1.74). Among women, however, the stroke incidence rate did not differ between educational level groups (HR= 1.05, 95% CI 0.79-1.38).

Table 9.2. Age-standardised stroke incidence rates and Hazard Ratios by educational level among men and women aged 25 years and over

SEX	Socioeconomic status	No. strokes	P-years	Incidence rate	Hazard ratio	95% CI
Men	Educational level					
	High	30	22434.6	218.7	1.00	
	Middle	113	52215.7	267.6	1.22	0.82-1.81
	Low	110	14429.1	354.0	1.58	1.07-2.36*
	Middle/high vs. low				1.36	1.06-1.74
Women	Educational level					
	High	11	17443.2	197.1	1.00	
	Middle	82	58238.0	180.3	1.08	0.57-2.04
	Low	126	22459.7	189.1	1.12	0.59-2.14
	Middle/high vs. low				1.05	0.79-1.38

*p-value for trend effect of educational level <0.05

Table 9.3 shows the age-adjusted prevalence (per 1,000) of precursors of stroke. Men and women with a low educational level had a less favourable risk profile. A low educational level was associated with a higher prevalence of hypertension, hypercholesterolemia, diabetes mellitus, angina pectoris, heart failure and peripheral artery disease. There was a marked educational level gradient in the prevalence of these factors for both men and women (p for trend < 0.05). A low educational level was associated with a higher prevalence of TIA (transient ischaemic attack) in women, but not in men. Odds ratios in Figures 2 and 3 show that men and women with a low educational level consistently had a higher prevalence of precursors of stroke than those with a middle or high educational level.

Table 9.3. Age-adjusted prevalence (per 1,000) of precursors of stroke according to educational level among men and women aged 25 years and over

Stroke precursor	**Men**				**Women**			
	Educational level				Educational level			
	High	Middle	Low	Total	High	Middle	Low	Total
Hypertension	77.3	84.5	87.6*	82.1	97.6	114.6	127.2*	115.8
Hypercholesterolemia	28.0	33.3	34.8*	32.3	19.0	25.5	28.2*	25.0
TIA†	5.5	6.0	5.2	5.6	3.4	5.8	5.5	5.6
Diabetes Mellitus	27.7	36.1	53.8*	37.9	19.9	34.0	59.4*	40.9
Angina pectoris	13.6	18.8	23.5*	19.0	11.1	13.5	17.9*	15.3
Heart failure	7.2	9.8	13.2*	10.7	7.2	9.5	13.6*	11.6
PAD†	3.6	6.0	7.6*	5.9	1.8	3.3	4.4*	3.4

*p-value for trend effect of educational level <0.05

†TIA indicates transient inschaemic attack; PAD indicates peripheral artery disease

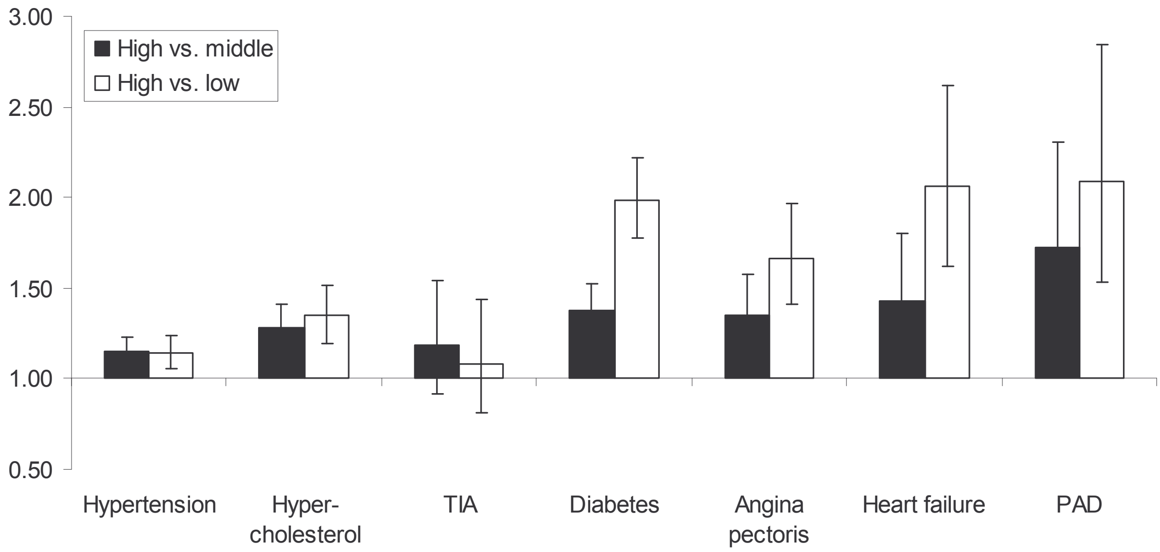

Figure 9.2. Age-adjusted odds ratios of precursors of stroke according to educational level for men aged 25 years and above

PAD indicates Peripheral artery disease; TIA indicates transient ischaemic attack

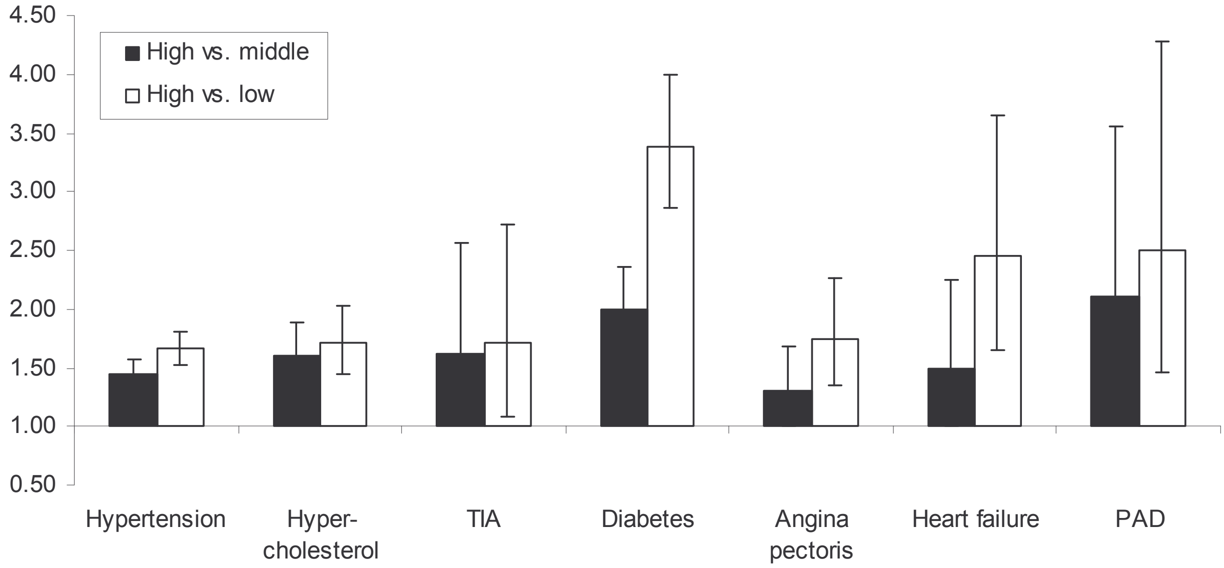

Figure 9.3. Age-adjusted odds ratios of precursors of stroke according to educational level for women aged 25 years and above

PAD indicates Peripheral artery disease; TIA indicates transient ischaemic attack

Table 9.4 shows the profile of health care for precursors of stroke, on the basis of eight quality of care indicators. GPs overall compliance with some guidelines was low: only about one third of men and half of women with uncomplicated hypertension received diuretics as first-step of second line medication treatment (indicator 1). Approximately half of patients with a diagnosis of TIA, peripheral artery disease or angina pectoris had received an aspirin prescription (indicator 3). Similarly, only about two thirds of heart failure patients had a combined prescription for ACE-inhibitors and diuretics (indicator 4). Nevertheless, the quality of care for patients with a low educational level was similar or better than the quality care for patients with a higher educational level. A prescription for diuretics as first-step of second line medication treatment for uncomplicated hypertension (indicator 1) was somewhat more common in lower educated patients for both men (OR= 1.22, 95%CI 1.05-1.42) and women (OR=1.10, 95% CI 1.00-1.22). The patterns of prescription for aspirin (indicator 3) and ACE-inhibitors and diuretics combined (indicator 4) did not differ according to educational level. Similarly, cardiovascular patients with a low educational level were referred to the specialist as often as patients from the higher educational categories (indicator 5). Among diabetes patients, blood pressure and weight were measured as frequently in all socioeconomic groups (indicators 6 and 7). Individuals aged 60 years and over with a low educational level had their blood pressure measured as frequently as patients with a higher educational level (indicator 8). Thus, overall, the quality of care for stroke precursors was of a similar quality for patients with different socioeconomic status. This pattern was observed even after adjusting for health need (Table 9.4).

Table 9.4. Age-standardised percentages and adjusted odds ratios* of GPs' compliance with guidelines for stroke prevention among men and women aged 25 years and above

Indicator	Men			Women		
		Educational level			Educational level	
	N	Middle/high	Low	N	Middle/high	low
1. Diuretics for uncomplicated hypertension patients under medication	5,274	33.1% 1.00	37.3% 1.22 (1.05-1.42)	9,279	46.1% 1.00	49.3% 1.10 (1.00-1.22)
2. Statins for hypercholesterolemia patients under medication	2,869	97.5% 1.00	95.4% 0.64 (0.37-1.11)	2,361	97.9% 1.00	95.3% 0.60 (.34-1.05)
3. Aspirin prescription for TIA†, PAD‡ and angina pectoris patients	3,207	55.5% 1.00	56.0% 0.97 (0.82-1.15)	2,885	51.8% 1.00	51.6% 1.01 (0.85-1.21)
4. ACE-inhibitors and diuretics prescription combined for heart failure patients	570	64.8% 1.00	62.7% .97 (0.65-1.46)	661	66.5% 1.00	60.1% 0.74 (0.49-1.10)
5. Specialist referral for TIA†, PAD‡, angina pectoris and heart failure patients	4,186	10.6% 1.00	12.0% 1.01 (.82-1.24)	4,061	8.7% 1.00	10.1% 1.13 (0.91-1.41)
6. Weight measurement for diabetes mellitus patients	934	28.7% 1.00	26.0% .94 (.64-1.38)	1,133	28.2% 1.00	22.3% 0.83 (0.59-1.17)
7. BP measurement for diabetes mellitus patients	934	41.5% 1.00	36.4% .87 (.62-1.22)	1,133	39.5% 1.00	39.3% 1.05 (0.78-1.42)
8. BP measurement for patients 60 years and over	3,886	17.7% 1.00	18.5% 1.03 (0.85-1.25)	5,366	17.1% 1.00	18.4% 1.06 (0.89-1.25)

*Odds ratios are adjusted for differences across educational level groups in health need, as measured by age, self-perceived health, number of cardiovascular symptoms, specific cardiovascular diseases, diabetes, other comorbidities and specialist referrals
†TIA indicates transient ischaemic attack
‡PAD indicates peripheral artery disease

Most patients with a hypercholesterolemia diagnosis who were under medication (and therefore in the second-line treatment phase) received a prescription for statins as recommended by the guidelines (Table 9.4). However, patients with a lower educational level were less likely to receive a prescription for statins. Although we did not have enough power to detect this difference separately for men and women, pooled analyses revealed significant educational level disparities in the prescription for statins for men and women together (OR= .62, 95% CI .42 - .91). This suggests that there were some disparities in the second-line treatment for hypercholesterolemia as recommended by practice guidelines.

9.4 Discussion

Previous research suggests that there are socioeconomic disparities in stroke in most European countries[4,5,8]. In the Netherlands, we found evidence of socioeconomic disparities in stroke incidence in men, but not in women. Among men, socioeconomic disparities in stroke are likely to be due to a higher prevalence of stroke precursors in the lower socioeconomic groups. We observed socioeconomic disparities in the prevalence of hypertension, hypercholesterolemia, diabetes mellitus, angina pectoris, heart failure and peripheral artery disease. GPs were less likely to comply with guidelines on statin prescriptions for second-line treatment of hypercholesterolemia in patients with a lower socioeconomic status, which can have implications for the prevention of ischaemic stroke.

However, the quality of care for other precursors of stroke was similar for all socioeconomic groups, or somewhat better for the lower socioeconomic classes. Overall, results emphasize the contribution of socioeconomic disparities in the prevalence of precursors of stroke to disparities in stroke incidence, whereas disparities in the quality of care might play only a minor role.

Evaluation of data and study limitations

We used the most recent data on general practice care in the Netherlands, which comprised a large sample of patients. Nevertheless, some methodological issues should be considered in this study. Stroke or other diseases may have been wrongly diagnosed by the GP. This would have biased our results only if misclassification had occurred differently across educational levels. There is no evidence to suggest that this occurred in our data. Therefore, any bias caused by this problem is likely to have been small. Furthermore, stroke occurrences in patients who went directly to hospital may not have been reported to the GP, which may have led to an underestimation of stroke incidence. However, in the Netherlands, the GP plays a gate-keeping role, so that hospital contacts are generally reported to the GP. Similarly, due the large scale and population registry character of our study, we were not able to determine to what extent the diagnosis of stroke was ascertained by sophisticated diagnostic techniques such as computer tomography or magnetic resonance imaging. However, a linkage of data from our study with data on cardiovascular diagnoses from the national hospital registration system in the Netherlands showed high correspondence[26]. Thus, it is unlikely that these problems influenced our results to a great extent.

Data on stroke subtypes were not available in our study. Thus, we used a broad category of stroke comprising both ischaemic and haemorrhagic events. We were therefore unable to assess the effect of socioeconomic status on different stroke categories. However, previous studies indicate that lower socioeconomic status is consistently associated with higher incidence of ischaemic[5], intracerebral[6] and subarachnoid haemorrhage[7], and associations for the three categories seem to be of similar magnitude[5-7]. Furthermore, our study was primarily focused on assessing disparities in the quality of care for precursors for stroke prevention at general practice. Thus, although it can provide further insight, it is unlikely that including data on stroke subtypes would substantially alter the main conclusions of our study.

Data on prescriptions, referrals and GP contacts were collected for a period of 12 months. However, information on blood pressure and weight measurements was available for a period of only 6 weeks. Since patients may have had these measurements at time points outside this period, estimates of their prevalence cannot be interpreted in absolute terms. Nevertheless, we used these estimates solely to assess disparities between socioeconomic groups, rather than overall compliance of GPs with guidelines on hypertension and weight measurements. Thus, odds ratios estimating disparities in these care factors are likely to be comparable to estimates based on a longer data collection period.

Although we obtained a high response rate in the baseline survey (76.5%), the exclusion of non-respondents may have biased our results to some extent. However, there is evidence that response bias has only a negligible effect on risk estimates of heath care utilization by background characteristics[27]. In order to further test the impact of non-response, we analysed differences in the quality of health care according to health insurance type, which was available for the total study population. In the Netherlands, health insurance type is a proxy for income, because individuals above an income threshold are required to have a private health insurance. Results for health insurance were identical to results for educational level: Men with public insurance (i.e., below the income threshold) had a higher incidence of stroke than men with private insurance (OR= 1.59, 95%CI 1.23-2.05). Similarly, among both men and women, there were large disparities in the prevalence of precursors of stroke, but not in the quality of preventive care. These results suggest that the effect of non-response is likely to be small, and further confirm our findings for educational level.

We assessed socioeconomic disparities in eight quality of care indicators. It is possible that there are disparities in other aspects of preventive care not included in this study. However, analyses were also conducted for other indicators regarding blood measurements, prescription of hypertension medication (other than diuretics), referrals of diabetes patients to an ophthalmologist, and ECG examinations among specific groups of patients (results not shown). Similarly, no major socioeconomic disparities were observed in the compliance of GPs to practice guidelines. Nevertheless, further research should assess whether the same pattern applies for other indicators of the quality of preventive care for precursors of stroke.

Comparison with previous studies

The results of this study add to a large body of research showing that a lower socioeconomic status is associated with a higher risk of stroke among men[2,4-9]. Previous studies have observed consistent socioeconomic disparities in stroke mortality in Europe[4,8], which are due partly to socioeconomic differences in stroke incidence[5-7,9]. In contrast with findings from previous studies[4,8,28], however, we observed no socioeconomic disparities in stroke incidence for women. This may reflect differences between men and women in the effect of educational level on cardiovascular risk factors. Previous studies have shown that socioeconomic disparities in several cardiovascular risk factors such as smoking and excessive alcohol consumption tend to be larger among men than women[29-31], which may have resulted in larger socioeconomic disparities in stroke for men.

Previous studies have also observed socioeconomic disparities in precursors of stroke such as hypertension[10,28,32], diabetes[33], heart failure[34] and hypercholesterolemia[35] . However, studies on socioeconomic differences in care for these conditions are controversial. On the one hand, socioeconomic disparities have been reported in some aspects of care for hypertension[10,32], diabetes[10,36] and heart failure[34] . In contrast, other studies have observed no socioeconomic disparities in care for these factors[37,38]. The results of our study support the view that the quality of cardiovascular preventive care is relatively equal for all socioeconomic classes. This is consistent with previous research suggesting that health care plays only a limited role in the explanation of socioeconomic differences in health, which may be due to the equal access to health care services enjoyed by the Dutch population[39]. However, this is unlikely to apply to other countries such as the United States, where access to medical care differs between socioeconomic groups[40].

The prescription rate for statins has recently increased among the lower socioeconomic groups[41]. Although patients with a lower socioeconomic status were less likely to be treated with statins during the mid-1990s, these disparities have recently disappeared[41]. However, no research on GPs' compliance with guidelines on statin prescriptions had previously been conducted. This is the first study to report that lower socioeconomic status patients with hypercholesterolemia initiated on cholesterol-lowering medication therapy are less likely to receive statins as choice of medication. This suggests that there may be still socioeconomic disparities in GPs' compliance with guidelines for the prescription for statins for hypercholesterolemia. Although the mechanisms remain unclear, statins have been shown to significantly reduce the risk of ischaemic stroke[42]. Thus, these disparities may partly contribute to existing socioeconomic differences in ischaemic events[5].

Patients with a low socioeconomic status receive more prescriptions for medication than patients with a high socioeconomic position[43]. Similarly, we found that diuretics were somewhat more often prescribed to hypertension patients with a lower socioeconomic position. However, we did not observe disparities in GPs' compliance with guidelines on the prescription for other medications such as aspirin and ACE-inhibitors. Overall, this suggests that GPs' compliance with guidelines for medication prescriptions is largely similar for patients from different socioeconomic groups.

Explanation of results

In this study, we found no evidence of major disparities in the quality of care provided by GPs to patients from different socioeconomic groups. These findings raise questions regarding factors of the Dutch primary care system that may have helped to generate equal care for all patients. Firstly, in the Netherlands, health care is available to all through health insurance schemes. In our study, the majority of patients with a low educational level were publicly insured, whereby health care services were free of charge. This may have contributed to eliminating any financial barriers to access general practice care among the lower socioeconomic groups[11,12]. Secondly, quality indicators were constructed on the basis of national guidelines for care in general practice. These are evidence-based guidelines aimed not only at improving the quality of care but also at preventing unnecessary interventions. After adjusting for health need, we observed no differences in the quality of care between patients from different socioeconomic groups. Guidelines may have contributed to the provision of equal and standardised diagnostics and care for patients on the basis of health need, thereby leaving limited room for variability in care according to factors such as socioeconomic status. Conversely, there might be disparities in aspects of care for which evidence is scarce and therefore no guidelines have been developed. Thus, general practice guidelines may not only contribute to improving the quality of care, but may also promote equal and standardised preventive care across socioeconomic groups.

We found that GPs' compliance with guidelines on the prescription for diuretics as first-line treatment for uncomplicated hypertension[14,18] was somewhat higher for patients with a lower socioeconomic status. This suggests that, for some aspects, the quality of care my indeed be better for these patients. These findings are interesting in the light of substantial research showing that lower socioeconomic status is associated with more general practice care consultations and prescriptions[11,12,44]. More frequent contacts with lower socioeconomic groups may provide GPs with more opportunities to comply with preventive guidelines in these patients. For instance, GPs discuss preventive care topics more often with patients from a lower socioeconomic background[45]. Thus, individuals with low socioeconomic status do not only use more general practice care[11,12,44] but might also receive care of a better quality than their higher socioeconomic status counterparts.

Despite this positive scenario, socioeconomic disparities in stroke incidence persist among men. This suggests that general practice care may be merely part of a broader picture, and raises questions about stroke risk factors and precursors that may play a more prominent role in the origin of stroke disparities. Hypertension is a major risk factor for stroke, accounting for up to 60% of ischaemic strokes[20]. The disparities observed in the prevalence of hypertension are likely to contribute to socioeconomic differences in stroke incidence in men[2]. Factors such as hypercholesterolemia and diabetes are also likely to contribute to socioeconomic differences in stroke incidence[2,20]. This may be exacerbated by the fact that men with a low socioeconomic status have a higher prevalence of smoking[29], excessive alcohol consumption[46], physical inactivity[47] and overweight[30]. Research indicates that these factors all together explain about half of socioeconomic differences in stroke incidence[2]. On the other hand, despite observing disparities in stroke precursors, we did not find evidence of socioeconomic disparities in stroke incidence in women. The fact that equal care for stroke precursors was provided for women from different socioeconomic categories may have helped preventing the emergence of disparities in stroke in women.

GPs' compliance with guidelines for the prescription for statins as second-line treatment for hypercholesterolemia was lower in patients with a lower socioeconomic status. This may reflect socioeconomic differences in communication patterns between GPs and patients[12]. Higher educated patients may have a greater awareness of treatment options and therefore be more likely to request certain types of medication. This is consistent with studies showing that patients with a higher socioeconomic position are more likely to be treated with newer or brand-name medications[48]. Further research should explore the explanation of disparities in the management of hypercholesterolemia, and how these differences can contribute to socioeconomic variations in the incidence of ischaemic stroke.

Previous studies on health care disparities have mostly been focused on health care utilization[11-13,38,44]. We developed an innovative approach, whereby indicators of quality of care were constructed and adherence of general practitioners to guidelines assessed. Thus, our study represents one of the first attempts to systematically assess disparities in the quality of preventive care, taking into account patients' health need and general practice variations using multi-level analysis techniques. Nevertheless, the mechanisms through which health care can play a role in stroke disparities involve several mechanisms[13]: Firstly, socioeconomic status may determine the proportion of individuals receiving high quality care. Our findings suggest that this mechanism does not play a major role. On the other hand, socioeconomic status may modify the host response to therapeutic interventions, due to differences in factors such as patients' adherence to therapy and in susceptibility to the impact of interventions[13]. Thus, even in the absence of disparities in the quality of care by the GP, preventive interventions may still be less effective in the lower socioeconomic groups. Future research should assess whether health care may contribute to stroke disparities through this alternative mechanism[13].

Finally, despite the absence of disparities in the quality of care for most stroke precursors in our study, there may still be socioeconomic differences in specialist care relevant for stroke prevention. Although patients with a low socioeconomic status use more general practice care, this is offset by an excess recourse of patients from the high socioeconomic categories to specialist care[11,12]. Furthermore, there are socioeconomic differences in treatment and survival after stroke even in countries with universal health care systems[5,9], which may contribute to socioeconomic disparities in stroke mortality in Europe[4,8]. Thus, disparities in the quality of care for stroke may exist at more specialised levels of the health care system.

Implications

Universal access to general practice care and the implementation of general practice guidelines are likely to have promoted the provision of equal and standardised care for stroke precursors across socioeconomic groups. However, this has not been sufficient to eliminate socioeconomic disparities in stroke occurrence. Therefore, reducing the prevalence of stroke precursors such as hypertension, hypercholesterolemia and diabetes in the lower socioeconomic groups is still necessary. Interventions focused on the primary prevention of factors such as an unhealthy diet, smoking and obesity may play a major role in reducing stroke disparities. Furthermore, improvements in GPs' compliance with guidelines for the prescription for statins as second-line treatment for hypercholesterolemia may contribute to reduce disparities in ischaemic stroke incidence. Overall, reducing disparities in the primary occurrence of stroke precursors may be more important than reducing disparities in subsequent preventive care. General practitioners may thus play a key role in reducing disparities in stroke through primary prevention of risk factors for stroke.

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Chapter 10

Socioeconomic disparities in the use of statins in general practice

Avendano M, Van Dijk L, Boshuizen H, Van den Bos GAM, Mackenbach JP, Lenthe FV, Westert GP. Socioeocnomic disparities in the use of statins in general practice. *Submitted 2006.*

Abstract

Objective and background: No consistent disparities in statin use have been observed in secondary prevention. This study assesses social inequity in statin prescription for primary and secondary prevention in general practice for various patient sub-groups.

Methods and setting: 263,053 patients aged 25 years and over registered in 96 practices were followed up for twelve months. Data were collected on demographics, prescriptions, diagnoses and specialist referrals. Multilevel logistic regression was used to assess the association between educational level and statin prescriptions in patients free of CVD (cardiovascular disease) (primary prevention) and with CVD (secondary prevention), adjusting for health-need indicators.

Results: Overall, 5.2% of patients were prescribed with statins. For primary prevention, statins were more often prescribed in the lower socioeconomic groups in men (OR=1.39, 95%CI 1.25, 1.54) and women (OR=1.91, 95%CI 1.63, 2.24). However, this difference was largely attenuated after adjusting for health-need. Although most patients under lowering-cholesterol medication were prescribed with statins, patients with lower socioeconomic status were less likely to be receiving statins for cholesterol treatment after a diagnosis of hypercholesterolemia (OR=0.61, 95% 0.39, 0.95) or hypertension (OR=0.48, 95%CI 0.29, 0.80). There were no disparities in the prescription for statins among patients with Ischaemic heart disease. In contrast, there were large disparities in the prescription for statins in men diagnosed with a cerebrovascular accident (CVA) (OR=0.48 95% CI 0.26, 0.88). Furthermore, there was substantial gender inequity in the prescription for statins for both primary (OR=0.61 95%CI 0.58, 0.63) and secondary prevention (OR=0.67 95%CI 0.59, 0.77).

Conclusion: Despite overall improvements, disparities remain in the prescription for statins as first choice of cholesterol treatment, and for secondary prevention among patients with cerebrovascular accident. Strategies to build up consensus and reassure physicians through clear-cut recommendations might contribute to reduce disparities in the prescription for statins in patients with CVA.

10.1 Introduction

During the last decade, several clinical trials have demonstrated the effectiveness of statins in the prevention of cardiovascular disease (CVD). Statins can reduce the risk of coronary events, both in the context of primary[1,2] and secondary[3-5] prevention. Furthermore, statin treatment can reduce the risk of stroke by about 17%-21%[6-10], and by as much as 27% among hypertensive patients[11]. Despite this evidence, the rate of statin prescription in the population remains well below recommended levels[12-14] and varies considerably between general practices[15,16]. There is considerable potential for cardiovascular prevention by increasing access to statin treatment in specific groups of the population.

Most studies have found no consistent association between socioeconomic status and statin prescriptions in Europe[12,17,18]. Although disparities were observed in the mid-1990s in some countries[19-21], overall increases in the prescription of statins resulted in no disparities during recent years[17,19-22]. However, most studies have been conducted in the UK using ecological measures of social deprivation, without adjusting for differences in healthcare need[12,17,18]. Furthermore, research has only being conducted among coronary heart disease patients, for which guidelines have been explicitly developed. Statins can also prevent major vascular events in patients with prior stroke or transient ischaemic attack (TIA)[6,23]. However, explicit guidelines for stroke and TIA patients have not yet been developed, despite major sources endorsing the potential benefit of statins in these patients[9,24-27]. Less clear-cut recommendations for clinicians might lead to higher variation in the pattern of statin prescriptions to these patients.

We assessed the impact of socioeconomic status on the prescription for statins in primary and secondary prevention among various general practice patient groups. This is the first study to use individual measures of socioeconomic status adjusting for healthcare need in patients with several diagnoses, including stroke and TIA. Furthermore, we assessed GP's (general practitioners) adherence to national guidelines regarding the prescription for statins as primary choice for the second-line treatment of hypercholesterolemia[28]. This study provides the first estimates of the quality of care in the prescription for statins distinguishing primary and secondary prevention.

10.2 Methods

Subjects and data collection

In the framework of the second Dutch national survey of general practice, 104 general practices participated in a study of general practice carried out between May 2000 and April 2002. Details of the study have been described elsewhere[29]. In order to obtain a representative sample, practices were selected on the basis of three classification criteria: region (north, central and south), level of urbanisation (five categories) and practice type (individual vs. group). GPs from these practices (n=195) were representative of the Dutch GP population in terms of age, gender, residence and level of urbanization. Similarly, patients were a representative sample of the Dutch population in terms of age, gender and type of health insurance.

In order to obtain information on demographic variables and socioeconomic status, a baseline survey was carried out among all registered patients. A response rate of 76.5% was obtained. Data on patients' contacts with the GP were collected during a follow-up period of 12 months. For each contact, GPs recorded information on diagnoses, referrals and drug prescriptions. Information was recorded electronically at the practice and subsequently integrated into a central information system. Contacts for the same diagnosis were grouped into disease episodes.

Socioeconomic status

Educational level was used as an indicator of socioeconomic status, as it can be used in a comparable way for both men and women. As opposed to other indicators such as occupational class, educational level can be applied to both the economically active and inactive population[30,31]. Previous studies have also shown that educational level is consistently related to stroke and heart disease in Europe[30,32]. Individuals were asked about the highest level of education they had completed. Reported levels were recoded into three categories: Low (no schooling or solely elementary education), middle (secondary school) and high (post-secondary education).

Indicators of health need and diagnoses

Diagnoses by the GP were coded according to the ICPC (International Classification of Primary Care) coding system[33], using the following classification: Hypercholesterolemia (T93), hypertension (K86, K87), diabetes mellitus (T90), heart failure (K77), ischaemic heart disease (IHD) (K74, K75, K76), stroke (K90), Transient Ischaemic attack (TIA) (K89), angina pectoris (K74), acute myocardial infarction (K75), other chronic ischaemic heart diseases (K76), peripheral artery disease (K92) and atrial fibrillation (K78). Other (non-cardiovascular) chronic diseases incorporated in the models included: Migraine and headache, arthritis, severe neck and shoulder complains, asthma and major respiratory conditions, Sever elbow, wrist & hand complains, chronic eczema, incontinence, cancer, vertigo/dizziness, intestinal disorders, psoriasis, neurological diseases, cataracts and fractures.

Medication prescriptions by the GP were coded according to the ATC (Anatomic, Therapeutic and Chemical) classification of pharmaceutical drugs[34], using the following classification: cholesterol-lowering medication agents (C10) and statins (C10AA01, C10AA03, C10AA04 and C10AA05).

Methods of analysis

Eight practices were excluded from the analyses due to problems in data collection and quality. The base population at risk consisted of 385,461 individuals registered in 96 practices. We excluded individuals aged less than 25 years, and those with missing information on educational level. The final sample comprised 190,664 subjects.

There was significant practice variation in diagnoses and health care use patterns. Therefore, multilevel analysis techniques were applied to assess the effect of educational level on the prescription of statins. Two major groups of patients were distinguished: Firstly, analyses were conducted for participants free of CVD, distinguishing patients with hypercholesterolemia, hypertension and diabetes (primary prevention). Secondly, we conducted analyses for patients diagnosed with three major cardiovascular conditions: Heart failure, IHD, and cerebrovascular accident (stroke and TIA) (secondary prevention). For each patient group, we followed a step-wise approach: Firstly, the age-standardized prevalence of statin prescriptions was calculated. Secondly, multilevel regression was used in order to quantify the effect of socioeconomic status on the prescription of statins, adjusting for age (model 1). Thirdly, in order to adjust for health need, the following variables were incorporated (model 3): A diagnosis of hypercholesterolemia, diabetes and hypertension, number of circulatory diagnoses, chronic disease comorbidity (non-circulatory), and self-perceived health. Due to the fact that patients may receive certain types of care from the specialist, analyses were also adjusted for specialist referrals. Multilevel analyses were conducted using the statistical package MLWIN version 1.02.

10.3 Results

Characteristics for the entire sample and for patients prescribed with statins are summarised in Table 10.1. During the study period, 9,996 (5.2%) participants were prescribed with statins. The mean age was significantly higher among patients prescribed with statins (62.2) than among all eligible participants (50.1). 2.8% of all participants were diagnosed with hypercholesterolemia, whereas 43.7% of patients who received statins had a hypercholesterolemia diagnosis. This suggests that statins were also prescribed for other purposes than lowering cholesterol. Patients prescribed with statins were more likely to have a diagnosis of hypertension, diabetes, heart failure, TIA, stroke, periphery artery disease, atrial fibrillation and other chronic diseases. These patients were also more likely to report less-than-good self-perceived health and to have been referred to the specialist.

Table 10.1. Characteristics of participants in the Dutch National study of general practice aged 25 years and older

	Eligible sample		Sample with statin prescriptions	
	n/mean	% (std)	n/mean	% (std)
n	190,664	100.0%	9,996	100%
Mean age (std)	50.0	15.9%	62.2	10.6%
Women	99,945	52.4%	4,265	42.7%
Hypercholesterolemia	5,432	2.8%	4,367	43.7%
Hypertension	19,030	10.0%	3,072	30.7%
Diabetes	7,532	4.0%	1,826	18.3%
Heart failure	2,138	1.1%	331	3.3%
TIA	1,070	0.6%	207	2.1%
Stroke	1,283	0.7%	284	2.8%
Periphery artery disease	872	0.5%	249	2.5%
Ischaemic heart disease	4,945	2.6%	2,135	21.4%
Atrial fibrillation	1,489	0.8%	212	2.1%
Other cardiovascular	372	0.2%	56	0.6%
Any cardiovascular disease	8,512	4.5%	2,714	27.2%
Specialist referral	7,863	4.1%	1,231	12.3%
Less-than-good self-rated health	5,635	3.0%	570	5.7%
Other chronic diseases	67,823	35.6%	4,471	44.7%

TIA indicates transient ischaemic attack

Overall, statins were less often prescribed for women (3.5%) than for men (5.5%), and this disparity remained consistent even after adjusting for health-need indicators (OR=0.61 95%CI 0.58, 0.63). Furthermore, large practice variation in the prescription of statins was evident after adjusting for health-need (OR=1.81 95%CI 1.52, 2.15). Table 10.2 shows the prescription of statins according to educational level among participants free of cardiovascular disease (primary prevention). There was a general tendency for higher prescription of statins among the lower socioeconomic groups. This pattern was consistent for both men (OR=1.39 95%CI 1.25, 1.54) and women (OR=1.91, 95%CI 1.63, 2.24) free of CVD, and was particularly marked among hypertensive women (1.71, 95% 1.26, 2.33). However, these differences were largely explained by a worse health profile in the lower education groups, so that differences were largely attenuated after adjustment for health-need, and only remained significant for women (OR=1.40, 95% 1.20, 1.64). No disparities in the prescription for statins were observed among diabetes patients.

Table 10.2. Age standardised prevalence and odds ratio of statin prescriptions in primary prevention in general practice according to educational level in men and women 25 years and over free of cardiovascular disease (CVD)

Population	Men			Women		
	Educational level			Educational level		
	High	Middle	Low	High	Middle	Low
Population free CVD	3.3%	4.1%	4.5%	2.3%	3.2%	3.7%
Model 1*	1.00	1.24 (1.14, 1.36)	1.39 (1.25, 1.54)	1.00	1.64 (1.41, 1.91)	1.91 (1.63, 2.24)
Model 2†	1.00	1.10 (1.00, 1.21)	1.08 (0.97, 1.21)	1.00	1.38 (1.19, 1.61)	1.40 (1.20, 1.64)
Hypercholesterolemia	68.9%	73.1%	73.8%	72.3%	75.7%	78.1%
Model 1	1.00	1.27 (0.98, 1.65)	1.44 (1.01, 2.06)	1.00	1.16 (0.79, 1.70)	1.28 (0.83, 1.96)
Model 2	1.00	1.16 (0.89, 1.53)	1.25 (0.86, 1.80)	1.00	1.07 (0.72, 1.58)	1.10 (0.71, 1.70)
Hypertension	13.5%	15.8%	15.2%	8.6%	12.0%	12.4%
Model 1	1.00	1.22 (1.00, 1.48)	1.29 (1.02, 1.62)	1.00	1.63 (1.21, 2.21)	1.71 (1.26, 2.33)
Model 2	1.00	1.30 (1.02, 1.66)	1.22 (0.92, 1.62)	1.00	1.40 (0.99, 1.96)	1.32 (0.93, 1.87)
Diabetes	22.4%	23.9%	22.3%	19.6%	20.8%	17.7%
Model 1	1.00	1.10 (0.84, 1.44)	1.01 (0.75, 1.35)	1.00	1.21 (0.76, 1.93)	1.01 (0.63, 1.62)
Model 2	1.00	1.03 (0.75, 1.42)	0.92 (0.67, 1.36)	1.00	1.00 (0.59, 1.72)	0.87 (0.51, 1.50)

*Odds ratios in model 1 are adjusted for age

†Odds ratios in model 2 are adjusted for health need, as defined by age, hypercholesterolemia, hypertension, diabetes, non-circulatory chronic comorbidity, self-perceived health and specialist referrals

The pattern of statin prescription among patients diagnosed with major CVD conditions (secondary prevention) is summarized in Table 10.3. A disadvantage for women diagnosed with CVD was evident in the prescription for statins in secondary prevention (OR=0.67 95%CI 0.59, 0.77). Among men with ischaemic heart disease, there were no socioeconomic disparities in the prescription for statins. In contrast, men in the lowest education group diagnosed with stroke or TIA were half as likely to be prescribed with statins than their highest education counterparts (OR=0.48 95% CI 0.26, 0.88). A similar pattern was observed for men diagnosed with heart failure (OR=0.51, 0.26, 1.00). Among women diagnosed with CVD, there was a tendency for higher statin prescriptions in the lower education groups (OR=1.53, 1.01, 2.33). However, these differences were attenuated and no longer significant after adjustment for health-need.

Table 10.3. Age standardised prevalence and odds ratio of statin prescriptions in secondary prevention in general practice according to educational level in men and women aged 25 years and over with cardiovascular disease (CVD)

Population	Men			Women		
	Educational level			Educational level		
	High	Middle	Low	High	Middle	Low
IHD	47.8%	50.7%	46.6%	26.6%	39.1%	35.1%
Model 1*	1.00	1.11 (0.88-1.40)	1.01 (0.78-1.30)	1.00	1.80 (1.07-3.04)	1.67 (0.99-2.83)
Model 2†	1.00	1.12 (0.83-1.51)	0.94 (0.68-1.31)	1.00	1.71 (0.83-3.51)	1.44 (0.70-2.97)
Stroke/TIA	21.1%	27.7%	17.8%	19.1%	18.5%	17.1%
Model 1	1.00	1.24 (0.81-1.92)	0.77 (0.47-1.25)	1.00	1.66 (0.74-3.71)	1.59 (0.70-3.60)
Model 2	1.00	0.84 (0.49-1.43)	0.48 (0.26-0.88)	1.00	0.95 (0.33-2.75)	1.13 (0.39-3.27)
Heart failure	24.8%	20.8%	17.7%	11.0%	14.5%	9.8%
Model 1	1.00	0.64 (0.37-1.10)	0.70 (0.41-1.20)	1.00	0.88 (0.25-3.17)	1.19 (0.33-4.32)
Model 2	1.00	0.62 (0.32-1.20)	0.51 (0.26-1.00)	1.00	1.10 (0.11-11.20)	1.10 (0.11-11.14)
All CVD	38.3%	40.4%	36.1%	20.5%	27.0%	24.0%
Model 1	1.00	1.07 (0.88-1.30)	0.94 (0.76-1.16)	1.00	1.64 (1.08-2.49)	1.53 (1.01-2.33)
Model 2	1.00	1.02 (0.80-1.30)	0.84 (0.64-1.10)	1.00	1.34 (0.76-2.36)	1.23 (0.69-2.18)

*Odds ratios in model 1 are adjusted for age

†Odds ratios in model 2 are adjusted for health need, as defined by age, hypercholesterolemia, hypertension, diabetes, number of circulatory diagnoses, non-circulatory chronic comorbidity, self-perceived health and specialist referrals

Figure 10.1 shows odds ratios of statin prescription comparing low and middle/high education groups, among patients who were under lowering-cholesterol medication (second-line treatment phase). As results were similar for men and women, pooled estimates were calculated to increase precision. Most patients (96.6%) who were under cholesterol-lowering medication received a prescription for statins as recommended by guidelines. However, even after adjusting for health-need, a lower educational level was associated with less statin prescription rates among patients diagnosed with hypercholesterolemia (OR=0.61, 95% 0.39, 0.95) and hypertension (OR=0.48, 95%CI 0.29, 0.80). This suggests that patients with lower socioeconomic status might be less likely to receive statins as primary choice of medication treatment for primary prevention.

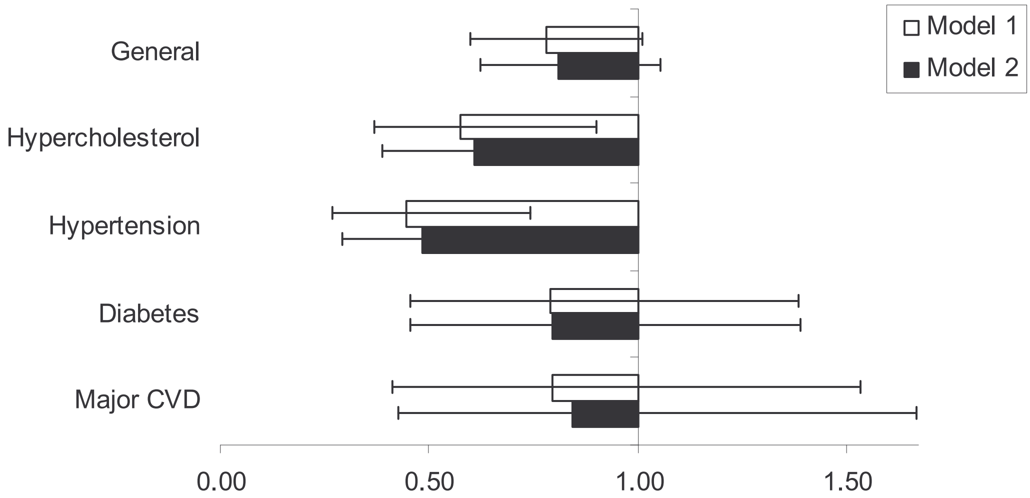

Figure 10.1. Second-line medication therapy for hypercholesterolemia in general practice: Odds ratios of statin prescription among patients under cholesterol-lowering medication between low and middle/high education groups for men and women aged 25 years and older.

CVD indicates cardiovascular disease

Middle/high education group is the reference category; Odds ratios in model 1 are adjusted for age; Odds ratios in model 2 are adjusted for health need, as defined by age, hypercholesterolemia, hypertension, diabetes, number of circulatory diagnoses, non-circulatory chronic comorbidity, self-perceived health and specialist referrals

10.4 Discussion

During the last decade, clinical trials have demonstrated the effectiveness of statins in both primary and secondary CVD prevention. Overall, we observed no major social disparities in the prescription of statins for primary prevention. However, although most patients under cholesterol-lowering medication received statins as recommended by guidelines, hypercholesterolemia and hypertensive patients in the lower socioeconomic groups were less likely to receive statins as primary choice of treatment for primary prevention. We observed no disparities in the prescription of statins for secondary prevention among IHD patients. In contrast, our study evidences large socioeconomic disparities in the prescription for statins in men diagnosed with CVA. Findings show disparities in the quality of care in statin treatment favouring the higher socioeconomic groups in patients with CVA, for which evidence of effectiveness has been less widespread among clinicians.

Strengths and limitations

Previous studies have mostly been conducted in the UK or have only focused on specific patients groups[17,19,20,22,35]. This is the first study to assess disparities explicitly distinguishing statin prescription for primary and secondary prevention in various patient groups, adjusting for health-need indicators. Nevertheless, some limitations should be considered. Our study comprised data on statin prescriptions at general practice only, whereas some patients may be receiving statins from the specialist. As patients in the higher socioeconomic groups are more likely to be treated by the specialist[36,37], we may have underestimated disparities in statin prescriptions in our study. Nevertheless, general practitioners play a gate-keeping role for access to specialist care in the Dutch healthcare system, and a central role in the management of patients even after major diagnoses. Furthermore, adjustment for specialist referrals did not alter our results. Thus, any bias caused by this problem is likely to be minor.

Data on stroke subtypes were not available in our study. Therefore, we were unable to distinguish patients with ischaemic and haemorrhagic stroke. Although statins have been shown to be beneficial for the prevention of ischaemic events, controversy remains on their impact on haemorrhagic stroke[6,9,38]. Thus, a higher proportion of haemorrhagic events in the lower socioeconomic groups may have partly contributed their lower rate of statin prescription. However, disparities in the prescriptions for statins were also observed for TIAs alone. Furthermore, differences in stroke sub-type distribution are unlikely to be of sufficient size to explain the large disparities in statin prescriptions. These problems are therefore unlikely explain our results.

Finally, we did not have data on over-the-counter (OTC) therapies in addition to prescribed medications. However, in the Netherlands, statins are only provided under doctor's prescription. Furthermore, we did not have estimates of the dose of statin prescription, and were therefore unable to assess disparities in this outcome. Future studies should assess whether there might be disparities in the dose of statin use, and in the adherence of patients to treatment regime.

Comparison with previous studies

Previous research in the UK observed an inverse relation between social deprivation and rates of prescribing statins at the population level up to 1996[21]. However, due to larger increases in statin prescription rates in socially deprived groups, these differences had disappeared by 1997-98[21]. Our results indicate that, in the period 2000-02, statins were more often prescribed to patients in lower socioeconomic groups for primary prevention. However, these disparities were largely explained by differences in health-need, so that no major social inequity in the prescription of statins was evident after multivariate adjustment. On the other hand, in an attempt to assess GP's adherence to guidelines on the prescription of statins as primary choice for lowering-cholesterol, we found that about 4% of patients under hypercholesterolemia treatment were prescribed with other drugs than statins. Interestingly, among this group, those in the lower socioeconomic groups were less likely to have statins prescribed, implying that social disparities in the adherence to guidelines for primary prevention may persist for certain groups of patients.

The vast majority of studies on secondary prevention have found no evidence of social disparities in the prescription for statins in patients diagnosed with coronary heart disease or angina[15,17,35,39]. A study in Ireland reported lower prescription rates in more socially deprived IHD patients, but this study was based on a crude deprivation measurement[22]. Some studies observed disparities in statin prescriptions in earlier periods, but these disparities had disappeared or decreased substantially by 2002[19,20]. Consistent with these findings, after adjusting for health-need, we observed no socioeconomic disparities in the prescription of statins among IHD patients. If anything, women with a lower socioeconomic status were more likely to have statins prescribed. On the other hand, this is the first study to report that stroke and TIA patients with lower socioeconomic status are less often prescribed with statins than patients in the highest socioeconomic groups. Stroke patients in deprived areas have been found to have almost twice the risk of receiving sub-optimal care[40]. These patients experience worse health outcomes and have poorer survival and prognosis[41-44], and are more likely to be disabled up to five years after stroke[44]. Lower access to statin prescriptions in lower socioeconomic groups may reflect sub-optimal care in these patients. This may have contributed to their poorer survival and prognosis[41-43], and might partly contribute to the consistent social gradient in stroke mortality observed across Europe[30].

Previous studies have reported gender inequity in the prescription of statins among IHD patients (secondary prevention)[19,35,45]. Our results further suggest that women are less likely than men to be prescribed with statins for both primary and secondary prevention.

These findings are consistent with previous evidence of a systematic bias favouring men with respect to women in the quality of care for the prevention of IHD[35,45-47].

A previous study in the UK found that only 19% of patients diagnosed with coronary heart disease (CHD) were receiving statins in 1998[39], whereas the corresponding figure for IHD patients in our study was 47-50% for men and 26-35% for women. This difference may reflect an increase in the rate of statin prescription during recent decades. Accordingly, a more recent study estimated that about half of CHD patients in the UK were prescribed with statins in 2000-2002[19]. These results indicate improvements in the compliance with guidelines for the prescription of statins. However, according to guidelines, about 85% of IHD patients should be treated with statins[48]. Thus, particularly among women, statin prescription rates for secondary prevention remain well below recommended levels.

Explanation of Results

Results from this study suggest that there is no major social inequity in the prescription of statins for primary prevention in The Netherlands. These findings are likely to reflect universal access to primary health care as provided through health insurance schemes, thus eliminating financial barriers for accessing preventive interventions[36,37]. Furthermore, the implementation of national guidelines for cholesterol treatment in general practice[49] may have contributed to the provision of equal care on the basis of health need, thereby preventing social inequity in the prescription of statins. On the other hand, hypercholesterolemia and hypertensive patients with lower socioeconomic status under lowering-cholesterol medication were less likely to be prescribed with statins. This may reflect some level of inequity in the quality of treatment for cholesterol, suggesting that GP's adherence to guidelines is less common among lower socioeconomic groups for some patients. Alternatively, this pattern may also reflect a higher prevalence of contra-indications among lower socioeconomic groups due to their higher prevalence of other health problems, resulting in statins less often been prescribed to this group.

A mixed picture emerges in regard to the prescription of statins for secondary prevention. On the one hand, we observed no social inequity in the prescription of statins in IHD patients. A possible explanation of this pattern comes from the theory of innovation diffusion in the adoption of advanced medical technologies[50]. As firm evidence for the effectiveness of statins for secondary prevention in patients with a history of IHD started to emerge in clinical trials in the mid-1990s[51-53], guidelines recommending statin prescriptions in these patients were first developed[48,49]. Evidence was not immediately translated into extensive prescribing of statins, as less than one fifth of patients diagnosed with CHD were being prescribed with statins during the late-1990s[19,39], and more often in patients with higher education and economic affluence[19-21]. During recent years, however, the prescription of statins in CHD patients has more than tripled, with larger increases occurring in the most deprived socioeconomic groups[19,21]. As a consequence, as evidence in our study, social inequity in the prescription for statins in CHD patients disappeared in recent years[19-21,39].

In contrast, men diagnosed with TIA or stroke in the lowest socioeconomic groups were half as likely to be receiving statins than those at the highest end of the social stratification. This might reflect the early stage of a similar innovation diffusion pattern as observed in IHD patients. Evidence of the effectiveness of statins in preventing major vascular events among patients with prior stroke or TIA was first provided by the Heart protection study (HPS) in 2002-2004[6,7]. Following this, although guidelines have not explicitly been provided, major publications have endorsed the benefits of statins in the aftermath of stroke and TIA[9,24-27]. In our study, only about one fourth of patients with prior stroke or TIA were being prescribed with statins, with higher prescription rates in the higher socioeconomic groups. This suggests a delay in the prescription for statins in socially disadvantaged patients. A similar diffusion pattern has been observed for the progression of the smoking epidemic in different socioeconomic groups[54]. This pattern may thus reflect a universal principle of delayed implementation of evidence-based interventions in the more deprived socioeconomic groups, which might vanish following the development of consensus and explicit guidelines as observed for CHD patients[19-21,39].

Several explanations can be provided for this pattern in the prescription of statins in patients with prior stroke or TIA. The publication of strong scientific evidence might be in itself insufficient to alter treatment patterns among general practitioners[55]. Thus, results from clinical trials may only be implemented in everyday practice after they are reiterated by other sources and underpinned by a clear local consensus[39,55]. This consensus may still be lacking for the prescription of statins following a stroke or TIA[9,24,38,56,57], resulting in differential prescription patterns by clinicians. Patients in the higher socioeconomic groups may be more aware of prophylactic treatment options and have better communication skills, and thus be more likely to be prescribed statins for conditions for which guidelines do not yet provide clear-cut recommendations[20]. Consistently, studies suggest that patients with higher income can influence physician decisions on prescriptions, and are thus more likely to be prescribed newer and more expensive drugs[22,58,59]. Better knowledge about health among higher educated patients may also influence GP's prescribing behavour[58,59]. Thus, prescribing drugs is not simply the result of critical appraisal of evidence, but also of the mode of exposure of pharmacological information and social influences on decision-making[59]. Only after sufficient time has elapsed and enough evidence been gathered, might clinicians prescribe statins to patients with prior stroke or TIA for the prevention of vascular events.

Finally, several mechanisms might account for gender disparities in statin prescriptions, including gender differences in doctor-patient relationships, physician bias and patient preferences[47]. Clinical profiles, presentation of symptoms, and outcomes also differ between men and women with acute coronary syndromes[60]. Furthermore, physicians consider male patients to be at higher risk for CVD and therefore prescribe lipid-lowering medications more often for male patients[61], leading to less aggressive treatment in women. Women are also less likely to attend cardiac rehabilitation after myocardial infarction, resulting in reduced clinicians' opportunities to implement preventive measures[19,62].

Clinical implications

This study highlights improvements in the prescription for statins in primary prevention for the management of hypercholesterolemia. However, strategies are needed to maximise the use of clinical evidence and reassure physicians on the prescription for statins as first choice in the treatment for hypercholesterolemia regardless of patients' social class. Adherence to guidelines on statin treatment in patients with IHD has improved and reaches patients in all social strata. However, particularly among women, strategies are needed to increase statin use after IHD, which remain well below recommended levels[48,49]. Large social disparities in the prescription for statins in patients with prior stroke or TIA are unacceptable, and reflect lack of consensus and clear-cut guidelines on statin treatment in these patients. Results from on-going trials may provide further re-assurance on the effectiveness of statins after stroke or TIA and thus contribute to build-up consensus[63]. In the meantime, however, these uncertainties should not discourage the widespread use of statins after ischaemic stroke or TIA in patients that may require them, regardless of social disadvantage or other demographic characteristics[25,26].

Acknowledgements

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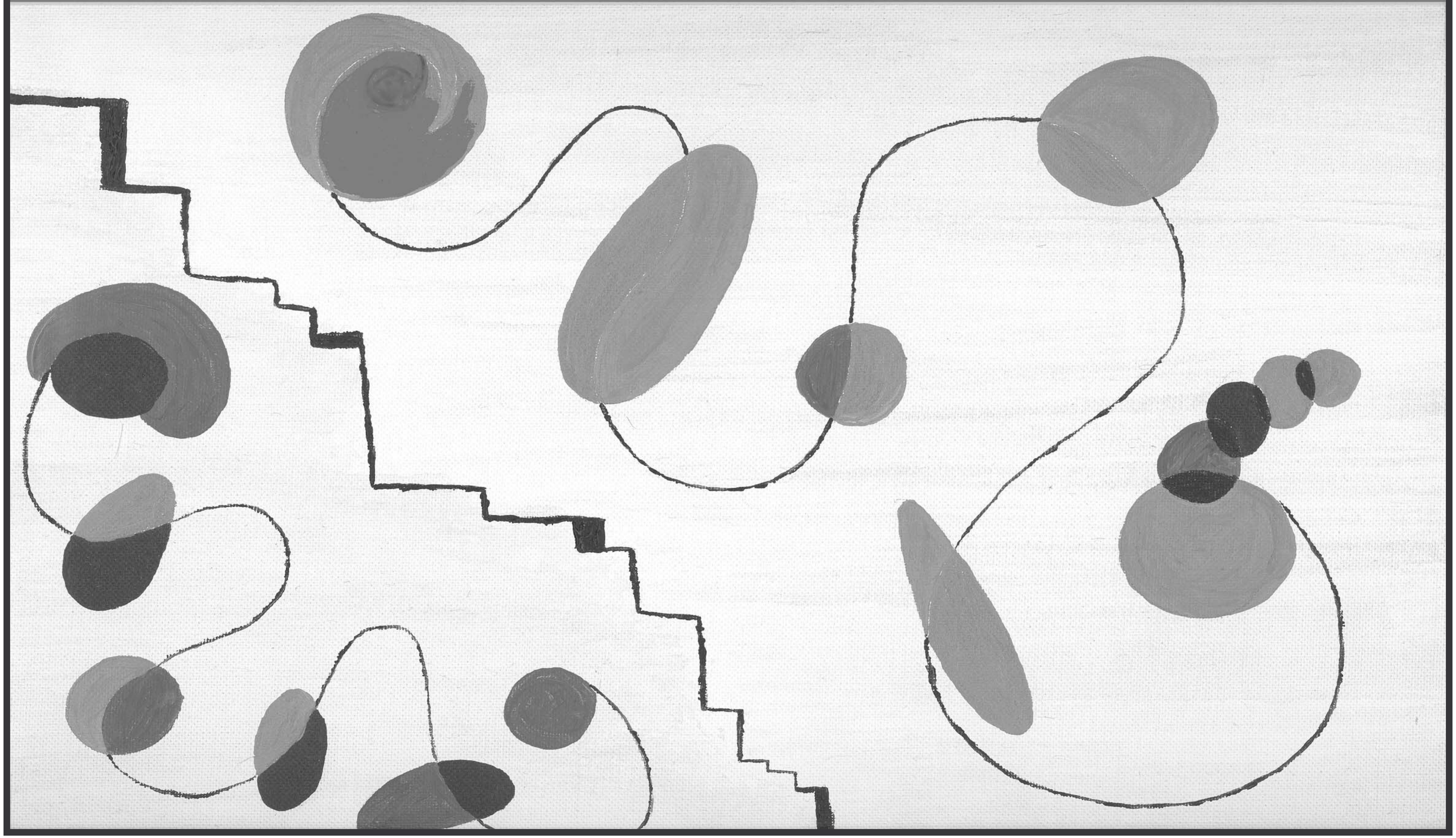
Part V General discussion



Chapter 11

Discussion

The purpose of this work was to estimate the magnitude of socioeconomic differences in stroke in different world populations, and to assess the contribution of biological, behavioural, psychosocial and preventive care related risk factor to socioeconomic disparities in stroke. This thesis is based on data from several studies conducted in 10 European countries and the United States. In this discussion, the main findings of this thesis will be first summarised. This will be followed by an analysis of data sources and methodological limitations relevant to the interpretation of results. Thirdly, we will discuss the possible explanations and interpretation of findings. This chapter ends with a discussion of the clinical and public health implications, as well as recommendations for future research.

11.1 Summary of findings

International pattern of socioeconomic differences in stroke

Results from this thesis suggest that socioeconomic status is associated with stroke mortality in many European populations including Finland, Norway, Denmark, England and Wales, Belgium, Switzerland, Austria, Turin (Italy), and Barcelona and Madrid (Spain). Previous studies during the 1980s indicated that socioeconomic differentials in stroke mortality were relatively small in most Nordic countries (Sweden, Norway and Denmark), Italy and Spain, whereas larger differences were observed in England and Wales, Ireland and Finland[1]. Our results confront these findings and suggest that during the 1990s, socioeconomic differences in stroke mortality were remarkably similar across Europe among both men and women. The only exception was Austria, where socioeconomic differences in stroke mortality among women tended to be larger than in other populations. Differences between our study and those in the 1980's may be due to improvements in the quality of or data, which comprised broader age groups and longer follow-up. Overall, among those aged 30 years and older, stroke mortality was about 30% higher among those with lowest than highest educational level in Europe. Furthermore, we found that socioeconomic differences in stroke mortality had a modest but important contribution to socioeconomic differentials in life expectancy. Overall, socioeconomic differences in stroke mortality accounted for approximately 7% of socioeconomic differentials in life expectancy among men and 14% among women in Europe.

Stroke mortality has been declining consistently during the last decades[2], although this decline might have ceased during recent years in some populatons[2-5]. In the period 1981-1995, we observed a consistent stroke mortality decline among both men and women in several European countries. Relative stroke mortality declines ranged from approximately 17% in Finland to 40% in Turin (Italy). Contrary to expectations, a similar stroke mortality decline occurred among those with high and low socioeconomic status in Europe, both in relative and absolute terms. The only exception was Norway, where a larger relative decline occurred in non-manual than manual classes. Despite this favourable pattern, socioeconomic disparities in stroke mortality persisted and remained of a similar magnitude in the 1990s as in the 1980s in most populations. In fact, in Norway, occupational class differences in stroke mortality significantly widened during this period.

Substantial research has been conducted on the association between socioeconomic status with ischaemic heart disease (IHD)[6-9]. As IHD and stroke share a number of risk factors related to the development of atherosclerosis[10,11], comparing socioeconomic differentials in stroke and IHD mortality can shed light on common determinants that might explain socioeconomic variations in the two main cardiovascular diseases. Overall, lower socioeconomic status was associated with higher stroke and IHD mortality. However, the international and time patterning of these associations was noticeably different for stroke and IHD mortality. Firstly, more favourable IHD mortality declines were observed among higher than lower socioeconomic groups, so that socioeconomic differences in IHD mortality widened in the period 1981-1995. This contrasted with stroke mortality declines of a similar magnitude across socioeconomic groups, and persisting but steady socioeconomic differentials in stroke mortality in most populations. Second and most interestingly, socioeconomic differences in IHD mortality were larger in northern European populations, of a moderate size in Belgium, Austria, and Switzerland, and smaller in southern European populations during the 1990s. This largely resembled the north-south gradient in lung cancer[12] and smoking socioeconomic differentials in Europe[13]. In contrast, socioeconomic differentials in stroke mortality were of a similar magnitude in most European countries and did not show a north-south gradient. These findings raise questions about possible differences in the risk factors that explain socioeconomic differences in stroke and IHD mortality in Europe.

Data from European populations are not directly comparable to data from the United States (US) in our study. However, results from the health and retirement survey (HRS) study indicated that socioeconomic status is also associated with higher stroke rates in the US population. Each year of additional schooling was associated with a 6% decrease in the risk of stroke at ages 50 to 64. At these ages, those in the lowest income and wealth quintiles had two to three times the risk of developing stroke than those in the highest quintiles. These findings add to the universality and consistency of socioeconomic differentials in stroke in the developed world.

Overall, socioeconomic differentials in stroke were of similar magnitude among both men and women. Although the association tended to be stronger among women in some populations, these differences were inconsistent and not significant. On the other hand, age modified substantially socioeconomic status and stroke associations, but this occurred in a different way in European and US populations. In European countries, relative socioeconomic differences in stroke declined with age but persisted into the oldest age groups in all countries. Among those aged 75 years and over, stroke mortality was about 20% higher in the lowest as compared to the highest educational level group. Furthermore, due to the fact that stroke mortality is highest at old age, absolute socioeconomic differences in stroke mortality increased with age and were largest at ages 75 and over. In the US, relative socioeconomic differences in stroke incidence also declined with age. However, this decline was much stronger in this population so that socioeconomic difference in stroke incidence did not persist into old age. In the EPESE population, a crossover of the association occurred so that stroke rates became higher in those with high education or income. In the HRS representative sample of US adults, socioeconomic status was associated with stroke up to age 65, but only income remained associated with stroke at ages 65 to 74. Beyond age 75, socioeconomic status was no longer a predictor of stroke incidence in this population. These results suggest that there might be differences between European and US populations in the age patterning of socioeconomic differences in stroke.

Explaining the gradient: How does socioeconomic status increase stroke risk?

This thesis examined some of the potential pathways through which socioeconomic status might have an impact on stroke incidence and mortality (Figure 11.1). Analyses were based on a decomposition approach to assess the contribution of risk factors to socioeconomic differences in stroke. This contribution was defined as the proportional attenuation in basic hazard or rate ratios after additional adjustment for stroke risk factors[14,15]. Table 11.1 summarizes the proportional attenuation in basic ratios for the effect of socioeconomic status on stroke after additional adjustment for risk factors included in this thesis. These percentage changes should not be interpreted as absolute estimates, but only as indicators of relative importance. Three main conclusions can be drawn from these findings: Firstly, the explanation of socioeconomic differentials in stroke is not straightforward. The relatively high rates of stroke in those with lower socioeconomic status do not result from the higher prevalence of a single but a combination of multiple risk factors in these groups. Secondly, biological, behavioural and psychosocial factors can explain a large part of socioeconomic differentials, whereas nutritional factors seem to account for only a small part of these disparities. Thirdly, the mechanisms through which socioeconomic status increases stroke risk differ according to age and population. These three contentions are discussed in more detail below.

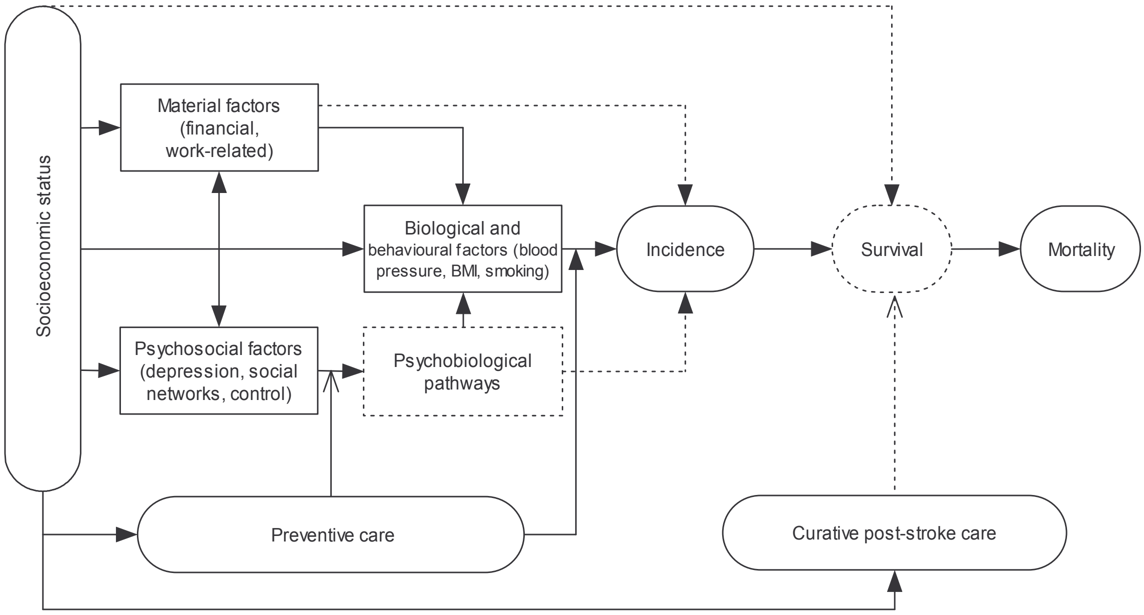


Figure 11.1. Model of the pathways through which socioeconomic status might influence stroke incidence, survival and mortality; nutritional factors are included in the behavioural factors category

Dotted lines refer to factors that were not examined in the present thesis

As observed in previous studies, biological and behavioural risk factors explained less than half of socioeconomic differentials in stroke[16-18]. Among these factors, blood pressure seemed to contribute the most to socioeconomic differentials in stroke among those aged 30 to 74 years in the EPIC study. Adjustment for blood pressure attenuated the effect of education on stroke by about 13% in northern and continental Europe and 29% in southern European populations, reflecting the higher levels of blood pressure among European low educated. However, this pattern was not observed in a cohort of US elderly, where blood pressure had only a limited role in explaining socioeconomic differentials in stroke at ages 65 to 74. Although blood pressure remained a strong predictor of stroke at these ages, blood pressure levels did not vary consistently by educational level or income. These findings might suggest that blood pressure plays a more important role in explaining socioeconomic differences in stroke in European than in US populations, due to larger blood pressure disparities in the former. However, it may also suggest that blood pressure contributes to socioeconomic differentials at mid-age, whereas it plays a smaller role after age 65 as differences in blood pressure attenuate.

Smoking was the second most important contributor to socioeconomic differences in stroke among those aged 30 to 74 in northern Europe, accounting for about 7-19% of these disparities. However, smoking did not contribute to stroke differentials neither in southern European populations nor among those 65 to 74 in the US. This suggests differences in the contribution of smoking to stroke disparities in different populations and age groups. Thirdly, diabetes and BMI (body mass index) contributed considerably to stroke differentials among US elderly, highlighting the important role of these factors at early old age in the US. However, these factors did not contribute to socioeconomic differences in stroke at younger ages in the EPIC and Globe European populations. Other conventional risk factors that contributed to socioeconomic differences in stroke included previous heart disease, excessive alcohol intake (Globe population only) and physical activity (Globe and EPESE studies).

Table 11.1. The contribution of risk factors to socioeconomic differences in stroke: Proportional attenuation of basic model rate or hazard ratio after adjusting for indicated risk factors*

	Risk factors	Epic (30-74)	Globe (40-74)	EPESE (65-74)
Biological	Blood pressure	13-29%	N.A.†	1-4%
	Body mass index	5%	0%	8-16%
	Height	2%	N.A.	N.A.
	Diabetes mellitus	2%	3-5%	16-30%
	Heart disease	2%	7-8%	N.A.
	Hypercholesterolemia	0%	N.A.	N.A.
Behavioural	Smoking	0-12%	7-19%	0
	Alcohol intake	0%	7-21%	0
	Physical activity	7%	0%	9-15%
	Physical/cognitive functioning	N.A.	N.A.	26-28%
	All biological/behavioural	29%	14-40%	22-43%
Psychosocial	Depression	N.A.	0%	23-30%
	Social networks / support	N.A.	6-19%	27-37%
	Difficult life events	N.A.	4-13%	1%
	Locus of control	N.A.	19-32%	N.A.
	All psychosocial	N.A.	48-50%	43-50
Nutrition	Fruit & vegetables	5%	N.A.	N.A.
	Fish consumption	2%	N.A.	N.A.
	Total energy intake	0%	N.A.	N.A.
	Saturated fatty acids	0%	N.A.	N.A.
	Calcium intake	0%	N.A.	N.A.
	Potassium intake	0%	N.A.	N.A.
	All nutritional factors	7%	N.A.	N.A.
	All factors	33%	51-73%	62-87%

*Attenuation is calculated using the following formula:

(100 * [Rate ratio Basic model - Rate ratio adjusted model]/[Rate ratio basic model - 1])

†N.A. indicates not available

Interestingly, a substantial share of unexplained stroke differentials was accounted for by psychosocial risk factors included in our study. Of particular interest were depression and social networks, each accounting for about one quarter of socioeconomic differentials in stroke among the US elderly. Depressive mood did not contribute to stroke differentials among Dutch participants aged 30 to 74 years. However, depressive mood may not be a good proxy for clinical depression, which involves a more extensive measurement than used in the Globe study. Among Dutch participants, locus of control was the most important psychosocial contributing factor, followed by the level of social support and difficult live events.

Fruit and vegetables consumption was a predictor of stroke and was less common in lower educated individuals among EPIC participants. It explained about 5% of socioeconomic differences in stroke among Europeans aged 30 to 74 years, whereas other nutritional risk factors did not contribute to these disparities.

The small contribution of some risk factors to socioeconomic differences in stroke was partly due to their weak association with socioeconomic status in specific populations. For instance, blood pressure and smoking were associated with socioeconomic status in the EPIC population, but were weakly associated with socioeconomic status in the US elderly (EPESE study). This explains their limited contribution to socioeconomic differentials in stroke in the EPESE study, and may suggest that these factors play a more important role in relatively young cohorts. On the other hand, physical activity, diabetes and BMI contributed to stroke differentials in the Epese elderly (65 to 74) but not in the relatively younger Globe participants (30 to 74). Although these factors were strongly associated with socioeconomic status in both cohorts, they were weakly associated with stroke in the Globe study. Thus, physical activity, diabetes and BMI might be associated with both stroke and socioeconomic status among the elderly, and therefore influence stroke differentials among older cohorts only. In contrast, factors such as smoking, alcohol consumption (Globe) and blood pressure might be more consistently associated with socioeconomic status and stroke in relatively young cohorts, and may therefore play a more prominent role in explaining stroke differentials in younger populations. Finally, although fruit and vegetable consumption was related to stroke risk, other nutritional factors were weakly associated with stroke in the EPIC population. As a consequence, despite their relatively strong association with socioeconomic status, these factors did not yield a large contribution to stroke differentials in stroke.

Absolute vs. relative stroke differentials

In a recent study, Lynch et al[19] showed that four major cardiovascular risk factors (hypertension, smoking, diabetes and dyslipidemia) explained only about one quarter of the social gradient in coronary heart disease (CHD) in a cohort of Finish men. However, eliminating these risk factors from the same population led to a reduction of about 72% in absolute socioeconomic differences in CHD[19]. These paradoxical results suggest that risk factors that explain little of the relative association between socioeconomic status and CHD can in turn explain a large part of absolute rate differences[19]. Following this line of enquiry, we estimated the contribution of risk factors to absolute rate differences in stroke incidence in a cohort of Dutch men and women.

Two important conclusions can be drawn from these analyses: Firstly, we found that reducing high blood pressure, smoking, excessive alcohol consumption, heart disease, internal locus of control, and low social support to the theoretical minimum population level would diminish absolute socioeconomic stroke rate differentials by more than three thirds. In contrast, these factors explained approximately half of relative socioeconomic differences in stroke only. Interestingly, adjustment for (self-reported) hypertension did not attenuate the relative association between education and stroke. However, eliminating hypertension from the population would reduce stroke differentials by about 20%. Secondly, psychosocial risk factors contributed more than behavioural and biomedical risk factors to relative socioeconomic differences in stroke. However, both groups of risk factors contributed to a similar extent to absolute socioeconomic differences in stroke.

Inequity in the quality of preventive care: Does it contribute to stroke differentials?

In a large cohort of general practice patients in the Netherlands, we found no evidence of major socioeconomic disparities in the quality of preventive care provided by GPs for major precursors for stroke. No systematic socioeconomic variations were observed in GP compliance with guidelines for care aspects such as the prescription for diuretics for hypertension, aspirin after a transient ischaemic attack (TIA), and ACE-inhibitors and diuretics combined after heart failure. The only exception to this rule referred to the prescription for statins. Firstly, lower socioeconomic status patients with hypercholesterolemia or hypertension under cholesterol-lowering medication therapy were somewhat less likely to receive statins as choice of medication. Secondly, men in the lowest socioeconomic groups diagnosed with TIA or stroke were half as likely to be receiving statins as those at the highest end of the social hierarchy. No disparities were observed in other aspects of care relevant for stroke prevention. In conclusion, although some social disparities in the prescription for statins remain, social inequity in the quality of preventive care for stroke precursors is unlikely to play a major role in the explanation of socioeconomic differentials in stroke.

11.2 Methodological considerations and validity of the thesis

Measurement of stroke

In the present thesis, stroke occurrence was ascertained by a variety of methods including follow-up through mortality, hospital discharge and general practice registries, and respondent and proxy follow-up interviews. Follow-up of stroke outcomes was complete for almost all participants in the different studies. We have missed non-hospitalised fatal stroke cases through linkage with hospital discharge databases (Globe study), which may have led to over or underestimation of socioeconomic differentials in stroke incidence. Most importantly, due to the large population sizes, we were unable to ascertain stroke using brain imaging techniques in all participants. Therefore, accurate data on stroke subtypes were not available in our study, so that the effect of socioeconomic status on different stroke subtypes could not be assessed. Two potential problems might arise from this limitation:

Firstly, the magnitude of the association between socioeconomic status and stroke might be different for ischaemic and haemorrhagic strokes, as well as the distribution of stroke subtypes for different populations. However, previous studies indicate that the association between socioeconomic status and stroke does not differ for different stroke sub-types. Jakovljevic et al. conducted a large study of socioeconomic status and stroke sub-types using data from the FINMONICA registry in Finland. Results from this study indicate that lower socioeconomic status is associated with higher incidence of ischemic stroke[20], intracerebral hemorrhage[21] and subarachnoid hemorrhage[22], with associations being in the same direction and of similar magnitude for the three stroke sub-types. Similar associations between socioeconomic status and different stroke subtypes have also been reported in Sweden[23]. Thus, these studies suggest that analyses of data for specific stroke sub-types is likely to yield similar results to those observed in our study by pooling data on all sub-types.

Secondly, although ischaemic and haemorrhagic stroke share several risk factors, differences exist in the determinants of the major stroke subtypes. This may have led to underestimation of the contribution of specific risk factors to stroke differentials, particularly for factors that are associated with a specific stroke sub-type. Example of this is hypercholesterolemia, which is associated with ischaemic but not haemorrhagic stroke[10]. Sensitivity analyses using a rough distinction between ischaemic and haemorrhagic strokes in the EPIC population showed a similar contribution of most risk factors. However, the contribution of fruit and vegetables to socioeconomic differences in stroke was evident for ischaemic but not for haemorrhagic events. Thus, although the overall contribution of major risk factors is unlikely to differ by stroke sub-type, future studies should examine the contribution of sub-type specific risk factors to socioeconomic differences in major stroke sub-types.

Validity of international comparisons

Major strengths of international studies in the present thesis (chapters 2, 3 and 4) included the longitudinal design and the use of data for the entire national or regional population.

However, two major data features may have had an impact on the validity of the thesis. Firstly, despite efforts at standardization, the measurement and distribution of educational level and occupational class differed between countries and may have changed over time. Secondly, cause-of-death certification and coding procedures differed between countries and may have changed over time. The potential impact of these limitations is discussed below.

The original distribution of educational level differs substantially by country. To increase comparability, national education levels were reclassified so that the proportion of participants with low education was similar across populatons[24]. Low education groups comprised a relatively large share of the population, so that this group did not represent the extreme end of the educational distribution. It is likely that a more refined classification of this group would have resulted in larger estimates of the association of educational level with stroke. However, reclassified categories corresponded roughly with the UNESCO standard classification of education[25], thus allowing valid cross-country comparisons. Furthermore, this problem is unlikely to influence the robust international pattern observed in our study and the similarities in the size of stroke differentials across countries. Thus, any bias cause by this limitation is unlikely to explain the overall international pattern observed in this thesis.

Analyses of trends in stroke by socioeconomic status may have been influenced by differences between countries in the accuracy of educational level and occupational class measurements. However, we did not strictly compare countries but analysed changes over time within each population. Nonetheless, although changes in the occupational class distribution were small, the proportion of the population in the low educational category decreased considerably over time. To assess the impact of these changes, sensitivity analyses were conducted using the relative index of inequality[26], an effect measure that is based on all educational levels and simultaneously adjusts for differences in the educational distribution. The pattern based on the relative index of inequality corresponded with that based on the rate ratio: Educational differences in stroke mortality persisted and remained relatively stable over time in most countries, whereas educational disparities in ischemic heart disease mortality widened in most populations. Similarly, the international pattern of educational level differences in stroke and IHD remained unchanged when using the RII as measure of effect in the cross-country comparisons. Thus, changes and cross-country differences in the distribution of education and occupation are unlikely to account for the international and trend patterns observed in this thesis.

There are large variations across countries in certifying and cause-of-death coding practices[27]. As this study was based on data from mortality registries, bias due to misclassification of cause of death may have influenced our results. However, our results would only be biased if misclassification of stroke occurred differentially across socioeconomic groups. Countries in our study enjoy universal healthcare access, although some differences in healthcare utilization remain[28]. Nevertheless, it is unlikely that these differences would result in large socioeconomic differences in the accuracy of cause of death classification. On the other hand, higher levels of misclassification of IHD in both southern countries and in lower educated individuals may explain the north-south south gradient in socioeconomic differences in IHD mortality. To test the impact of this problem, we assessed the pattern of educational disparities for a combined category of IHD and other heart diseases (OHD; ICD-9 codes 416 and 420-429), thus diluting the effect of heart disease misclassification. Although north-south gradients were somewhat less marked among women and young men, a marked north-south gradient remained for older men. Overall, although misclassification may have played a role, this problem is unlikely to fully explain the overall international pattern observed in our study for disparities in stroke and IHD mortality.

Finally, changes in the classification of causes of death may influence trends analyses. However, in most countries, the 9th version of the ICD code was used in all periods, and the overall stroke category is essentially the same in the 8th and 9th ICD revisions[2]. Furthermore, our results would only be biased if deaths from stroke were classified differently by socioeconomic status. There is no evidence that this has occurred in our data. However, replication of findings using reliable data such as those provided by the MONICA study might be necessary to assess the full extent of this problem[29].

Validity of explanatory studies

There are two potential threats to the validity of the present thesis. These comprise error in risk factor measurement and problems related to statistical adjustment for the assessment of mediation. These two sources of bias are discussed in detail below.

Measurement of risk factors

Two potential limitations in the measurement of risk factors may have influenced their contribution to stroke differentials: Firstly, measurement of some risk factors was not optimal in all studies. Although blood pressure was measured in the EPESE study according to the Hypertension Detection and Follow-up Program protocol[30], no standard procedures were followed in the different EPIC populations. Similarly, other factors such as diabetes and hypercholesterolemia were based on self-report. Error in the measurement of risk factors can bias their association with stroke and socioeconomic status[19,31]. As individuals in lower socioeconomic status groups are typically more prone to underreporting[32], we may have underestimated socioeconomic differentials in certain risk factors. Thus, the small contribution of some risk factors might at least be partly explained by imprecise measures of risk factors in these studies.

Secondly, risk factors in our study were measured at baseline only. A single measurement of highly variable factors such as blood pressure will not be fully representative of the long-term average blood pressure levels throughout the study period[33,34]. Such measurement error will not only lead to attenuation of the regression coefficient for the effect of this risk factor on stroke (regression dilution), but also to overestimation of the regression coefficients of variables that are associated with this factor[35]. Therefore, if data on long-term blood pressure levels had been used, a larger attenuation of the effect of socioeconomic status on stroke is likely to have occurred. Thus, we may have underestimated the contribution of risk factors such as blood pressure to socioeconomic differentials in stroke. Further research is necessary to assess the full extent of this underestimation in longitudinal studies that measure risk factors in sub-sequent waves.

Statistical approach and mediation analysis

In this thesis, we followed a decomposition approach by contrasting two estimates of the effect of socioeconomic status on stroke: An estimate adjusted for potential confounders, and an estimate adjusted for the same confounders plus one or more individual risk factors hypothesized to be intermediates of the effect of socioeconomic status on stroke[15]. Although this remain the most widely accepted approach to assess the contribution of risk factors to socioeconomic differences in health[14,15], there are two potential problems with this method: Firstly, recent studies have argued that that assumptions involved in the original development of this method such as the absence of unit-level interaction and the use of linear contrast measures are seldom met in the analysis of discrete events such as disease occurrence[36]. Since the causal assumptions required for the validity of the decomposition method are generally not verifiable from the observed data[36], we cannot discard the possibility that these problems might have influenced estimates of the contribution of risk factors to stroke differentials. However, previous studies have found similar results when using alternative methods to decomposition such as structural equation modelling. Thus, until alternative methods that address the problems inherent to the decomposition approach have been developed, the latter remains one of the preferred methods to assess mediation.

Absolute vs. relative stroke differentials: What do they tell us?

We assessed the effect of adjusting for risk factors on relative estimates of association between socioeconomic status and stroke. Recent studies indicate that the impact of risk factor adjustment might be larger for absolute (rate difference) than for relative (rate ratio) measures of effect. Therefore, we assessed the impact of risk factor elimination on absolute socioeconomic differences in stroke incidence rates in the GLOBE population. Overall, we found that the attenuation of the effect of socioeconomic status on stroke after risk factor adjustment was larger for absolute than for relative effect measures. This pattern applied to a similar extent for all risk factors. Therefore, comparisons of the relative importance of risk factors may not depend on the effect measure chosen.

Differences in the impact of risk factors on relative and absolute stroke differentials are partly due to the fact that these two methods address slightly different questions: The impact of risk factors on relative stroke disparities reflect the reduction that would be achieved in stroke disparities if the entire population experienced the population average risk factor prevalence or mean. In contrast, estimates of absolute change illustrate the reduction that would occur in absolute stroke disparities if a given risk factor would be entirely eliminated from the population (up to theoretical minimum), regardless of whether this is an attainable goal. In other words, these two approaches depart from different counterfactuals (i.e., population average prevalence vs. zero prevalence). As absolute stroke differentials are also partly dependent on the absolute stroke rates, the choice of a more extreme counterfactual (i.e., zero prevalence) will lead to a larger contribution of a risk factor to absolute stroke differentials as compared to a less extreme counterfactual (i.e., average smoking prevalence), simply because stroke rates are in itself reduced by eliminating the risk factor. However, even in a situation in which absolute differentials would be largely reduced, the remaining increased risk in the lower socioeconomic groups in relative terms will remain unexplained.

In conclusion, estimates of the contribution of risk factors to absolute differentials provide additional information but do not yield an answer to why relative differences remain. Furthermore, the impact of risk factors on relative disparities might yield a more realistic estimation, as achieving the population average risk factor prevalence or mean is a more attainable goal than the full elimination of a risk factor. Although reaching a level close to the theoretical minimum distribution might be an achievable goal in some cases, this is unlikely to be true for most risk factors. Therefore, in this thesis, we have placed special emphasis on the impact of risk factors on relative disparities.

Validity of analyses on the quality of preventive care

The present thesis comprised a large and representative study on general practice care for major precursors of stroke in the Netherlands. However, three main limitations should be considered in this study: Firstly, data on prescriptions, referrals and GP contacts were collected for a period of 12 months. However, information on blood pressure and weight measurements was available for a period of only 6 weeks. Since patients may have had these measurements at time points outside this period, estimates of their prevalence cannot be interpreted in absolute terms. Nevertheless, we used these estimates solely to assess disparities between socioeconomic groups, rather than overall compliance of GPs with guidelines on hypertension and weight measurements. Thus, odds ratios estimating disparities in these care factors are likely to be comparable to estimates based on a longer data collection period.

We assessed socioeconomic disparities in eight quality of care indicators. There may be disparities in other aspects of preventive care not included in this study. However, analyses were also conducted for other indicators regarding blood measurements, prescription of hypertension medication (other than diuretics), referrals of diabetes patients to an ophthalmologist, and electrocardiogram (ECG) examinations among specific groups of patients (results not shown). Similarly, no major socioeconomic disparities were observed in the compliance of GPs to these practice guidelines. Nevertheless, further research should assess whether the same pattern applies for other indicators of the quality of preventive care for precursors of stroke.

General practitioners are largely responsible for statin prescriptions for primary prevention in the Netherlands because of their gate-keeping role in the healthcare system. However, some patients with specific conditions such as heart disease and stroke may be receiving statins from the specialist. As patients in the higher socioeconomic groups are more likely to be treated by the specialist[28,37], we may have underestimated disparities in statin prescriptions. Nevertheless, statin prescription rates in our study were almost identical to those for the same period based on the Pharmo Record linkage system (Pharmo-RLS) database, which links pharmacies' prescriptions to hospitals' discharge records at the individual level[38]. Furthermore, adjustment for specialist referrals did not alter our results. Thus, although some level of underestimation might persist, it is unlikely that this problem can explain the overall pattern observed in our study.

11.3 Interpretation of findings

This thesis provides important indications of the magnitude and explanation of socioeconomic differences in stroke in different world populations. Explaining socioeconomic differentials in stroke involves at least two different perspectives: Firstly, from the societal point of view, the magnitude of socioeconomic differentials in stroke might be related to structural and macro-social forces such as the type of welfare regime of a nation[39,40]. Secondly, more adjacent explanations address the role of risk factors and how these vary across populations and socioeconomic groups[41]. In this thesis, emphasis has been be placed on the second perspective, namely how variations in risk factors can explain the effect of socioeconomic status on stroke.

Well-established risk factors for stroke

Socioeconomic differences in stroke mortality were of similar magnitude across Europe. This similitude in stroke differentials points at the possibility of a common explanation of socioeconomic differences in stroke across European populations. Hypertension is the most consistent powerful predictor of stroke[42], accounting for as much as 40% of ischaemic strokes and a third of haemorrhagic events[10,42-48]. On average, only about 8% of hypertensive individual have their condition controlled in Europe[49]. Results from the EPIC study (chapter 8) indicate that those with lower socioeconomic status have higher levels of blood pressure, a finding that is consistent with previous studies across Europe[50-52]. Consistently, adjustment for blood pressure partly attenuated the impact of socioeconomic status on stroke mortality. A higher prevalence of poor hypertension treatment has been observed among low socioeconomic groups[52], which may contribute to their higher hypertension prevalence and subsequent stroke rates. Overall, these results indicate that disparities in prevalence, detection and treatment of hypertension are likely to play a role in the explanation of socioeconomic differentials in stroke and their consistency across Europe.

In the EPIC study, socioeconomic differentials in blood pressure levels were larger in southern than northern European populations. This is at odds with the fact that socioeconomic differences in stroke mortality were similar across populations. Smoking is a major risk factor for both ischaemic and hemorrhagic stroke[10,42-44,47,48], and has shown a larger social gradient in northern than in southern populations[13,53]. Accordingly, adjustment for smoking attenuated the effect of education on stroke in northern countries, whereas it had the opposite effect in southern populations in the EPIC study. The combination of larger socioeconomic disparities in blood pressure in southern populations and larger smoking disparities in northern countries may have resulted in socioeconomic differentials in stroke of a similar magnitude across Western Europe. Thus, despite similar socioeconomic differences in stroke, the mechanisms behind these disparities might differ between populations.

Smoking might also play a major role in the explanation of differences in the international pattern of socioeconomic disparities in stroke and IHD mortality. Smoking diffuses within societies as an epidemic: It is first adopted by the higher socioeconomic classes, and subsequently spreads among the lower socioeconomic groups[13,54]. Whereas northern European countries and the USA have already experienced this transition, the smoking epidemic is less advanced in southern countries such as Spain and Italy[12,13,54,55]. Consistently, our study shows that socioeconomic disparities in lung cancer mortality tended to be larger in northern than in southern European populations (chapter 4). This lag in the progression of the smoking epidemic in southern population may partly explain why socioeconomic differences in IHD mortality are smaller in southern than northern Europe. This pattern contrasts with the similarities in socioeconomic disparities in stroke across Europe, which is also influenced by the consistent socioeconomic disparities in blood pressure levels across northern and southern Europe.

During recent decades, hypertension prevalence and blood pressure levels have generally declined in all socioeconomic groups in many European countries[56-59]. This is likely to explain the similar stroke mortality decline in all socioeconomic groups in most populations. Furthermore, improvements in the awareness, treatment, and control of hypertension have occurred in many European countries[60-62]. In contrast, recent trends in smoking and overweight may have contributed to the pattern for IHD mortality. Smoking prevalence has declined sharply among higher socioeconomic groups in several Nordic countries and the UK, whereas it has risen among the lower socioeconomic groups[58,59,63-65]. Similarly, the prevalence of overweight and obesity has shown more favourable trends among higher socioeconomic groups[59,66]. Smoking and overweight and obesity may thus have contributed to widening socioeconomic differentials in IHD mortality. In contrast, favourable trends in hypertension prevalence in all socioeconomic groups may have prevented widening of socioeconomic differentials in stroke mortality.

Previous studies have observed a slow down in the stroke mortality decline during recent years in some poplations[2]. For most countries, this pattern cannot be explained by less favourable trends in stroke mortality in the lower socioeconomic groups (chapter 3). However, we did observed less favourable trends in stroke mortality among lower socioeconomic groups in Norway, a country with relatively low stroke mortality rates. Whereas large declines occurred among men in non-manual classes, no declines were observed in manual classes. This resembles the pattern for other countries with low stroke mortality rates such as the United States[67,68] and Australia[69], where a slow down of the mortality decline has also been reported[2-4]. Thus, in certain countries with low stroke mortality rates such as Norway, the slow down in the stroke mortality decline might be largely due to less favourable declines in the manual classes. However, this pattern does not apply to other countries such as Sweden, where similar declines have occurred in all socioeconomic groups.

Psychosocial risk factors for stroke

Well-established risk factors for stroke explained less than half of socioeconomic differentials in stroke. As an alternative hypothesis, it has been suggested that psychosocial pathways are important mediators of the effect of socioeconomic status on cardiovascular disease[14,70-72]. In this study, we identified three potential psychosocial risk factors that contributed to socioeconomic differentials in stroke. Firstly, we found that depression partly mediated the association between socioeconomic status and stroke incidence among the US elderly. Depression is associated with an increased risk of atherosclerosis[73], thus increasing the risk of cerebral thrombosis. Potential biological explanations include altered autonomic tone as manifested by less heart rate variability, increased sympathetic nervous system activity and increased platelet reactivity[73,74]. On the other hand, the contribution of depression might also reflect the association of atherosclerosis with subsequent depression. Previous research suggests that atherosclerosis and severe coronary and aortic calcifications are associated with a higher prevalence of depressive disorders[75]. This is consistent with the vascular depression hypothesis, which postulates that structural changes in the brain due to atherosclerosis are involved in the development of late-life depression. Thus, part of the contribution of depression to stroke differentials might reflect the early stages in the development of atherosclerosis which lead to stroke.

Locus of control and social networks and support partly explained socioeconomic differences in stroke incidence in the Globe and EPESE studies. Less social networks are associated with higher functional limitations, which may lead to less physical activity and higher stroke risk[76]. Those with a low socioeconomic status have a lower sense of control, and are less likely to believe in their own efficacy[77]. An external locus of control might increase the risk of stroke partly through decreasing adherence to healthy behaviours[78]. However, their relatively large contribution suggests that social networks may not only influence stroke risk through health behaviour (Chapter 7), but that alternative mechanisms might also be involved.

In our study, the contribution of psychosocial factors to stroke differentials did not seem to occur entirely through behavioural factors included in our study. This was evidence by the fact that adjusting for psychosocial factors further attenuated the effect of socioeconomic status of stroke in models adjusted for behavioural factors (Chapters 6 and 7). This raises questions about the possibility that psychosocial factors influence stroke risk through more direct mechanisms. In particular, factors such as locus of control and social support may influence stroke risk via psychobiological pathways. Psychosocial factors can stimulate biological systems through central nervous system activation of autonomic, neuroendocrine and immunological responses[79]. Studies have found increased cardiovascular and blood pressure stress reactivity in lower socioeconomic groups[80,81], which is associated with higher stroke rates[80]. Control at work may influence cardiovascular risk partly through provoking greater fibrinogen stress responses[82,83], which is associated with lower socioeconomic status[82]. Thus, although our study does not provide direct evidence, findings are in agreement with the hypothesis that psychosocial factors contribute to stroke differentials independently of behavioural factors, possibly through psychobiological pathways that are relevant to stroke risk.

Although it is clear that these psychosocial risk factors contribute to socioeconomic disparities in stroke, it is not known whether this pattern applies to different world populations. Associations between socioeconomic status and psychosocial risk factors have mostly been reported in the UK and the Netherlands[14,71]. It is not known whether there are similar associations in southern European populations. Furthermore, the contribution of depression and social networks was largest among the US elderly in the EPESE study. Depression and social networks may thus be more important determinants of stroke at older ages, whereas other psychosocial factors such as locus of control may play a more prominent role in younger adults. Overall, further research is necessary to assess whether the contribution of psychosocial risk factors to stroke differentials might vary according to population and stage in the life course.

The unexplained part of the effect of socioeconomic status on stroke

Further to stressing the role of classical risk factors, the present study adds to previous literature by emphasising the additional contribution of psychosocial risk factors to socioeconomic disparities in stroke. However, factors in our study did not entirely account for these disparities, part of which remained unexplained. This pattern was particularly marked for the EPIC and Globe study, in which part of the effect of socioeconomic status on stroke was not attenuated after adjustment for risk factors. This raises questions about alternative pathways that may account for this effect. Firstly, as indicated previously, measurement error may be responsible for the small contribution of some risk factors. In particular, a single measurement of blood pressure and BMI may not represent their long-term average values through the study period. Failure to ascertain for these longitudinal variations may partly account for the unexplained part of stroke disparities.

Secondly, this pattern may also reflect the fact that well-established risk factors explain only part of stroke occurrence. For instance, conventional risk factors predict less than half of future events, and can only account for a small part of international variations in stroke occurrence[11,41,84]. Novel risk factors for stroke can therefore be hypothesized as potential contributors to stroke disparities. This includes factors such as fibrinogen[85], impaired fibrinolytic activity, platelet reactivity, hypercoagulability, lipoprotein(a), small dense low-density lipoprotein, and markers of inflammation including C-reactive protein and soluble intercellular adhesion molecule 1 (ICAM-1)[10,11]. Furthermore, alternative psychosocial risk factors such as stress[86] and stress reactivity[79] might also play a role in explaining the effect of social position on stroke risk.

A third alternative explanation draws attention to the role of early life conditions and infectious agents. Studies suggest that poor prenatal and childhood circumstances are associated with increased stroke risk[17,87]. The mechanisms behind this effect are still unclear but are likely to involve mother's and child's malnutrition, childhood illness and chronic infections acquired during childhood[17,87,88]. Indirect support to this hypothesis stems also from evidence that the number of siblings is associated with haemorrhagic stroke mortality[89]. Individuals who have more siblings will, on average, have grown up in more overcrowded accommodation, with greater exposure to early infections, and less access to adequate diet[89]. Overall, these studies indicate that factors acting early in life may be associated with both socioeconomic position and stroke incidence in adulthood, and may thus partly contribute to socioeconomic disparities in stroke at later ages.

Do socioeconomic differences in stroke persist into old age?

Socioeconomic disparities in stroke mortality decreased but persisted into old age in European populations (chapter 2). In contrast, stroke disparities declined sharply with age in the US, with null or reverse effects of socioeconomic status on stroke beyond age 75 (chapters 5 and 7). Methodological differences in aspects such as length of follow-up and stroke ascertainment might account for these differences. However, it is unlikely that they can explain the consistent age related crossover or diminishing gradient. Age-related weakening of the association of risk factors such as hypertension and smoking with stroke may have partly contributed to the reduced effect of socioeconomic status on stroke at later ages. Additionally, a more marked weakening or reversing of the association between hypertension and socioeconomic status might partly have contributed to the cross-over in socioeconomic disparities in stroke in the US elderly (EPESE study). Nevertheless, adjustment for these factors did not fully explain this age pattern, suggesting that there might be other mechanisms involved. Failure of education of income to represent the true socioeconomic resources of the oldest old in the US may also explain this pattern. However, we observed a similar age-decline in stroke differentials for wealth, a good indicator of socioeconomic status in the elderly[90-92]. Thus, it is unlikely that these problems fully explain this age patterning.

Further to these methodological limitations, there are two potential explanations for these findings: Firstly, entitlement programs such as social security and Medicare in the US may buffer the negative effect of social deprivation on stroke in the oldest old. As a consequence, socioeconomic status might truly cease to expert an effect on stroke at very old age in this country. However, European populations such as the Netherlands and Nordic countries encompass noticeably more generous social benefits and egalitarian policies as compared to the US, including universal access to healthcare. Furthermore, susceptibility to stroke is to a large extent developed throughout the life course, with factors in early and mid life playing a critical role[87,93-95]. Thus, it is unlikely that entitlement programmes and interventions for the elderly explain the lack of socioeconomic disparities in stroke at old age in the US.

A second and more plausible explanation draws attention on the concept of selective survival, an artefact phenomenon used to explain a similar crossover of black/white differentials in mortality in the US[96,97]. Individuals with lower socioeconomic status are more likely to die earlier from stroke or other competing causes, so that only the healthiest survive into old age[97]. Simultaneously, better survival might lead to postponement of death toward older ages among higher socioeconomic groups[97,98]. As a consequence, individuals with a low socioeconomic status who survive into very old age might no longer be comparable to those with a high socioeconomic status at the same age. Similarly, higher socioeconomic groups might be more likely to live ‘long enough’ to develop stroke at very old ages. Selective survival might thus explain why socioeconomic differentials in stroke mortality disappear or reverse at very old age in the US. This pattern might also explain the age-related decline in stroke disparities in Europe, where the effect of selective survival might be less marked.

But why would selective survival occur to a larger extent in the US than in Europe? Recent studies have suggested that socioeconomic differentials in health at mid age might be larger in the US than in Europe[99]. Due to methodological differences, we cannot reach any firm conclusion regarding differences in the magnitude of socioeconomic differences in stroke mortality between Europe and the United States. However, educational level differences in stroke at ages 65 to 74 in the New Haven (US) EPESE cohort (chapter 7) appeared to be larger than those in Europe at ages 60 to 74 (chapter 2). Previous research has also observed larger differences in all-cause mortality by educational level in the United States as compared to most European countries at ages 35 to 64[100,101].These findings could be indications of a larger effect of socioeconomic status on health at younger ages in the US than in Europe[100,101]. This larger impact would result in stronger selection of healthy survivors in the former, whereas in Europe this selection mechanism may only result in diminishing but still persisting socioeconomic differentials in stroke (chapter 2). Nevertheless, further research is required to assess this hypothesis in the context of comparable data for Europe and the US.

Preventive health care: Does it contribute to stroke disparities?

We found no evidence of major socioeconomic disparities in the quality of care for several precursors of stroke. In the Netherlands, health care is available to all through health insurance schemes. This may have contributed to eliminating any financial barriers to access general practice care among the lower socioeconomic groups[28,37]. Furthermore, national guidelines for general practice care may have contributed to the provision of equal and standardised care on the basis of patients' needs, thereby leaving limited room for variability according to socioeconomic status. Thus, general practice guidelines may not only contribute to improving the quality of care, but may also promote equal and standardised preventive care across socioeconomic groups.

However, socioeconomic disparities may still persist in other aspects of care not assessed in our study. For instance, individuals in the higher socioeconomic groups might be more likely to have their hypertension detected, which could contribute to disparities in stroke. Furthermore, there might be disparities in aspects of care for which evidence is scarce and therefore no guidelines have been developed. In agreement with this view, we found that men in the lowest socioeconomic groups diagnosed with TIA or stroke were half as likely to be receiving statins from the GP as compared to those in the highest end of the social stratification. Although major publications have endorsed the benefits of statins in the aftermath of stroke and TIA[102-106], current guidelines do not explicitly recommend the use of statins after stroke. As a result, only about one fourth of men with prior stroke or TIA were being prescribed with statins by the GP, as opposed to about half of those diagnosed with heart disease. Thus, consensus may still be lacking for the prescription of statins following a stroke or TIA[102,103,107-109], resulting in differential prescription patterns by clinicians. This pattern may thus reflect a delayed implementation of evidence-based interventions in the more deprived socioeconomic groups, which might only vanish after the development of consensus and explicit practice guidelines [110-113].

It is important to bear in mind that preventive health care can contribute to socioeconomic disparities in stroke through several mechanisms[114]: Firstly, socioeconomic status may determine the proportion of individuals receiving high quality care. Our findings suggest that this mechanism does not play a major role. On the other hand, socioeconomic status may modify the host response to therapeutic interventions, due to differences in factors such as patients' adherence to therapy and in susceptibility to the impact of interventions[114]. Thus, even in the absence of disparities in care provided by the GP, preventive interventions may still be less effective in the lower socioeconomic groups. Future research should assess whether health care may contribute to stroke disparities through this alternative mechanism[114].

Finally, despite the absence of disparities in the quality of care for most stroke precursors in our study, there may still be socioeconomic differences in specialist care relevant for stroke prevention. Although patients with a low socioeconomic status use more general practice care, this is offset by an excess recourse of patients from the high socioeconomic categories to specialist care[28,37]. Furthermore, there are socioeconomic differences in treatment and survival after stroke even in countries with universal health care systems[20,57], which may contribute to socioeconomic disparities in stroke mortality in Europe. In the Netherlands, it is estimated that 25% to 35% of patients diagnosed with stroke are not hospitalised[115], which may reflect deficiencies in the management of stroke in the acute phase. Thus, disparities in the quality of care for stroke may exist at more specialised levels of the health care system.

What are the 'causes behind the causes' of socioeconomic disparities in stroke?

This thesis describes how a range of biological, behavioural and psychosocial factors mediate the association between socioeconomic status and stroke risk. These multiple pathways seem to act in synergy and thus lead to higher stroke risk among the socially disadvantaged groups. But what are the mechanisms behind this clustering of unfavourable risk factors in the lower socioeconomic groups and how do they persist across diverging societies? Multiple explanations have been provided to explain why 'the poor have poor health'. Socioeconomic differences in stroke are partly explained by behavioural factors such as smoking, which at first might be considered the result of personal choices and individual responsibility. However, it has now been widely accepted that individual choices are strongly embedded within economic and political contexts, which influence the choice process and the behavioural options available to individuals[116]. Following this line of enquiry, material deprivation has often been suggested as one of the major underlying mechanisms explaining socioeconomic differences in health (figure 11.1)[14]. Socially disadvantaged groups are more likely to be exposed to negative working circumstances, financial strain, and poor housing conditions, and to live in a deprived and unhealthy environment[14,117-120]. This is consistent with the fact that income and wealth – which are strongly related to material deprivation– were both strong predictors of stroke, independently of childhood circumstances and educational level (Chapter 5). The effect of material deprivation is likely to begin early in life, with poor material circumstances accumulating from childhood to adulthood and subsequently influencing adult risk factors and stroke risk[17,82,121]. This process of disadvantage accumulation advocates for a life-course perspective, which postulates that the risk of stroke is determined early in life and throughout the entire life span[17,82,87,93].

Material factors, however, do not act on themselves and are in fact only one among other mechanisms through which socioeconomic status might increase stroke risk (figure 11.1). Recent studies have indicated that socioeconomic status has an impact on psychosocial factors through a number of mechanisms, including psychobiological pathways[71,79]. Socioeconomic status may exert an effect on responses to psychosocial stressors that are more prevalent in deprived groups, such as job strain, hostility and social support[71,79,83]. These physiological reactions involve neuroendocrine and immunological responses such as daily function, rhythm (e.g., heart rate variability) and cortisol output over the day[71,79,83,122]. The role of these factors is consistent with the important contribution of psychosocial factors such as depression and social networks reported in this thesis, and suggests that inappropriate biological responses to these psychological stressors may to some extent underlie socioeconomic disparities in stroke.

From this perspective, it could be argued that socioeconomic status determines an individual's capacity to have access to a broad array of both material (e.g., housing, working conditions) and psychosocial (e.g., job control, self-efficacy) resources, which are less readily available to those in the most deprived socioeconomic groups. Among populations that have reached a relatively high level of living and economic standards such as those in European countries and the United States, psychosocial resources are likely to be at least as important as material resources in the explanation of socioeconomic disparities in stroke. Furthermore, psychosocial and material factors are likely to exert mutual influences; for instance, material deprivation can lead to psychosocial stress, but at the same time, low levels of self-efficacy may lead to material deprivation. On the basis of this argumentation, it could be argued that socioeconomic disparities in stroke stem from reduced access of a combination of material and psychosocial resources, which subsequently influence behavioural and biological responses that have an impact on stroke risk.

The above mechanism is a plausible explanation of stroke differentials. However, it does not fully account for the broader macro-social and distal factors that explain socioeconomic disparities in stroke. Assessing the impact of these mechanisms was beyond the aims of our study, which focused on more proximal determinants of stroke disparities. Nonetheless, two assertions merit mentioning on the basis of our international comparative study: Firstly, among European countries, socioeconomic disparities in stroke seem to be unrelated to variations in egalitarian policies and welfare regimes across the region (Chapter 2). For instance, socioeconomic differentials in stroke in England and Southern Europe were as large in Scandinavian populations such as Finland and Norway, where wealth redistribution policies, social benefits and health insurance systems have traditionally been more generous[123,124]. These findings suggest that providing equal social and health care might not be enough to reduce socioeconomic disparities in stroke in the population.

On the other hand, we observed that the magnitude of socioeconomic differentials in IHD was associated with the geographic distribution of countries across Europe, with southern populations showing smaller disparities than northern states (chapter 4). Although this pattern was not observed for stroke, it is plausible that the advanced stage in the diffusion of the smoking epidemic in northern countries is associated with their higher level of economic development, which may not have yet been entirely realised in the southern states. In the absence of this north-south gradient in smoking disparities, larger socioeconomic disparities in stroke may have been observed in southern countries. On the contrary, we observed larger socioeconomic disparities in blood pressure levels in southern than in northern populations, as well as relatively small hypertension disparities within the United States. This may reflect higher levels of national awareness as a response to a more preventive orientation in northern European populations and the United States as opposed to southern European countries, which may have equally benefited all sub-groups in the population in the former regions.

Overall, results from our study raise multiple questions regarding the role of national policies on the magnitude of stroke disparities. Future research should elucidate how these marco-social mechanisms underlie the material circumstances that cause disparities in behavioural choices and psychosocial stress, and how these pathways ultimately lead to increased stroke risk among socially disadvantaged groups.

11.4 Implications

Implications for public health policy

The main implication of this thesis is that interventions aimed at reducing stroke incidence and mortality will need to place special focus on those with lower socioeconomic status. This targeted approach is likely to have the greatest impact on overall stroke mortality in many world populations. Following this line of enquiry, the present thesis raises three major important principles that should be considered in the development of policies and interventions to reduce stroke disparities: Firstly, combined interventions to reduce the prevalence of multiple stroke risk factors and precursors in lower socioeconomic groups will have the greatest impact on reducing their higher stroke rates, as opposed to interventions focused on a single risk factor. Secondly, the types of interventions needed to reduce stroke differentials are not the same for each population and age group, and are most likely to have an impact in the early stages of life. Thirdly, developing practice guidelines for the management of cardiovascular risk factors can contribute to the provision of standardized and equal preventive care for all. These three major recommendations will be discussed in more detail below.

Interventions and policies are likely to have the greatest impact if focused on a combined approach to reducing the prevalence of a few major risk factors in the most disadvantaged groups. Firstly, interventions to decrease blood pressure levels and hypertension prevalence in lower socioeconomic groups can have a major impact on European populations. This involves improvements in detection and management of hypertension aimed at decreasing the high blood pressure levels and increasing the low controlled hypertension levels among Europeans, which are evidenced already at ages 30 to 59[49]. Furthermore, populations-based prevention policies to stimulate a reduction in salt intake in lower socioeconomic groups can have a major impact. In particular, population-wide strategies to decrease salt concentration in processed foods have been shown to yield substantial reductions in blood pressure in the long-term[125], and will have the greatest impact on the socially disadvantaged groups. Furthermore, although action is needed in all European countries, interventions to decrease blood pressure levels are likely to have the greatest impact on stroke disparities in southern European populations.

Secondly, tobacco control policies focused on the lower socioeconomic groups will also contribute to reducing stroke disparities. Although smoking contributes to stroke differentials in continental and northern European populations, smoking disparities will most likely emerge in southern European populations in future decades as the smoking epidemic progresses in these countries[53,54]. An amalgam of interventions to reducing smoking prevalence is available and should be further implemented across borders. Measures at the macro-level include price and tax policies, mass media campaigns and publication education tailored to the lower socioeconomic groups, removing financial barriers to accessing smoking cessation programmes, and enforcement policies to restrict age of tobacco purchase. Smoking is adopted early in life[126]. Therefore, interventions to prevent smoking uptake among youngsters and adolescents from socially deprived groups are likely to have the greatest impact. Furthermore, interventions in multiple settings and the public environment might be necessary. For instance, workplace interventions targeted to those in the manual classes might contribute to reduce their higher smoking prevalence rates.

Thirdly, one of the central findings of this thesis is that tackling conventional risk factors for stroke will contribute but not eliminate stroke differentials. In addition, tackling the higher prevalence of psychosocial risk factors in lower socioeconomic groups is at least as important to eliminate stroke disparities. Depression was a major contributor to stroke differentials, particularly at early old age (65 to 74). Much of the effect of low income on the risk of depression seems to occur through increased financial strain[118], which might subsequently lead to stroke. Thus, tackling depression may require policies for improving material and financial conditions in the socially disadvantaged, through mechanisms such as better income redistribution, housing support and improved pension benefits for these groups. Furthermore, prevention strategies to increase self-esteem and improve depression management and detection tailored to those in low socioeconomic groups are required. Lower social networks among elderly with a low socioeconomic status also contributed significantly to their increased stroke risk. Interventions tailored to the socially disadvantaged elderly aimed at preventing isolation, promoting physical and cognitive function, and increasing mobility in the community can contribute to decrease their stroke risk. Additionally, interventions to increase socially disadvantaged individuals' sense of control at different settings such as the workplace might contribute to reduce their stroke risk.

This thesis evidences large socioeconomic differentials in diabetes prevalence. Interventions for improving diabetes awareness, detection and management tailored to the low socioeconomic groups can contribute to reduce their increased stroke risk, particularly at early old age (65 to 74). Furthermore, population wide-strategies to increase fruit and vegetable consumption tailoring the low socioeconomic groups can yield a modest reduction on their stroke risk. Other risk factors such as body mass index, alcohol consumption and hypercholesterolemia might be important but did not seem to yield a large contribution to stroke differentials in most of our studies.

We found no evidence of socioeconomic disparities in many aspects of preventive care for which clear-cut guidelines have been developed in the Netherlands. Translating the Dutch experience to a broader European or international level through the provision evidence-based guidelines can not only contribute to improving the quality of care, but also promoting equal and standardized preventive care across socioeconomic groups. In agreement with this view, increasing consensus among clinical practitioners and developing guidelines for the prescription of statins after stroke and TIA based on results from recent clinical trials such as the SPARCL (stroke prevention by aggressive reduction in cholesterol level) study[127] could contribute to reducing disparities among these patients. Overall, bridging the time gap between the point at which scientific evidence becomes available and the implementation of evidence-based practice guidelines can contribute to ensure standardized and equal preventive care for all.

Implications for clinical practice

Results from this thesis suggest that the quality of general practice care plays only a limited role in the explanation of socioeconomic disparities in stroke in the Netherlands. However, clinicians can still contribute to tacking stroke disparities in a number of different ways: Firstly, risk factor management should be dependent on the individual characteristics of each patient. Nevertheless, following basic general practice guidelines can significantly contribute to the reduction of stroke occurrence regardless of patients' social position or demographic characteristics. Thus, continued efforts by physicians to adhere to guidelines for the detection and management of hypertension, diabetes, hypercholesterolemia, and other stroke risk factors among patients from all socioeconomic groups can contribute to reduce socioeconomic differentials in stroke. Despite equal care among patients from different socioeconomic status, disparities in stroke remained in the population. Thus, even better levels of care in the low socioeconomic groups might be necessary to achieve equal outcomes.

Secondly, socioeconomic differentials in stroke are largely the result of higher prevalence of stroke risk factors and precursors. General practitioners can play a central role in providing advice for lifestyle changes among those from the lower socioeconomic groups. This could include individual recommendations for participation in smoking cessation programmes, decreasing the consumption of salt, and adhering to recommended levels of fruit and vegetable consumption and physical activity. General practitioners play a gate-keeping role in the healthcare system in most European countries and can thus ensure that prevention messages reach large groups of patients in all social strata.

Individuals with a low socioeconomic status may be less likely to have their depression detected, and therefore be less likely to be treated for this condition. General practitioners have frequent contact with older individuals and can therefore play an important role in the screening of depression among patients with a low socioeconomic status. Subsequently, general practitioners should ensure that individuals from all socioeconomic groups have access to adequate management and treatment for depression. General practitioners can also contribute to identifying individuals with lower social networks by placing emphasis on these aspects during doctor-patient encounters. Likewise, they can encourage elderly patients to participate in social activities and thus broader their social contacts.

Finally, we found that elderly patients with lower socioeconomic status are more likely to experience physical and cognitive limitations, which partly explains their increased risk of stroke. Clinicians should ensure that elderly patients with disability limitations from all socioeconomic groups have access to rehabilitation services, which can enhance their ability to participate in society, and increase their social networks and physical activity. As the toll of disability hits particularly the socially disadvantaged, improved access to these programmes may contribute to reducing socioeconomic differentials in the occurrence of stroke.

Implications for future research

The present thesis described socioeconomic differentials in stroke mortality across Europe. Further descriptive research should focus on overcoming three major problems in existing studies: Firstly, international studies that describe socioeconomic differentials in stroke subtypes based on the use of brain imaging techniques can contribute to assess whether a different international pattern might exist for ischaemic stroke and cerebral haemorrhage. Large international studies such as the MONICA project[128] could provide the necessary means for this purpose. Secondly, international comparisons of stroke incidence and survival after stroke can contribute to distinguish the effect of socioeconomic status on first occurrence and case-fatality, and how this may vary between countries. Thirdly, existing international comparisons have focused on the effect of educational level, a socioeconomic indicator that is established early in life[129]. However, most strokes occur at very old ages[130]. Therefore, international studies should assess how socioeconomic indicators that reflect material conditions of the elderly such as wealth have an impact of stroke in different populations. Such studies can contribute to reveal the potential impact of social, welfare and entitlement programme policies such as Medicare on the socially disadvantaged elderly by comparing the magnitude of stroke disparities in different countries.

Multiple studies have described the association between socioeconomic status and stroke. Therefore, future research should largely focus on revealing the mechanisms through which stroke disparities occur, by focusing in three major areas: Firstly, further research should focus on the contribution of psychosocial risk factors in different European countries. For instance, it has been established that the prevalence of depression is substantially larger in southern than northern European populations[131]. However, no studies have assessed the contribution of this factor to socioeconomic differentials in stroke in these countries. Conversely, social networks might be a more prominent factor in northern Europe, where the elderly might be less likely to remain in the community and more prone to institutionalisation. These studies can contribute information on specific areas on which psychosocial interventions should focus in each population.

Secondly, further explanatory research is warranted on the biological mechanisms through which psychosocial factors increase the risk of stroke among lower socioeconomic groups. Factors such as depression and social networks explained a large part of socioeconomic differentials in stroke, but the biological mechanisms through this effect takes place remain largely unknown. For instance, recent studies have established that biological markers of psychosocial stress such as heart rate recovery explain a considerable part of socioeconomic differences in all-cause mortality[122]. Future studies of this type that assess the impact of these factors on socioeconomic differences in stroke are necessary. Furthermore, further studies should examine the role of novel risk factors for stroke such as hyperhomocysteinemia, platelet reactivity, infectious agents and C-reactive protein as potential mediators of the association between socioeconomic status and stroke.

Thirdly, there is limited knowledge on the explanation of socioeconomic differentials in stroke survival[20-23]. Several studies indicate that post-stroke depression confers a high risk for subsequent mortality independently of conventional risk factors[132-136], and is associated with increased disability and cognitive impairments after stroke[137-139]. Therefore, future studies should assess whether depression after stroke is more common among stroke patients in lower socioeconomic groups and whether this contributes to their lower post-stroke survival. Other factors that may have a potential role on survival disparities include cardiovascular risk profile, disability impairments, speed of recovery after stroke and copying style.

Fourthly, substantial research suggests that childhood socioeconomic status is associated with stroke incidence and mortality[17,87,93-95,121,140]. Further studies should assess whether this association differs for ischaemic and haemorrhagic stroke, and address the potential pathways through which childhood circumstances increase the risk of stroke. Future research should adopt a lifetime perspective that considers socioeconomic position at different stages of the life course and how these interact to influence stroke risk.

Our study suggested that several aspects of preventive healthcare did not play a major role in explaining socioeconomic disparities in stroke in the Netherlands. Further research is required to ascertain whether this pattern is also observed in other countries such as the US, where no universal healthcare system is available. Most importantly, research should examine whether there might be socioeconomic disparities in the quality of post-stroke secondary care, and whether these might contribute to socioeconomic differences in survival. This comprises post-stroke acute procedures such as brain imaging, laboratory tests and aspirin within 48 hours; and secondary preventive measures such as carotid endarterectomy, antiplatelet agents, oral anticoagulants, antihypertensive agents, and statins prescription[141]. Particularly among stroke outpatients, shortcomings have been identified in the quality of secondary preventive care in the Netherlands[141]. Furthermore, research should examine whether there are socioeconomic differentials in host response to therapeutic interventions, due to differences in factors such as patient's adhere to therapy and susceptibility to the impact of interventions[114].

Finally, the present thesis had a number of methodological limitations that will need to be addressed in future research. Firstly, studies should attempt to replicate the age-decline or crossover in the association between socioeconomic status and stroke, and formally assess the contribution of selective survival to this pattern. Although this has been assessed for total mortality[142], the specific age patterning of stroke might yield a different outcome. Secondly, future studies should attempt to overcome the problems inherent to the decomposition approach, and to develop new methods to assess the contribution of risk factors to socioeconomic differences in health. Additionally, future explanatory studies should incorporate repeated measurements that take into account changes in factors such as blood pressure throughout the follow-up period, or apply correction methods to assess the potential effects of regression dilution[33,34]. Finally, future studies on trends in stroke mortality in populations with low stroke rates such as Norway, US and Australia[2] should assess the role of socioeconomic status in explaining the slow down in the stroke mortality decline during recent decades in these particular countries. Understanding these issues can help developing targeted interventions aimed at sustaining the stroke mortality decline in all populations.

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Summary

Summary

This thesis aimed to contributing to the understanding of socioeconomic differences in stroke from an international perspective. **The overall aim** of the thesis was to estimate the magnitude of socioeconomic differences in stroke across different world populations, and to assess the contribution of biological, behavioural, psychosocial and preventive health care related risk factors to socioeconomic differentials in stroke. Three research questions formed the basis for this thesis:

1. What is the international pattern of socioeconomic differences in stroke mortality during the last decades among men and women at middle and old ages in Europe and the United States?

2. What is the role of biological, behavioural and psychosocial risk factors in the explanation of socioeconomic differences in stroke?

3. What is the impact of inequity in the quality of preventive care and cardiovascular risk management on socioeconomic differences in stroke?

For this purpose, we studied the association between socioeconomic status and stroke using multiple data sources. In order to address the first research question, three data sources were used: Firstly, mortality data from 10 European populations were collated to assess the international pattern of socioeconomic disparities in stroke and how this varies by age and gender. Mortality data were obtained from death registries and linked with census data, in most cases comprising information for the entire population or a specific region. Data were longitudinal typically comprising five years of follow-up. Secondly, we used data for the periods 1981-85 to 1991-95 from six European countries to assess trends in socioeconomic disparities in stroke. Finally, we used data from the Health and retirement study (HRS) to assess socioeconomic disparities in stroke in the US. The HRS comprises a representative sample of the US population aged 50 years and older.

In order to address the second research question, three data sources were used: Firstly, we used data from Globe, a longitudinal study of men and women aged 40 to 74 years living in the south of the Netherlands. Data comprised information on biomedical, behavioural and psychosocial risk factors obtained through baseline interview. Stroke incidence was ascertained during 12 years of follow-up through linkage with the national hospital diagnosis registry. Secondly, data were used from the New Haven cohort of the EPESE (Established Populations for the Epidemiologic Studies of the Elderly) study. Individuals provided baseline information on demographics, functioning, cardiovascular and psychosocial risk factors, and were followed for 12 years for stroke outcomes. Finally, data from the EPIC (European Prospective Investigation into Cancer) study was used. EPIC comprises information on over half a million men and women from eight European countries who completed a validated diet and health questionnaire at baseline and were followed for mortality (mean 5.3 years).

For addressing the third research question, data from the NS2 (second national survey of general practice) in the Netherlands was used. This study comprises information on about 400,000 patients registered in approximately 100 general practices. A survey on demographic information was performed at baseline. Subsequently, data were collected on diagnoses, referrals, prescriptions and diagnostic procedures received by patients for a period of 12 months.

Part II of this thesis comprises chapters 2 to 6 and examines socioeconomic disparities in stroke from an international perspective (research question 1).

Variations between countries were reported in socioeconomic disparities in stroke during the 1980s among middle-aged men. **Chapter 2** presents results from analyses on educational level and stroke mortality in 10 European populations during the 1990s based on longitudinal data, and comprising information for men and women aged 30 years and older. Results suggest that socioeconomic disparities in stroke mortality according to educational level were of similar magnitude in most Western European countries. The only exception was Austria, where larger stroke disparities were observed. Overall, socioeconomic disparities were of similar magnitude in men and women and generally decreased with age. Importantly, we found that eliminating stroke disparities would on average reduce educational level differences in life expectancy by 7% among men and 14% among women. Although the association between socioeconomic status and stroke is similar across countries, the explanation of these disparities is likely to be different across populations. However, similarities point also at the potential role of common explanatory factors such as hypertension, which may contribute to stroke disparities in all populations. Overall, these results highlight the importance of socioeconomic disparities in stroke as a major public health problem in many Western populations.

Stroke mortality has been declining for several decades in most Western populations. **Chapter 3** examines whether these trends in stroke mortality were less favourable among lower than among higher socioeconomic groups in the period 1985-1995, using data for the entire population or a representative sample in six European populations. We compared trends in stroke mortality with trends in IHD (ischaemic heart disease) mortality. Results indicate that trends in stroke mortality were generally as favourable among lower as among higher socioeconomic groups, such that socioeconomic disparities in stroke mortality persisted and remained of a similar magnitude in the 1990s as in the 1980s. In Norway, however, occupational disparities in stroke mortality significantly widened, and a non-significant tendency for increasing disparities was observed in Finland. Stroke and IHD share several risk factors. However, socioeconomic disparities in IHD mortality showed a general tendency to widen in most populations during the same period. This suggests that there may be differences in the underlying causes of socioeconomic disparities in stroke and IHD mortality. Overall, results suggest that stroke mortality trends in all socioeconomic groups have been responsive to favourable changes in important risk factors such as hypertension. However, the persistence of socioeconomic inequalities in stroke mortality indicates that recent changes in policies and risk factors have not been sufficient to reduce these disparities.

Chapter 4 examines the international pattern of socioeconomic differences in IHD, stroke and lung cancer mortality in Europe. As these three causes of death share several risk factors, comparing the international pattern of disparities can provide information on common risk factors that may explain socioeconomic disparities in mortality. Socioeconomic disparities in IHD mortality were larger in the Scandinavian countries and England/Wales, of moderate size in Belgium, Switzerland, and Austria, and smaller in southern European populations among men and younger women. No socioeconomic disparities in IHD mortality existed among elderly men in southern Europe. These findings support the hypothesis of a north-south gradient in socioeconomic disparities in IHD mortality among men and younger women. Among elderly women, this north–south pattern was smaller and there was less variation between populations. A similar north-south gradient for lung cancer points at the role of smoking in explaining socioeconomic disparities in both lung cancer and IHD mortality. Instead, this north–south gradient was not observed for stroke: Socioeconomic disparities in stroke mortality are similar across countries, which may point at the role of other factors such as hypertension. These results indicate that the international pattern of socioeconomic disparities differs for the two main cardiovascular diseases, despite having common determinants. Furthermore, this study highlights the fact that the explanation of socioeconomic disparities in IHD mortality may differ by country.

Studies on socioeconomic disparities in stroke have been largely focused on the effect of education in middle-aged populations. **Chapter 5** examines the independent effect of wealth, income and education on stroke incidence in the US population, and assesses how these effects vary throughout age. Among men and women aged 50 years and over, lower wealth, income and education were associated with higher stroke incidence. This pattern was mainly attributable to a large effect in those aged 50 to 64. In this age strata, wealth was the strongest independent predictor of stroke net of other socioeconomic status indicators. The effect of all socioeconomic status indicators decreased sharply beyond age 65, resulting in no consistent effect of wealth and income among the elderly. Education was not a predictor of stroke beyond age 65. After adjustment for risk factors, income and wealth disparities in stroke at ages 50 to 64 were attenuated but remained consistent, whereas no effect of education persisted. Results suggest that wealth and income are independent predictors of stroke at ages 50 to 64, whereas disparities decrease considerably beyond age 65. The age-attenuation of socioeconomic disparities in stroke likely reflects selective survival, a consequence of the cumulative disadvantage faced by individuals throughout the life-course.

Part III of this thesis comprises chapters 6 to 8 and examines the role of behavioural, psychosocial and nutritional factors in explaining the association between socioeconomic status and stroke.

Studies aimed to explaining socioeconomic disparities in stroke have only assessed the role of conventional cardiovascular risk factors in accounting for relative disparities. **Chapter 6** extends these efforts by examining the impact of conventional but also psychosocial risk factor modification on both relative and absolute stroke disparities. Adopting a counterfactual analysis perspective, we estimated the potential reduction that would be achieved in absolute and relative stroke differentials, under a hypothetical scenario of optimal theoretical minimum population distribution of risk factors (e.g., zero-prevalence of smoking). Biomedical and behavioural risk factors such as hypertension and smoking contributed to stroke disparities, but they explained less than half of relative disparities. Interestingly, locus of control and emotional support explained an additional part of relative stroke differentials. Aggressive modification of blood pressure, smoking, excessive alcohol consumption, heart disease, locus of control, emotional and instrumental social support to the theoretical minimum distribution would lead to a substantial reduction of absolute stroke disparities. Overall, findings suggest that although conventional risk factors play a role, psychosocial risk factors contribute considerably to both relative and absolute stroke disparities. Therefore, interventions to reduce population exposure to both conventional and psychosocial factors are necessary to eliminate socioeconomic disparities in stroke.

Little research has examined whether socioeconomic disparities in stroke varies across age-groups, and the factors that mediate this association in the elderly. **Chapter 7** examines the effect of socioeconomic status on stroke incidence and how this varies for the old and oldest old in a sample of US elderly. Furthermore, it estimates the contribution of biomedical, psychosocial and functioning risk factor to these disparities. At ages 65 to 74 years, lower education and income were associated with higher stroke incidence. Adjustment for race, diabetes, depressive symptomatology, social networks, and cognitive/physical functioning reduced these associations considerably, whereas other conventional risk factors did not alter associations. Beyond age 75, higher socioeconomic status was associated with higher stroke rates, even after adjustment for risk factors. Results indicate that socioeconomic disparities remain up to age 74, whereas a crossover of the association occurs beyond age 75. Findings suggest that policies to improve social and economic resources at early old age, and interventions to improve diabetes management, depression, social networks and functioning in the disadvantaged elderly can contribute to reduce stroke disparities.

Chapter 8 examines socioeconomic disparities in stroke and IHD mortality in Europe, and estimates the contribution of biological, behavioural and nutritional risk factors to these disparities. Furthermore, it assesses whether the contribution of risk factors to socioeconomic differences in stroke and IHD mortality is different for northern and southern European populations. Based on data from a large prospective study, we found that lower educational level was associated with higher stroke and IHD mortality across Europe. These associations were partly attenuated after adjustment for blood pressure and hypertension, height, smoking, physical activity at work, and fruit and vegetable consumption. BMI (body mass index) contributed to socioeconomic differences in IHD mortality only, whereas other risk factors did not contribute to stroke or IHD socioeconomic differentials. Interestingly, smoking contributed to socioeconomic differentials in cardiovascular disease in northern but not in southern populations. In contrast, blood pressure and hypertension contributed to stroke socioeconomic differentials in all countries. Apart from a modest contribution of fruit and vegetable consumption, we found no evidence of a major role of nutrition patterns in explaining socioeconomic differentials in cardiovascular mortality. Overall, findings highlight differences in the explanation of socioeconomic differences in stroke and IHD, as well as variations between countries in these mechanisms.

Part IV of this thesis comprises chapters 9 and 10 and focuses on the role of preventive care in general practice in explaining socioeconomic disparities in stroke.

Previous studies on the role of healthcare have focused on the hospital setting, and have only assessed disparities in health care utilization. **Chapter 9** examines socioeconomic disparities in stroke incidence and in the quality of preventive care for precursors of stroke in the Netherlands. We developed quality indicators based on evidenced based guidelines for stroke prevention at general practice, and assessed deviations from these guidelines. We observed socioeconomic disparities in the prevalence of stroke precursors including hypertension, hypercholesterolemia, diabetes mellitus, angina pectoris, heart failure and peripheral artery disease. GPs were less likely to comply with guidelines on statin prescriptions for second-line treatment of hypercholesterolemia in patients with a lower socioeconomic status. However, the quality of care for other precursors of stroke was similar for all socioeconomic groups. Universal access to general practice care and the implementation of general practice guidelines in the Netherlands are likely to have promoted the provision of equal and standardised care for stroke precursors across socioeconomic groups. Overall, reducing disparities in the primary occurrence of stroke precursors may be more important than reducing disparities in subsequent preventive care.

Statin treatment can reduce the risk of stroke by about 17%-21%, and by as much as 27% among hypertensive patients. **Chapter 10** assesses social inequity in statin prescription for primary and secondary prevention in general practice for various patient sub-groups in the Netherlands. Overall, we observed no major social disparities in the prescription of statins for primary prevention. However, although most patients under cholesterol-lowering medication received statins as recommended by guidelines, hypercholesterolemia and hypertensive patients in the lower socioeconomic groups were less likely to receive statins as primary choice of treatment for primary prevention. We observed no disparities in the prescription for statins for secondary prevention among IHD patients. In contrast, our study evidences large socioeconomic disparities in the prescription for statins in men diagnosed with CVA (cerebrovascular accident). This may reflect the fact that evidence of effectiveness of statins among patients with CVA has been less widespread among clinicians. Despite overall improvements, disparities remain in the prescription for statins as first choice of cholesterol treatment, and for secondary prevention among patients with CVA. Findings suggest that strategies to build up consensus and reassure physicians through clear-cut recommendations might contribute to reduce disparities in the prescription for statins in patients with CVA.

Chapter 11 discusses the main findings of this study, the most important methodological limitations, and the possible explanations for socioeconomic disparities in stroke.

Furthermore, this chapter provides recommendations for policy and future research necessary to understand and address socioeconomic disparities in stroke.

Results from this thesis suggest that socioeconomic status is associated with stroke mortality in many countries, and that stroke disparities are remarkably similar across European populations. Furthermore, although a similar stroke mortality decline has occurred among those with high and low socioeconomic status, socioeconomic disparities have remained unchanged and persisted into recent years across Europe. The international and time patterning of disparities was noticeably different for stroke and IHD mortality. Whereas socioeconomic disparities in IHD mortality have widened, disparities in stroke have remained largely unchanged and persisted into recent years. Furthermore, whereas socioeconomic disparities in stroke were of similar magnitude, socioeconomic disparities a north-south gradient in socioeconomic differences in IHD mortality was observed. These results suggest that IHD disparities might be largely driven by disparities in factors such as smoking, which show a different patterning across north and south Europe. In contrast, results point at the possibility of a common explanation of socioeconomic differences in stroke across countries. In particular, disparities in prevalence, detection and treatment of hypertension are likely to play a role in the explanation of socioeconomic differentials in stroke and their consistency across Europe.

Our in-depth studies indicate that socioeconomic differentials in stroke result from the combination of multiple risk factors, and that explanations are not uniform in all countries. Blood pressure appears to be the most important conventional factor in Europe, particularly in Northern populations. However, blood pressure did not contribute to stroke disparities in the US elderly, where disparities in blood pressure appear to be smaller. Smoking was also an important mediating factor in Northern Europe, whereas it did not contribute to stroke disparities in southern Europe. This is likely to reflect differences between northern and southern countries in the progression of the smoking epidemic. Other factors that contributed to stroke disparities were BMI, previous heart disease, alcohol intake and physical activity. Overall, our results indicates that these conventional (biological and behavioural) risk factors are important but explain less than half of socioeconomic differentials in stroke.

Interestingly, we found that a substantial share of unexplained stroke differentials was accounted for by psychosocial risk factors. Of particular interest were depression and social networks among the US elderly, and locus of control and social support among Dutch participants. These results raise questions about the possibility that psychosocial factors influence stroke risk via psychobiological pathways. Although our study does not provide direct evidence, findings are in agreement with the hypothesis that psychosocial factors contribute to stroke differentials independently of behavioural factors. Further research is necessary to elucidate these biological pathways that may explain this effect.

Overall, our study suggests that the quality of preventive care may only play a limited role in explaining socioeconomic differences in stroke. We observed disparities in the prescription for statins as first choice of cholesterol treatment, and for secondary prevention among patients with CVA. Strategies to reassure physicians through clear-cut recommendations might contribute to reduce disparities in the prescription for statins in patients with CVA. However, overall, the quality of care for other precursors of stroke was similar for all socioeconomic groups. Universal access to general practice care and the implementation of general practice guidelines in the Netherlands are likely to have promoted the provision of equal and standardised care for stroke precursors across socioeconomic groups.

We argue that socioeconomic status determines an individual's capacity to have access to a broad array of both material (e.g., housing, working conditions) and psychosocial (e.g., job control, self-efficacy) resources, which are less readily available to those in the most deprived socioeconomic groups. Among populations that have reached a relatively high level of living and economic standards such as those in European countries and the United States, psychosocial resources are likely to be at least as important as material resources in the explanation of socioeconomic disparities in stroke. On the basis of this argumentation, it could be argued that socioeconomic disparities in stroke stem from reduced access of a combination of material and psychosocial resources, which subsequently influence behavioural and biological responses that have an impact on stroke risk.

Interventions aimed at reducing stroke incidence and mortality will need to place special focus on those with lower socioeconomic status. Combined interventions to reduce the prevalence of multiple stroke risk factors and precursors in lower socioeconomic groups will have the greatest impact, as opposed to interventions focused on a single risk factor. Further to interventions to tackle conventional cardiovascular risk factors, addressing the higher depression levels and increasing social support and networks in socially disadvantaged populations is necessary to reduce stroke disparities. The types of interventions needed to reduce stroke differentials are not the same for each population and age group, and are most likely to have an impact in the early stages of life. Finally, developing practice guidelines for the management of risk factors can contribute to the provision of standardized and equal preventive care for all, as observed in the Dutch population.

Overall, results indicate that socioeconomic disparities in stroke are a major public health problem that requires combined interventions and policies. Reducing these disparities is essential to sustain the stroke mortality decline in the developed world.

Samenvatting

Samenvatting

In dit proefschrift onderzoeken wij sociaal-economische verschillen in het cerebrovasculaire accident (CVA) in verschillende populaties, en de bijdragen van biologische, gedrags, psychologische en preventiezorg gerelateerde determinanten aan deze verschillen. De onderzoeksvragen die in dit proefschrift centraal staan luiden als volgt:

- Wat is het internationale patroon van sociaal-economische verschillen in CVA mortaliteit in de laatste decennia onder mannen en vrouwen van middelbare en oudere leeftijd in West-Europese landen en de Verenigde Staten?
- Wat is de bijdrage van biologische, gedrags en psychologische determinanten aan deze sociaal-economische verschillen in CVA?
- Wat is de bijdrage van verschillende in de kwaliteit van preventiezorg en behandeling van cardiovasculair risicofactoren aan sociaal-economische verschillen in CVA?

Verschillende soorten van gegevens zijn voor dit onderzoek gebruikt. Voor het beantwoorden van de eerste onderzoeksvraag zijn 3 databronnen gebruikt. Ten eerste zijn sterfte gegevens van een aantal bevolkingsgroepen van West-Europese lande verkregen. Deze sterfte gegevens bestaan uit een combinatie van informatie over het aantal sterftegevallen in verschillende sociaal-economische groepen binnen een afgebakende periode (deze informatie is afkomstig uit sterftestatistieken), en informatie over het totaal aantal personen binnen de sociaal-economische groepen. Deze longitudinale gegevens bevatten een follow-up van ongeveer 5 jaar. Ten tweede is gebruikt gemaakt van sterfte gegevens van sociaal-economische groepen van zes Europese landen in de periode 1981-1995. Te laatste zijn gegevens van de *Health and retirement survey (HRS) study* gebruikt om sociaal-economische verschillen in CVA onder oudere mannen en vrouwen in de Verenigde Staten te onderzoeken.

Drie soorten van gegevens zijn gebruikt om een antwoord op de tweede onderzoeksvraag te formuleren: Ten eerste zijn gegevens van de *Globe studie* gebruikt. Globe is een longitudinale studie onder mannen en vrouwen (40-74 jaar) die in het zuiden van Nederland wonen. Het databestand bevat gegevens over biologische, gedrags- en psychologische risicofactoren, verzameld door een baseline interview. Door 12 jaar follow-up zijn gegevens over CVA incidentie verkregen, via koppeling met de landelijke registratie van ziekenhuis opnamen (PRISMANT). Ten tweede zijn gegevens van de EPESE (Established populations for the Epidemiologic studies of the Elderly) studie gebruikt. Deze studie bevat informatie over demografische, functionerings, cardiovasculaire en psychologische risicofactoren onder mannen en vrouwen, met een follow-up van 12 jaar m.b.t. CVA incidentie. Ten laatste zijn gegevens dan de EPIC (European Prospective Investigation into Cancer) studie gebruikt. Deze gegevens bevatten informatie over voeding and gezondheid over een ongeveer half miljoen mannen en vrouwen in acht Europese landen.

Gegevens van de NS2 studie (Tweede Nationale Studie) zijn gebruikt om een antwoord op de derde onderzoeksvraag te formuleren. Deze studie bevat informatie over ongeveer 400,000 patiënten die zijn ingeschreven bij ongeveer honderd huisartsen in Nederland. Allereerst werd in deze studie een meting gedaan m.b.t. de demografische kenmerken van de patiënten. Vervolgens werden gegevens verzameld over diagnosen, verwijzingen, voorschriften en diagnostische procedures door middel van registratie van alle contacten tussen huisarts en patiënt over een periode van 12 maanden (registratie van een beperkt aantal basiskenmerken van alle patiënten ingeschreven bij de aan de studie deelnemende huisartsen, en een enquête onder patiënten ingeschreven bij de deelnemende huisartsen).

Deel II van dit proefschrift omvat hoofdstukken 2 tot en met 6. Deze Hoofdstukken gaan over sociaal-economische verschillen in CVA in verschillende landen (onderzoeksvraag 1).

Vorige studies hebben variatie tussen landen in sociaal-economische verschillen in CVA mortaliteit gerapporteerd onder middelbare mannen. **Hoofdstuk 2** beschrijft analyses over de relatie tussen opleidingniveau en CVA sterfte in tien Europese landen in de jaren negentig. Dit zijn longitudinale data over mannen en vrouwen van 30 jaar en ouder. Resultaten suggereren dat sociaal-economische verschillen (gebaseerd op opleidingsniveau) in CVA sterfte tussen landen niet verschillen. Oostenrijk is het enige land waar sociaal-economische verschillen in CVA groter zijn vergeleken met andere West-Europese landen. Sociaal-economische verschillen tussen mannen en vrouwen bleken niet te verschillen en namen over het algemeen af met de leeftijd. Het terugbrengen van sociaal-economische verschillen in CVA sterfte zou sociaal-economische verschillen in de levensverwachting verminderen tot 7% onder mannen en tot 14% onder vrouwen. Ondanks het feit dat sociaal-economische verschillen in CVA tussen landen niet verschilt, verschilt de verklaring van deze verschillen waarschijnlijk wel. Desalniettemin wijzen deze resultaten op mogelijk gedeelde risicofactoren in het verklaren van sociaal-economische verschillen in CVA in alle landen, zoals hypertensie. Resultaten van deze studie tonen dat het reduceren van sociaal-economische verschillen in CVA op zichzelf weer een vereiste voor het verbeteren van de volksgezondheid is.

In de afgelopen decennia is CVA sterfte in de meeste West-Europese landen afgenomen. In **Hoofdstuk 3** onderzoeken we of de CVA sterfte in alle sociaal-economische groepen evenzeer is afgenomen binnen West Europa in de periode 1985-1995. Gegevens van een aantal bevolkingsgroepen van zes West-Europese landen zijn daartoe gebruikt. Bovendien vergelijken we trends in CVA met trends in IHZ (ischemische hartziekten). De resultaten laten zien dat trends in CVA sterfte gelijk waren in de hoger en de lager sociaal-economische groepen, zodat sociaal-economische verschillen in CVA gelijk bleven in de jaren ’80 en ’90. Een uitzondering was Noorwegen, waar sociaal-economische verschillen in CVA sterfte significant toe zijn genomen. Een niet-significante toename zien we ook in Finland.

CVA en IHZ hebben een aantal risicofactoren gemeenschappelijk. Sociaal-economische verschillen in IHZ zijn echte de afgelopen jaren toegenomen in de meeste onderzochte populaties. Op basis van deze resultaten kan worden gesteld dat de determinanten van trends in sociaal-economische verschillen in CVA en IHZ zouden kunnen verschillen. In het algemeen suggereren deze resultaten dat CVA sterfte in alle sociaal-economische groepen afgenomen heeft als gevolg van veranderingen in risicofactoren zoals hypertensie. Niettemin suggereren de resultaten dat beleidsinterventies om sociaal-economische verschillen in CVA te reduceren in de laatste jaren niet succesvol zijn geweest, zodat sociaal-economische verschillen in CVA blijven bestaan in West-Europese landen.

Hoofdstuk 4 geeft een overzicht van de sociaal-economische verschillen in IHZ, CVA en longkanker in Europa. Deze drie doodsoorzaken hebben een aantal risicofactoren gemeenschappelijk. Vergelijking van sociaal-economische verschillen in deze doodsoorzaken kan inzicht geven in de gemeenschappelijke risicofactoren die sociaal-economische verschillen in sterfte kunnen verklaren. Sociaal-economische verschillen in IHZ onder mannen en jongere vrouwen blijken groter te zijn in Scandinavië landen en Engeland/Wales, gemiddelde in België, Zwitserland en Oostenrijk, en kleinere in Zuid-Europese landen. We vonden geen sociaal-economische verschillen in IHZ sterfte onder oudere mannen in Zuid-Europa. Deze resultaten bevestigen de hypothese dat er een Noord-Zuid gradiënt is in de mate van sociaal-economische verschillen in IHZ sterfte onder mannen en jongere vrouwen. Onder oudere vrouwen is deze Noord-Zuid gradiënt in sociaal-economische verschillen minder duidelijk en was er kleinere variatie in sociaal-economische verschillen in IHZ sterfte tussen de landen. Dezelfde Noord-Zuid gradiënt in sociaal-economische verschillen wordt waargenomen voor longkanker. Noord-Zuid gradiënten in sociaal-economische verschillen in IHZ en longkanker vormen een sterke aanwijzing dat roken een belangrijke factor is in het verklaren van sociaal-economische verschillen bij deze aandoeningen. Aan de andere kant verschillen de sociaal-economische verschillen in CVA sterfte tussen de landen niet, wat een aanwijzing is dat andere factoren zoals hypertensie belangrijke determinanten van sociaal-economische verschillen in CVA sterfte kunnen zijn. Op basis van deze resultaten kan worden gesteld dat sociaal-economische verschillen in CVA en IHZ verschillen, ondanks dat zij gezamenlijke risicofactoren hebben. Verder tont deze studie aan dat de verklaring van sociaal-economische verschillen in IHZ kan verschillen per land.

Hoofdstuk 5 besteedt aandacht aan het onafhankelijke effect van rijkdom, inkomen en opleidingsniveau op CVA incidentie onder mannen en vrouwen van 50 jaar en ouder in de Verenigde Staten. Bovendien wordt in dit hoofdstuk geëvalueerd in hoeverre deze effecten veranderen met de leeftijd. Onder mannen en vrouwen ouder dan 50 jaar blijkt lager inkomen en opleidingsniveau geassocieerd zijn met hogere CVA incidentie. Dit patroon is met name toe te schrijven aan een sterke effect onder de 50-64 jarigen. In deze leeftijdsgroep was rijkdom de sterkste onafhankelijke voorspeller aan CVA sterfte, ongeacht de invloed van andere sociaal-economische status indicatoren. De effecten van alle sociaal-economische status indicatoren namen af bij mensen ouder dan 65 jaar, zodat er geen effect van rijkdom en inkomen meer bestond onder ouderen. Opleidingsniveau was geen voorspeller van CVA incidentie bij mensen ouder dan 65 jaar. Na correctie van de invloed van de risicofactoren verminderden de effecten van inkomen en rijkdom in mensen van 50-64 jaar, hoewel een duidelijke effect bleef bestaan. Deze resultaten suggereren dat rijkdom en inkomen onafhankelijk voorspellers zijn van CVA incidentie onder mensen van 50-64 jaar, terwijl sociaal-economische verschillen in CVA boven de leeftijd van 65 jaar afnemen. Deze resultaten kunnen waarschijnlijk verklaard worden door het effect van ´selective survival´, een gevolg van de cumulatieve ongunstige situatie die mensen in de lagere sociaal-economische groepen gedurende hun levensloop meemaken.

Deel III van dit proefschrift bestaat uit de hoofdstukken 6 tot en met 8 en onderzoekt de rol van gedrags -, psychosociale, en voedingsfactoren in de verklaring van de associatie van sociaal-economische status met CVA.

Voorgaande studies die het doel hadden om sociaal-economische verschillen in CVA te verklaren hebben slechts de rol van traditionele cardiovasculaire risico factoren bepaald. **Hoofdstuk 6** bouwt hierop voort door niet alleen de impact van deze conventionele risico factoren te bepalen in relatieve en absolute sociaal-economische verschillen, maar ook de bijdrage van psychosociale risico factoren. Door gebruik te maken van een ‘counterfactual’ analyse perspectief, bepaalden we de mogelijke reductie in absolute en relatieve verschillen in CVA die bereikt zou worden in de hypothetische situatie dat de verdeling van risico factoren over de bevolking optimaal minimaal is (bijvoorbeeld door de prevalentie van roken op nul te zetten). Biomedische en gedragsfactoren zoals hypertensie en roken droegen bij aan de verschillen in CVA, maar zij verklaarden minder dan de helft van de totale relatieve verschillen. Interessant genoeg verklaarden locus of control en emotionele en instrumentele steun een additioneel deel van de relatieve verschillen. Het aanpassen van bloeddruk, roken, excessieve alcoholconsumptie, hartziekte, locus of control, en emotionele en instrumentele steun tot de theoretisch meest optimale waarden in de bevolking zou een substantiële bijdrage leveren aan het reduceren van absolute verschillen in CVA. Deze uitkomsten wijzen uit dat conventionele cardiovasculaire risico factoren een bijdrage leveren aan de verklaring van absolute en relatieve verschillen, maar dat daarboven psychosociale factoren een belangrijke rol spelen. Interventies dienen zich daarom te richten op zowel conventionele risico factoren als psychosociale factoren om sociaal-economische verschillen in CVA terug te dringen.

Maar weinig onderzoek is verricht naar mogelijke variaties in sociaal-economische verschillen in CVA tussen leeftijdsgroepen, en de specifieke factoren die de associatie mediëren onder ouderen. **Hoofdstuk 7** beschrijft het effect van sociaal-economische status op de incidentie van CVA, en leeftijdsvariaties onder ouderen en de oudste ouderen in een steekproef van ouderen uit de VS. Tevens beschrijft het de bijdrage van biomedische, psychosociale en functionele risico factoren aan verschillen in incidentie. In de leeftijden 65 tot 74 jaar bleken een lager niveau van opleiding en inkomen gerelateerd te zijn aan een hogere incidentie van CVA. Controleren voor ras, diabetes, symptomen van depressie, sociale netwerken, en cognitief en fysiek functioneren reduceerden de verschillen aanzienlijk, terwijl andere conventionele risico factoren niet van invloed waren op de associatie tussen sociaal-economische status en incidentie. Onder 75 plussers bleek dat een hogere sociaal-economische status gerelateerd was aan een hogere incidentie van CVA, ook na controle voor risico factoren. Deze resultaten geven aan dat er sociaal-economische verschillen in CVA blijven tot 74 jaar, maar dat er daarna een omslag plaatsvindt van de associatie van sociaal-economische status met CVA incidentie. Maatregelen om de sociale en economische middelen van ouderen te bevorderen en interventies om diabetes management, depressie, sociale netwerken en functioneren van de ouderen met een lagere status te verbeteren kunnen een aanzienlijke bijdrage leveren aan het verminderen van verschillen in CVA.

Hoofdstuk 8 onderzoekt sociaal-economische verschillen in CVA en Ischemische Hartziekte (IHZ) sterfte in Europa, en bepaalt de bijdrage van biologische, gedrags – en voedingsfactoren aan deze verschillen. Tevens onderzoekt het of de bijdrage van risico factoren aan sociaal-economische verschillen in CVA en IHZ sterfte verschilt tussen Noord – en Zuid-Europese populaties. Resultaten gebaseerd op data van een groot prospectief onderzoek toonden aan dat een lager opleidingsniveau gerelateerd was aan hogere sterfte aan CVA en IHZ in Europa. Controleren voor bloeddruk en hypertensie, lengte, roken, fysieke inspanning tijdens het werk, en consumptie van fruit en groente leidde tot een gedeeltelijke reductie van de associatie. Roken bleek bij te dragen aan sociaal-economische verschillen in cardiovasculaire ziekten sterfte in Noord-Europese, maar niet in Zuid-Europese populaties. Bloeddruk en hypertensie droegen juist wel bij aan sociaal-economische verschillen in CVA in alle populaties. Buiten een geringe bijdrage van fruit en groente consumptie vonden we geen indicatie van een belangrijke rol voor voedingsfactoren in het verklaren van sociaal-economische verschillen in cardiovasculaire sterfte. Deze bevindingen vestigen de aandacht op de verschillende verklaringen van sociaal-economische verschillen in CVA enerzijds en IHZ anderzijds, en op de verschillen in verklaringen van sociaal-economische verschillen in cardiovasculaire sterfte tussen Europese landen.

Deel IV van dit proefschrift bestaat uit de hoofdstukken 9 en 10 en richt zich op de rol van preventieve zorg in de huisartsenpraktijk in het verklaren van sociaal-economische verschillen in CVA.

Voorgaande studies naar de rol van de gezondheidszorg richtten zich op ziekenhuissettings en hebben tot nu toe slechts verschillen in gebruik van gezondheidszorg vastgesteld. **Hoofdstuk 9** onderzoekt sociaal-economische verschillen in de incidentie van CVA en in de kwaliteit van preventieve zorgverlening bij 'precursors' van CVA in Nederland. We ontwikkelden kwaliteitsindicatoren gebaseerd op evidence based richtlijnen voor de preventie van CVA in de huisartsenpraktijk en we onderzochten wanneer van deze richtlijnen werd afgeweken. We observeerden sociaal-economische verschillen in de prevalentie van precursors: hypertensie, hypercholesterolemia, diabetes mellitus, angine pectoris, hartfalen en perifere arteriële aandoening. Huisartsen bleken minder geneigd om aan de richtlijnen voor het voorschrijven van statines te voldoen in het geval van tweedelijns behandeling van hypercholesterolemie in patiënten met een lage sociaal-economische status. Echter, de kwaliteit van de zorg voor andere precursors van CVA was gelijk in alle sociaal-economische groepen. Algemene toegankelijkheid van de huisartsenpraktijk en de implementatie van algemene richtlijnen voor behandeling in Nederland hebben waarschijnlijk bijgedragen aan de levering van gelijke en gestandaardiseerde zorg voor CVA precursors aan alle sociaal-economische groepen. Het reduceren van verschillen in het optreden van CVA precursors is waarschijnlijk belangrijker dan het reduceren van verschillen in de daarop volgende preventieve zorg.

Behandeling met statines kan het risico op CVA met ongeveer 17%-20% verminderen, en met 27% in het geval van patiënten met een verhoogde bloeddruk. **Hoofdstuk 10** onderzoekt sociale ongelijkheid in het voorgeschreven krijgen van statines voor primaire en secundaire preventie in de huisartsenpraktijk in verschillende patiënten subgroepen in Nederland. Over het geheel genomen observeerden we niet veel sociale ongelijkheid in het voorgeschreven krijgen van statines voor primaire preventie. Maar hoewel de meeste patiënten met cholesterol verlagende medicatie statines kregen, zoals de richtlijnen aanbevelen, bleken patiënten met hypercholesterolemie en hypertensie in lagere sociaal-economische groepen minder vaak statines te hebben gekregen als de eerste keus van behandeling voor primaire preventie. We vonden geen ongelijkheid in het voorgeschreven krijgen van statines voor secundaire preventie onder patiënten met IHZ. Dit was in tegenstelling tot de grote sociaal-economische verschillen die we vonden onder mannen met een CVA (Cerebrovasculair accident) in het voorgeschreven krijgen van statines. Dit laatste kan te maken hebben met het feit dat bewijs voor de effectiviteit van statines in patiënten met CVA minder verspreid is onder clinici. Ondanks algemene verbeteringen is ongelijkheid in het voorgeschreven krijgen van statines voor cholesterol behandeling en voor secundaire preventie in patiënten met CVA blijven bestaan. Deze resultaten geven aan dat strategieën om consensus te bevorderen en artsen gerust te stellen door middel van duidelijke aanbevelingen kunnen helpen bij het terugdringen van ongelijkheden in het voorgeschreven krijgen van statines in patiënten met CVA.

Hoofdstuk 11 behandelt de belangrijkste bevindingen van dit onderzoek, alsmede de belangrijkste methodologische beperkingen ervan en de mogelijke verklaringen van sociaal-economische verschillen in CVA. Daarnaast geeft dit hoofdstuk aanbevelingen voor beleid en nieuw onderzoek.

De resultaten van dit proefschrift geven aan dat sociaal-economische status is gerelateerd aan CVA sterfte in verschillende landen en dat verschillen in CVA opmerkelijk vergelijkbaar zijn tussen landen. Hoewel zich een vergelijkbare afname in sterfte als gevolg van CVA heeft voorgedaan in zowel lage als hoge sociaal-economische groepen, zijn de sociaal-economische verschillen hierin niet veranderd en zijn blijven bestaan tot in recente jaren in Europa. Het internationale en tijdspatroon van verschillen was duidelijk verschillend voor CVA en IHZ sterfte. Zo zijn de verschillen in IHZ sterfte bijvoorbeeld toegenomen, terwijl de verschillen in CVA gelijk bleven gedurende afgelopen jaren. Verder bleek dat sociaal-economische verschillen in CVA van gelijke grootte waren, terwijl verschillen in IHZ sterfte een noord-zuid gradiënt in Europa vertoonden. Deze resultaten suggereren dat verschillen in IHZ grotendeels voortkomen uit verschillen in een factor als roken, waarvan het patroon sterk verschilt tussen Noord en Zuid-Europa. In tegenstelling daartoe geven de resultaten aan dat er een gemeenschappelijke verklaring kan zijn voor sociaal-economische verschillen in CVA voor verschillende landen. Vooral de verschillen in de prevalentie, detectie en behandeling van hypertensie spelen waarschijnlijk een belangrijke rol in de verklaring van sociaal-economische verschillen in CVA, en hun consistentie patroon over Europa.

Onze verklarende studies geven aan dat sociaal-economische verschillen in CVA het resultaat zijn van de combinatie van multipele risico factoren en dat de verklaringen niet uniform zijn in alle landen. De meest belangrijke conventionele factor in Europa blijkt bloeddruk te zijn, vooral in noordelijke populaties. Echter, bloeddruk droeg niet bij aan verschillen in CVA in ouderen uit de VS, waar verschillen in bloeddruk lager blijken te zijn. Roken was ook een belangrijke mediërende factor in Noord-Europa, terwijl dat niet het geval was voor verschillen in CVA in het zuiden van Europa. Dit heeft waarschijnlijk te maken met noord-zuid verschillen in de progressie van de rookepidemie. Andere factoren die bijdroegen aan verschillen in CVA waren Body Mass Index, eerdere hartziekten, alcohol inname en lichaamsbeweging. Over het algemeen geven onze resultaten aan dat de conventionele (biologische en gedrags -) factoren belangrijk zijn in de verklaring, maar dat zij minder dan de helft van sociaal-economische verschillen in CVA verklaren.

Resultaten van deze studie geven aan dat psychologische factoren een relatief grote bijdrage leveren aan sociaal-economische verschillen in CVA incidentie. Onder oudere mensen in de Verenigde Staten bleken depressie en (ontbreken van) sociale netwerken de belangrijkste risicofactoren, terwijl locus of control en sociale steun van belang bleken te zijn in de Nederlandse bevolking. Deze resultaten suggereren dat psychosociale factoren via psycho-biologische mechanismen direct het risico op CVA kunnen beïnvloeden . Hoewel onze studies geen direct bewijs leveren, komen de resultaten overeen met de hypothese dat psychosociale factoren onafhankelijk van gedragsgerelateerde risicofactoren een bijdrage leveren aan sociaal-economische verschillen in incidentie van CVA. De biologische mechanismen die sociaal-economische verschillen in incidentie van CVA verklaren zouden de focus van verder onderzoek kunnen zijn.

Resultaten van dit proefschrift suggereren dat sociaal-economische verschillen in de kwaliteit van preventiezorg een relatief kleine rol spelen in de verklaring van sociaal-economische verschillen in incidentie van CVA. Niettemin vinden wij sociaal-economische verschillen in het voorschrijven van statines als eerste keuze van cholesterolverlagend middel, en in het geven van secundaire preventie aan CVA patiënten. Onze bevindingen suggereren dat er een groot potentieel is om sociaal-economische verschillen in het voorschrijven van statines onder CVA patiënten te reduceren wanneer daarvoor duidelijke richtlijnen ontwikkeld kunnen worden. Desondanks suggereren onze resultaten dat de kwaliteit van preventiezorg voor mensen met een verschillende sociaal-economische afkomst gelijk is. De universele toegang tot huisartszorg in Nederland en de implementatie van standaard richtlijnen hebben vermoedelijk aan vergelijkbare zorg in alle sociaal-economische groepen bijgedragen.

Wij beargumenteren dat sociaal-economische status bepaalt in hoeverre iemand toegang heeft tot een breed scala aan zowel materiele (bijv. huisvesting en arbeidsomstandigheden) als psychosociale (bijv. autonomie in het werk en 'self-efficacy') bronnen, die minder beschikbaar zijn in de meest 'deprived' sociaal-economische groepen.

In landen met relatief hoge economische en materiële standaarden, zoals de Europese landen en de Verenigde Staten, zijn zowel psychosociale factoren als materiele middelen belangrijk in de verklaring van sociaal-economische verschillen in incidentie van CVA. Op basis van deze argumentatie kan worden gesteld dat sociaal-economische verschillen in incidentie van CVA het gevolg zijn van ongelijke toegang tot een combinatie van materiele en psychosociale middelen. Het gebrek van deze middelen in de lagere sociaal-economische groepen heeft een grote invloed op het gedrag en de biologische factoren die het risico op CVA verhogen.

Uit dit onderzoek blijkt dat bij interventies om CVA incidentie te reduceren speciale aandacht aan mensen met een lagere sociaal-economische status dient te worden besteed om optimaal succesvol te kunnen zijn. Geïntegreerde interventies om de prevalentie van veelvoudige risicofactoren in de lagere sociaal-economische groepen te reduceren zullen een grotere impact hebben dan interventies die zich slechts concentreren op een enkele risicofactor. Interventies om de prevalentie van conventionele risicofactoren te reduceren zijn nodig. Niettemin is er een groot potentieel om sociaal-economische verschillen in CVA terug te dringen door de prevalentie van depressie en andere psychosociale risicofactoren in de lagere sociaal-economische groepen te verminderen. Bovendien suggereren onze bevindingen dat noodzakelijke interventies om sociaal-economische verschillen in CVA te reduceren niet hetzelfde zijn voor alle landen en leeftijdsgroepen. Interventies om een te hoge bloeddruk te verminderen zouden bijvoorbeeld de grootste invloed op verschillen in CVA incidentie kunnen hebben in Zuid-Europese landen, terwijl het terugdringen van verschillen in roken een belangrijkere stap is voor het reduceren van verschillen in CVA incidentie in Noord-Europese landen. De invloed van deze interventies neemt toe wanneer zij vroeg in de levensloop worden toegepast. Tenslotte is het implementeren van richtlijnen een effectieve strategie om de kwaliteit van preventiezorg gelijk te maken voor alle sociaal-economische groepen. Artsen kunnen een belangrijke rol spelen in het reduceren van sociaal-economische verschillen in incidentie van CVA door primaire preventie van risicofactoren.

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Curriculum Vitae

Curriculum Vitae

Mauricio Avendaño Pabon was born on 28 January 1976 in Bogota, Colombia. He finished his secondary education at the San Tarsicio School, after which he went on to study Psychology at the University of Los Andes in Bogota. As part of his Psychology Degree, Mauricio was a visiting student at Goldsmiths College, University of London. During the same period, Mauricio worked as research assistant at the Centre for Research on Drugs and Health Behaviour, Imperial College, where he was involved in a study on the delivery of pharmacy-based needle exchange programmes for injecting drug users in south London, and was first introduced to the field of public health. Subsequently he returned to Bogota where he obtained his Psychology degree in 1999. His dissertation examined the drug policy decision-making process in Colombia, by assessing the alternatives for implementing harm-reduction policies among policy makers. In January 2000 he was appointed full-time lecturer at the University Bolivariana in Bucaramanga, where he taught methods in Psychology and co-ordinated the centre for research on social and health services. In the summer of 2001 he was awarded a fellowship from the Dutch institute for Higher Education for his postgraduate studies. He received a Master of Public Health degree from the Netherlands Institute of Public Health and the Erasmus Medical Center. In the summer of 2002 he started working as a PhD researcher at the Department of Public Health of the Erasmus Medical Center on a project focused on the social determinants of stroke, during which he also obtained a Master of Science degree in Epidemiology at the Netherlands Institute of Health Sciences. During the summer of 2005 he was visiting scholar at the Harvard School of Public Health, where he conducted a study on the impact of socioeconomic status on stroke in the US elderly. Mauricio has also been closely involved in the Survey of Health, ageing and retirement in Europe (Share) study, publishing a chapter on social inequalities in health in the first results book. Since September 2006 he works as postdoc researcher at the Department of Public Health, Erasmus Medical Center.

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