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SOCIOECONOMIC INEQUALITIES IN HEALTH

**Epidemiological studies of disease burden,
mechanisms, and gender differences**

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The cover picture symbolizes the four estates;
Coat of arms of the noble family Skjöldebrand representing the nobility (courtesy of Riddarhuset), Geneva bands and a bible representing the clergy, a town representing the burghers, and a plow representing the peasantry.

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Pretentious? Moi?

(Fawlty Towers; The Psychiatrist, 1979)

ABSTRACT

The overall aim of this thesis was to study inequalities in health, in particular, focusing on the risk of myocardial infarction and etiologic mechanisms from a life course perspective and on epidemiological measures and methodology.

Paper I uses the Swedish Burden of Disease Study together with the Social Database managed by the Swedish National Board of Health and Welfare. The analyses in Paper II-IV are based on the Stockholm Heart Epidemiology Program (SHEEP), a population-based case-control study of first myocardial infarction, in total 2,246 cases and 3,206 controls, among all Swedish citizens aged 45-70 living in Stockholm County 1992-1994.

Ischemic heart disease, depression and neurosis, and stroke are the three diseases with the largest contribution to the burden of disease, measured as disability-adjusted life years (DALY), in Sweden. Approximately one third of the burden of disease is unequally distributed, to a large extent this burden is put on the manual workers. The diseases with the largest contribution of DALYs to the total burden are also the diseases that stand for the largest part of the unequally distributed burden.

Misclassification of socioeconomic position among women has been proposed to affect the gender comparison of socioeconomic inequalities in health. In Paper II we find women to be categorized into fewer occupational groups and more often into unclassifiable subgroups than men. However, male occupational groups are nevertheless socioeconomically more heterogeneous. Furthermore, regarding the gender comparison of socioeconomic inequalities; empirical simulation of varying degrees of misclassification of men and women show that the dilution of the socioeconomic gradient among women, due to random misclassification of socioeconomic position, may be compensated by less misclassification among men.

The accumulation model in life course epidemiology hypothesizes that the longer time spent in socioeconomic adversity the greater is the risk of disease. In Paper III each year from birth till inclusion in manual position for men and women has been defined as in socioeconomic adversity. The number of years in adversity has been used to calculate the proportion in life spent in adversity. Men always in adversity have a relative risk of 2.36 (95% CI: 1.79 – 3.11) for myocardial infarction and women in always adversity have a relative risk of 2.54 (95% CI: 1.70 – 3.78) compared to the reference groups of those never in adversity. Adjustment for unhealthy behavior, social factors, and social trajectories decreased the observed accumulation effect. The increased risk of myocardial infarction is present even after just a few years in socioeconomic adversity.

Men in non-manual socioeconomic position in both childhood and adulthood have the lowest prevalence of seven cardiovascular risk factors, i.e. diabetes, hypertension, low life control, low social network, obesity, physical inactivity, and smoking. For women the pattern is similar. Those with adulthood manual experience have the highest prevalence of exposure to three or more risk factors, whereas those with non-manual adult socioeconomic position have the highest prevalence of null-exposed. Men born in non-manual position but who end up in manual position have high prevalence of exposed to three or more risk factors and a strong tendency to cluster risk factors on the individual level. Though it is notable that the largest observed-to-expected ratio for both men and women is in the always non-manual group exposed to three or more risk factors, indicating that individual clustering is most common in this socioeconomic trajectory.

We do not find that risk clustering plays an important role in the accumulation process leading to higher prevalence of multi-exposed in the most adverse socioeconomic groups. Together the findings in Paper III and IV question an overly simplistic interpretation of the accumulation hypothesis, i.e. the longer time spent in socioeconomic adversity the higher the morbidity, as they indicate that it also depends on how (social mobility) and when (critical period) the accumulation occurs.

Key words: Burden of disease, disability-adjusted life years, socioeconomic factors, gender, misclassification, myocardial infarction, life course, risk accumulation, risk clustering

LIST OF PUBLICATIONS

The thesis is based on the following publications, which will be referred to in the text by their Roman numerals:

- I. Ljung R, Peterson S, Hallqvist J, Heimerson I, Diderichsen F. Socioeconomic differences in the burden of disease in Sweden. *Bulletin of the World Health Organization* 2005;83:92-99.
- II. Ljung R, Hallqvist J. Misclassification of occupation-based socioeconomic position and gender comparisons of socioeconomic risk. *Scandinavian Journal of Public Health (in press)*.
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- III. Ljung R, Hallqvist J. Accumulation of adverse socioeconomic position over the entire life course and the risk of myocardial infarction among men and women: results from the Stockholm Heart Epidemiology Program (SHEEP). *Journal of Epidemiology & Community Health (in press)*.
Doi: 10.1136/jech.2006.047670
- IV. Ljung R, Hallqvist J. Multi-exposure and clustering of risk factors, socioeconomic trajectories and the risk of myocardial infarction in men and women: results from the Stockholm Heart Epidemiology Program (SHEEP). *(submitted)*.

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LIST OF ABBREVIATIONS

AF	Attributable fraction
BMI	Body Mass Index
CI	Confidence interval
DALY	Disability-Adjusted Life Years
ECG	Electro Cardio Gram
ILO	International Labour Organization
LO	Swedish confederation of Trade Unions (Landsorganisationen)
MI	Myocardial Infarction
NYK	Nordic Occupational Classification (Nordisk yrkesklassificering)
OR	Odds Ratio
PTO	Person Trade-off
RD	Risk Difference
RERI	Relative Excess Risk of Interaction
RII	Relative Index of Inequality
RR	Relative Risk
SCB	Statistics Sweden (Statistiska Centralbyrån)
SHEEP	Stockholm Heart Epidemiology Program
SI	Synergy Index
SII	Slope Index of Inequality
TTO	Time Trade-off
WB	World Bank
WHO	World Health Organization
YLD	Years Lived with Disability
YLL	Years of Life Lost

INTRODUCTION

Health is fundamental to our well-being and good health enables us to be part of society and fully benefit from lifetime chances and opportunities. Socioeconomic inequalities in health deny some groups of people their rights to equality of opportunity.¹

The association between adverse socioeconomic position and poor health has repeatedly been observed. Those in the upper end of the social stratification in society are less ill and lead a healthier life than those at the bottom. This is true for the stratification by income,²⁻⁴ education,⁵⁻⁸ occupation-based measures of socioeconomic position,⁹⁻¹¹ characteristics of the residential area,¹²⁻¹⁴ social capital,¹⁵⁻¹⁷ and by employment status.¹⁸⁻²⁰ The inequalities in health are present in all ages and through the whole spectrum of the socioeconomic gradient. Children with parents from the upper end of the social stratification have more healthy life style patterns,²¹⁻²³ fewer injuries,²⁴ lower prevalence of chronic disease,²⁵ better well-being,²⁶ and lower risk of dying young,²⁷ than children born into less fortunate circumstances. The inequalities persist throughout young adulthood,²⁸ the middle-aged,^{8,29,30} and till old age.³¹⁻³⁴ Even early fetal life is affected by the socioeconomic position of the pregnant mother. For example, those whose mothers lived in adversity³⁵⁻³⁷ or were exposed to starvation³⁸ during pregnancy are shown to have a higher risk of heart disease later in life. Accumulated exposures to socioeconomic adversity throughout the entire life course increases the risk of disease.^{39,40} Although measures of socioeconomic position are not uniform, socioeconomic inequalities in health are found in low-income,⁴¹⁻⁴³ middle-income,^{44,45} and high-income^{2,46} countries in all parts of the world.

Most diseases follow the socioeconomic gradient over the whole spectrum of socioeconomic adversity. Those higher up in the social hierarchy, richer or more well-educated have better health than those slightly lower in the hierarchy, less rich or not as well-educated. In general, the greater the adversity the greater is the risk of disease. Those in adversity have higher mortality,⁴⁷ rate their own general health and it's consequences worse,^{48,49} have higher rates of acute diseases,⁵⁰ express higher prevalence of psychiatric symptoms,^{51,52} show less coping capabilities,⁵³ have a higher overall burden of disease,⁵⁴ rate their quality of life lower,⁴⁹ and the consequences of disease, especially sick leave and early retirement are more common among those in adversity.^{55,56} Inequalities in health-seeking behavior,⁵⁷ and access to and utilization of health care,^{58,59} and in treatment of disease⁶⁰ are also present.

Sweden is an affluent,⁶¹ democratic country. It is one of the most egalitarian countries in the world and has acknowledged gender equity issues.⁶² Sweden also has one of the lowest levels of corruption.⁶³ Still socioeconomic inequalities in health are and have been clearly present. In the beginning of the twentieth century those children living in poor areas in Stockholm, with overcrowding and lack of clean water, had higher rates of measles and diarrhea.^{64,65} At present men in the most affluent suburbs of Stockholm in general live five years longer than men from the least affluent areas.⁶⁶ It has been possible to follow the trends in cancer incidence, myocardial infarction and overall mortality by computerized registers since the mid 1960's. The trends are rather consistent over time; those in adversity have worse health.^{66-72,73}^{1998,74} Hence, socioeconomic inequalities in health are present all over the world, including Sweden, for the most commonly used measures of socioeconomic position,

in all ages and for most definitions of ill health. Though, for some specific outcomes the association between socioeconomic adversity and ill health is not as clear.⁷⁵⁻⁷⁷

The intention of this thesis was to study inequalities in health, in particular focusing on the risk of myocardial infarction and etiologic mechanisms from a life course perspective and on epidemiological measures and methodology.

Health variation, inequality or inequity?

In a widely cited paper on *The concepts and principles of equity in health*, Margaret Whitehead in 1992 defined health inequities as differences in health that are unnecessary, avoidable, unfair and unjust.⁷⁸ Braveman and Gruskin further state that

*“ The concept of health equity focuses attention on the distribution of resources and other processes that drive a particular kind of health inequality – that is, a systematic inequality in health (or in its social determinants) between more or less advantaged social groups, in other words, a health inequality that is unjust or unfair.”*⁷⁹

Most of the differences in health between individuals are determined by variation in biology. Some variations between old and young, men and women are also determined by biology; the elderly are more ill than the children, men have prostate cancer, women have cervix cancer. Not many would argue that these variations in health are unfair. However, some variation in health between groups or so called inequalities in health in society are determined by how the society is culturally, economically, politically, and socially stratified. These systematic inequalities in health, hereafter referred to as socioeconomic inequalities in health, are therefore unfair, synonymous to inequities in health. Women live longer than men, often hypothesized to be the effect of differences in the biological composition and hormone levels in the male and female body. It could be argued that these differences are part of natural biological variation and therefore not unfair. If, on the other hand, men being exposed to more health-damaging experiences than women caused these differences, and these health-damaging experiences were determined by the social construct of male gender then these differences would be unfair. Whitehead argued that health differences determined by natural biological variation would normally not be classified as inequities in health as these can be regarded as “unavoidable”. However, the term unavoidable is time and place dependent, and others have proposed that “avoidable” should be removed from the definition of health inequities.^{79,80} It has further been argued that even if the cause of disease is unavoidable the consequences of a sick person losing her job or lowering her income are preventable and unjust.⁷⁸ Kawachi et al state that health inequity refers to inequalities in health that are seen as unfair or due to some form of injustice, not necessarily taking into account whether they also are preventable and unnecessary.⁸⁰

How to measure ill health?

Mankind has always strived for increased longevity. Life expectancy and mortality are easily measured. Hence, many studies on inequalities in health have analyzed differences in mortality rates and longevity between socioeconomic groups and between geographical areas.^{46,81-83} We are also hoping to lead a life free of disease, i.e. we want to postpone morbidity and mortality by extending the area of disease-free time under the survivorship curve as long as possible within the constraints of a finite biological life. These values of extending life free of disease are the fundament for public health work. The concept of measuring morbidity in studies of inequalities in health has several dimensions; should we measure the incidence or prevalence of disease, or measure self-rated health, or care-seeking behavior, or treatment of disease, or should we measure the socioeconomic consequences of disease? For all of these dimensions of health we find socioeconomic inequalities.

Summary measures of population health that integrate mortality and morbidity into a single measure have been developed to assist in the process of developing public health policy.⁸⁴ These summary measures make it easier to compare different settings and trends over time. These simplified measures of a more complex situation can be easier to comprehend for public policy makers, though the risk of oversimplification is always present. Summary measures of population health can roughly be divided into those measuring health expectancy and those measuring health gaps. Health expectancy represents the life expectancy at birth but also take into account years lived in less than full health. In figure 1 represented by area A (full health) and area B (less than full health) where the area of B is assigned a weight-function (f) according to severity of disease on a scale from 0 to 1 where 0 is equal to death and 1 is equal to full health.

$$\text{Health expectancy} = A + f(B)$$

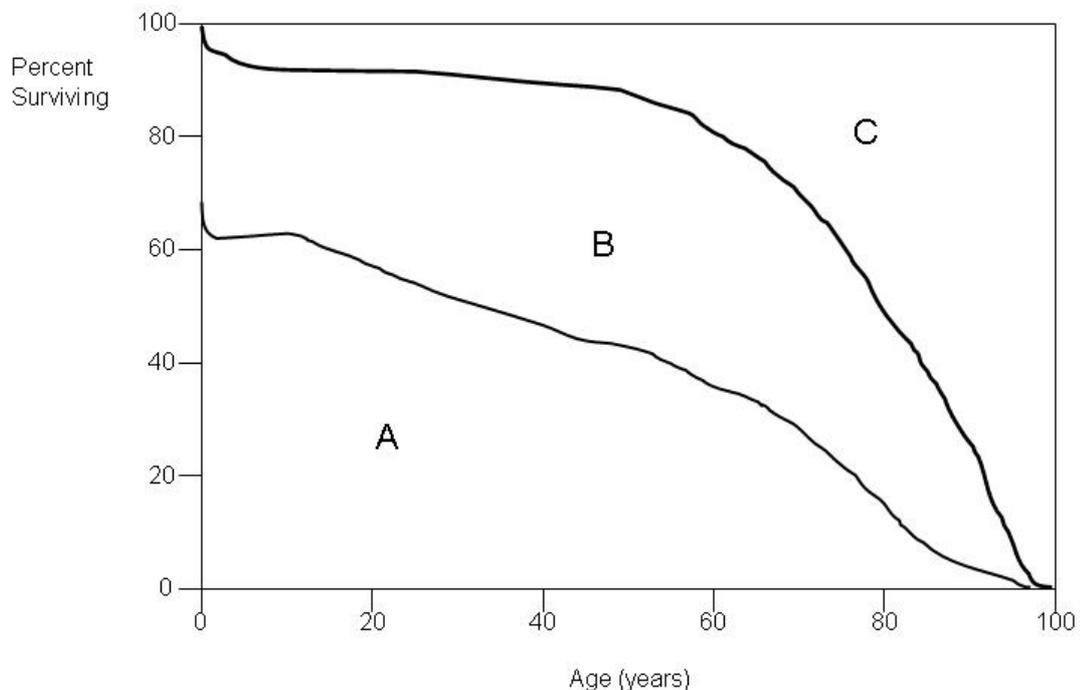


Figure 1. The survivorship curve.

On the other hand, a health gap measure instead compares the actual health status to some desired norm or goal. In figure 1 represented by area C (life lost due to premature mortality) and area B (life lived with disability) where area B is assigned a weight function (g) according to severity of disease on a scale from 0 to 1 where 0 is equal to full health and 1 is equal to death.

$$\text{Health gap} = C + g(B)$$

There are several different measures of health expectancies and health gaps.^{85,86} The disability-adjusted life year (DALY) which combines the burden of mortality and morbidity for different diseases is a health gap measure and was developed by the World Bank (WB) and the World Health Organization (WHO).⁸⁷ The Global Burden of Disease study, calculating the burden of disease measured in DALY for the different regions of the world was presented in 1996.⁸⁸⁻⁹² Since then, burden of disease measurements have been carried out at regional,⁹³⁻⁹⁵ national,⁹⁶⁻⁹⁹ and sub-national^{100,101} levels in high-income, medium-income, and low-income countries, and also globally for specific diseases.¹⁰²⁻¹⁰⁴ The DALY makes it possible to disaggregate burden of disease by risk factors.¹⁰⁵⁻¹⁰⁷ Child underweight for age and hypertension are the leading global risk factors for the total global burden of disease in 2001.¹⁰⁸ Gwatkin et al have calculated the burden of disease among the global poor.⁵⁴ They showed that a shift of focus from communicable to non-communicable diseases, although it is beneficial from a global perspective, will widen the poor-rich gap in life expectancy between the poorest 20 percent and the richest 20 percent of the world's population. The DALY is increasingly used as a summary measure of population health but as it incorporates value judgments there is an ongoing debate on the subjects of disability weighting, discounting, where burden in the future is valued less than present burden, age weighting, and gender issues.¹⁰⁹⁻¹¹⁵

Summary measures of population health are used for describing inequalities in population health and some can be disaggregated by risk factors. On the other hand, studies of the mechanisms of socioeconomic adversity leading to poorer health are better studied by using better-defined outcomes. A high validity of diagnosis and high reliability in case definition is preferred, with as little misclassification of disease as possible. As we are studying mechanisms of disease onset an incidence measure is preferred over a prevalence measure. Incident first event of myocardial infarction (MI) is a well-defined outcome recorded in high quality data registers in Sweden. The incidence and mortality in MI in Sweden has been decreasing the last twenty-five years.¹¹⁶ The decrease is seen in all socioeconomic groups but large differences still persist, with those in manual socioeconomic position or with low education having the highest incidence.^{50,117} The social patterning of MI is well known, and conventional risk factors have been established, though the contribution of these to explaining the socioeconomic inequalities in MI is under debate.^{118,119} Proximal and distal exposures acting throughout the entire life course contribute to the risk of MI, though all mechanisms and pathways are not fully understood.¹²⁰ This lends MI to be an interesting outcome when studying the social patterning of health from a life course perspective.

Across what groups should we measure inequality?

The idea of indicators of socioeconomic position in social epidemiology is to describe the social stratification. The socioeconomic stratification distributes structural positions in society. These positions within the stratification are powerful determinants of the likelihood of health-damaging and health-enhancing exposures, behaviors and resources.¹²¹ With a measure of this social stratification it is possible to study how resources, living conditions, and lifetime opportunities are related to individuals' structural positions in society and how this affects the likelihood to achieve good health.¹²¹⁻¹²³ Lynch and Kaplan have in an overview of the concept of socioeconomic position in social epidemiology research briefly discussed three major sociological traditions, Marxian, Weberian, and Functionalist.¹²¹ They argue in short that, according to Marx the society is stratified into classes that are determined by the nature of exploitative production and that this forms a relationship between those who own and those who do not own property in the means of production. And according to Weber that society was stratified in multiple ways, class, status and political power; and that this stratification leads to unequal distribution of economic resources and skills. The Functionalist view is described as that social stratification in society is natural and necessary, with a tacit consent of the existence of social inequalities.^{121,123}

Throughout this thesis an occupation-based measure of the social stratification will be used as the measure to define socioeconomic position. The scheme used is the socioeconomic classification of Statistics Sweden.¹²⁴ This classification is similar to the Erikson-Goldthorpe scale, and will be described in the methods section.¹²⁵ As mentioned, the concept of social class refers to Marx and the conflict between classes with different relation to the means of production. Social status or socioeconomic status reflect more the position in a hierarchy, or social prestige or honor accorded to an individual.¹²⁶ Socioeconomic group is in this thesis used to define a specific socioeconomic position, e.g. unskilled manual worker.

Apart from occupation, indicators of income and education have also been commonly used in social epidemiology research to define the social stratification in society.

Occupation

The intention of the occupation-based measures of socioeconomic position is to group occupations where the individuals in these occupations have similar labor market and work situation.^{121,122,127} Classification based on occupation has more resemblance with the concept of social class than does classification based on education or income. Occupation-based measures do not only reflect the exposure to hazardous working conditions or psychosocial work environment, with the concepts of psychological demands, decision latitude, and social support. They also reflect the individual's market situation and lifetime opportunities. The, in Europe, most commonly used occupation-based measures reflect the above mentioned relation to the market and work situation, whereas occupation-based measures in the United States more often only reflect the social prestige or income of the particular occupation.^{121,123,127,128} One drawback of measures of socioeconomic position that do not reflect social status or prestige is that they are not intended for rank ordering of socioeconomic groups.

Income

Income as a measure of socioeconomic position is attractive as it is continuous and has a broad range from the very poor to the very rich. Though, the usual way of measuring income does not fully capture the economic status of the individual. Often wealth or ownership of property and transfers in the informal economy are not accounted for. Individual income as a measure must also be adjusted for the number of adults and children supported by the income. The basic idea of income is that the richer one is the greater is one's possibility to add benefits that can improve health. The gains in health per income unit is smaller in the upper end of the income distribution than in the lower end.^{121,123,129,130}

Education

Even though education is easy to measure, either categorized into highest achieved educational attainment or even used as a continuous measure, it is not a direct measure of position within the social stratification. Educational credentials are one way but not the only mechanism to gain access to positions in society. Education is less affected by reverse causation of disease, with the exception of some psychiatric disorders, than income or occupation. The benefits and conceptualized pathways of educational attainment leading to better health can have different social implications depending on time period and cultural settings.^{121,123,126}

Gender

In most societies the distribution of social and political power is disfavoring the female population, though the effect on female health is not as clear-cut. Women generally live several years longer than men except in some of the most gender inequitable countries of the world.¹³¹ The predominant conclusion has been that women instead have higher morbidity, though the picture does not seem as clear. Macintyre et al have shown that women in high-income countries have higher levels of psychological distress across the life span, but that men have higher levels of more severe diseases.¹³²

Regardless of whether the social construct of female gender causes women having better or poorer health than men, the discussion on how to measure women's social position is ongoing.^{123,133-136} Sen et al argued that occupational classification systems differentiate more poorly between women's jobs than between men's, and that studies of socioeconomic inequalities in health thus will underestimate the inequalities more among women than among men.¹³⁷ Though, the major discussion on misclassification of socioeconomic position is more on whether women should be classified according to their own socioeconomic position or by the position of their male spouse. A gender neutral or household dominance order has been proposed, equally applied to both men and women, where the dominant socioeconomic position in the household, regardless of sex, is used to define both spouses.^{127,138}

Other measures of systematic division of individuals are language, religion, sexuality, and race and ethnicity more commonly used in the United States. Race and ethnicity are being discussed as they often are used as proxies for the more accurate and informative variables of socioeconomic position.¹³⁹⁻¹⁴² Several indices of asset ownership are also frequently used as indicators of socioeconomic position, especially in settings where registry data are poor, foremost in low-income

countries.^{143, 144} It seems that socioeconomic positions at all ages throughout the entire life course affects health, but being in adversity in some periods in life may be more important than in others in the risk of developing disease and health-damaging behaviors.¹²⁰

What effect measure to use?

Risk, or incidence proportion, is the number of subjects developing disease during a time period divided by the number of subjects followed for the time period. Risk is often used to reflect a single individual's risk whereas the term incidence proportion is used to reflect the average risk in a group. Incidence rate, on the other hand, is the number of subjects developing disease divided by the total time experienced for the subjects followed. The most commonly used effect measures in epidemiology research are the relative risk (RR), and the risk difference (RD), both comparing the risk or incidence rate in two groups, in relative and absolute terms, respectively. To study the causal effect of exposure the experience of those exposed is compared with the experience of the unexposed. In social epidemiology this is most often the effect of increased socioeconomic adversity on health. The RR and RD do not reflect the distribution of health across all socioeconomic groups in the population and does not take group size into account. The two groups compared should preferably not be too extreme apart or too broad in group size. Too extreme or broad groups could fail to spot or conceal the extent of health inequalities in the population. The RD always expresses the absolute difference between two studied groups, whereas the magnitude of the RR will depend on the baseline level of the reference group.^{145, 146}

Attributable fraction is used as a comprehensive term of fractional measures according to Greenland and Robins.¹⁴⁷ The family of attributable fraction measurements calculate how the burden of disease today would have been had we chosen a counterfactual distribution of exposure. Four types of counterfactual distributions of exposure have been identified; theoretical minimum risk, plausible minimum risk, feasible minimum risk and cost-effective minimum risk. In general theoretical minimum risk is the burden when hazardous exposure is set to zero (no one is exposed). Plausible minimum risk is when exposure is set to some plausible distribution of exposure that would minimize population risk (an imaginable or possible exposure level). Feasible minimum risk is when exposure is set to some existing low level of exposure achieved in a subgroup population (an actually achieved exposure level). In social epidemiology the counterfactual distribution of feasible minimum risk is commonly used, where we suppose to reduce the risk factor burden of some adverse group to the level of the least adverse group. Cost-effective minimum risk is when an exposure level is defined given that all feasible interventions costing less than some defined value were implemented.¹⁴⁸

In a milestone paper on how to measure socioeconomic inequalities in health Wagstaff et al have put forward three “minimal” requirements of an inequality measure when studying socioeconomic inequalities;¹⁴⁵

“That it reflect the socioeconomic dimension to inequalities in health; that it reflect the experiences of the entire population (rather than just, say, social classes I and V); that it be sensitive to the changes in the distribution of the population across socioeconomic groups”.

The measures of slope index of inequality, and relative index of inequality are measures that fulfill the above recommended requirements by Wagstaff et al, as does measures of attributable fraction. These measures will be further described in the methods section; in short they take the distribution of health across all socioeconomic groups and the group size into account.

Mackenbach and Kunst further argue in another widely cited paper on the measurement of inequalities in health that to only measure “total impact” on the population as proposed in Wagstaff et al’s third requirement could miss relevant information.¹⁴⁶ A more simple measure, like the RR, of the “effect” between specified groups could reveal relevant information for public health policy, for example the evaluation of targeted interventions for specific groups.¹⁴⁶ Manor et al have shown the more simple group comparison measures of “effect” to yield comparable estimates of the “total impact” measures of the population proposed by Wagstaff et al.¹⁴⁹

In epidemiology effects can be measured either on the absolute or the relative scale. Only relying on relative differences without taking the underlying risks into account can lead to wrong conclusions. This is illustrated by a study of mortality among manual and non-manual male workers in 13 countries in Europe where the greatest inequality was noticed in the Nordic countries when comparing the relative risks of manuals compared to non-manuals,⁴⁶ but as pointed out by Vågerö and Erikson the absolute mortality level for manual workers in the Nordic countries was much lower than the rate in the other studied countries.¹⁵⁰ This correlation between relative and absolute differences is further illustrated by a hypothetical example adopted from Finn Diderichsen;

A percentage reduction of the burden due to cardiovascular disease equally among socioeconomic groups will reduce the absolute inequalities in health by the same amount. On the other hand the relative differences between the socioeconomic groups will be constant. To illustrate this, if one group has a burden of 150 units and another has a burden of 100 then if we could reduce the burden by 40 percent for both groups by preventing some known risk factor the result in burden would be 90 for the first group and 60 for the second. The relative difference is unchanged, 1.5, but the absolute difference has decreased from 50 units to 30 units. Wrongly focusing on only the relative difference we would draw the conclusion that the inequality is unchanged and that this intervention is not appropriate if our aim is to reduce inequalities in health.

Distributional sensitivity or in other words how we value health along the health distribution is a value choice not reflected by most measures of health inequalities.^{151, 152} What if we would rather improve the health for the most ill or for some disadvantaged group than for those with average health?¹⁵³ It could be argued that improving health among the least healthy should be valued more than improvement for the healthiest.¹⁵⁴ Though studies using measures that also reflect these value choices are rare.

Life course epidemiology

Mechanisms of how social inequalities in health emerge

From a life course perspective socioeconomic inequalities in health have their origin in differential exposure. These differential exposures of biological and social factors act independently, cumulatively, synergistically or antagonistically throughout the entire life course. They will affect health-damaging and health-enhancing behaviors and as a consequence health outcomes in later life.^{120, 155-158} A life course approach stresses the importance of time and timing in understanding causal links between exposure and outcome.¹⁵⁹ The mechanisms of risk factor acquisition and how risk factors interact to influence the risk of disease are key aspect in life course epidemiology. In their classification of potential causal models Kuh and Ben-Shlomo distinguish between critical period models and accumulation of risk models.¹²⁰ The critical period models address the importance of the timing of exposure and have their origins from studies of intrauterine growth and development and later risk of heart disease.³⁵⁻³⁷ Critical period models refer to a longer or shorter exposure window in time when an individual is more susceptible to exposures. An illustrative example of the critical period model is exposure to thalidomide, where there is a high risk of developing limb malformations if exposed during foetal life, whereas exposure later in life does not imply any risk at all of malformations. Early exposures with later life effect modification can also be seen as critical period models if only those who were exposed early in life will develop disease when experiencing some other exposure later in life, interacting with the early exposure.

Accumulation of risk has been introduced as a key concept in the life course approach to the study of chronic disease etiology.¹²⁰ Accumulation of risk models suggests that throughout the life course exposures or insults gradually accumulate through episodes of illness, adverse environmental conditions and behaviors increasing the risk of chronic disease and mortality. A further distinction is made between accumulation of correlated insults or of independent and uncorrelated insults. The models with correlated risks can be either models of chains of risk where one health-damaging exposure leads to another, or clustering of multiple risk factors within the lives of the same individuals. Another feature of interest is that accumulated exposure provides a possible explanation that is alternative to hierarchical stress mechanisms, for the socioeconomic gradient in mortality risk often found to be preserved across a large number of hierarchically ordered socioeconomic positions.¹⁶⁰⁻¹⁶² An important problem is that the theoretically distinct concepts of accumulation and critical periods cannot be measured independently making it difficult to empirically disentangle their effects.¹⁶³

Accumulated exposure to adverse socioeconomic positions across the life course increases the risk of disease,^{39, 164-174} Though, with the increasing interest in research with a life course approach there is a discussion on how to measure accumulated exposure to social adversity.^{126, 138, 172} Different measures of social class, social status or material circumstances have been shown to affect health through different causal pathways, predominantly from studies in England.¹⁷⁵⁻¹⁷⁹ The measures of accumulated adverse socioeconomic positions are in most studies rather crude and

based on a combination of father's socioeconomic position (childhood), highest educational attainment or first occupation (young adulthood) and current occupation-based socioeconomic position (adulthood).^{39,40,164,166-169,180,181} Other studies have used a combined accumulation-score of exposures to both specific risk factors and to socioeconomic adversity.^{172,182} In a large cohort study of Swedish conscripts, childhood socioeconomic circumstances and adolescent life style behavior explained a substantial part of socioeconomic differences in coronary heart disease in middle-aged men.¹⁸³ Health-damaging behavior in adolescence are related to future adverse socioeconomic position.¹⁸⁴⁻¹⁸⁶ A study of six Western countries found socioeconomic adversity in childhood to increase the risk of obesity and reduce the probability of quitting smoking irrespective of adult socioeconomic position.¹⁸⁷ A life course perspective is used in the understanding of inequalities in health through the social patterning of exposures acting over the entire life course but also by acknowledging biological and social transmission of risk across generations.¹⁵⁵

AIMS

The overall aim of this thesis was to study inequalities in health, in particular focusing on the risk of myocardial infarction and etiologic mechanisms from a life course perspective and on epidemiological measures and methodology.

Specific objectives

- To assess how much of the total burden of disease that is a result of inequalities in health between socioeconomic groups: which disease groups that contribute the most to the socioeconomic inequalities in health, and how the unequal burden of disease is distributed across different socioeconomic groups. (I)
- To calculate and discuss the use of different effect measures in the study of socioeconomic inequalities in health, especially from a public health perspective. (I,II)
- To assess how the comparison of gender-specific socioeconomic differences in the risk of myocardial infarction is affected by misclassification of socioeconomic position among both men and women. (II)
- To analyze the effect of cumulative life course exposure to adverse socioeconomic positions on the risk of myocardial infarction and whether it matters how and when the accumulation occurs. (III)
- To evaluate to what extent established biological risk factors and health-damaging behaviors explain the effect of accumulated adverse socioeconomic positions. (III)
- To analyze seven major risk factors of myocardial infarction and their distribution between and within socioeconomic groups, and also to assess whether the risk of myocardial infarction is similar between socioeconomic groups exposed to increasing number of risk factors. (IV)
- To analyze the accumulation of risk model with risk clustering conceptualized in life course epidemiology and its contribution to the understanding of how socioeconomic inequalities in the risk of myocardial infarction emerge. (IV)

MATERIAL AND METHODS

Burden of disease

Study base

In Paper I we analyzed data from the Swedish Burden of Disease Study.⁹⁹ The Swedish Burden of Disease Study calculated the burden of disease in Sweden for the 20 largest disease groups for men and women separately, see table 1. In Paper I the study base consists of all Swedish men and women aged 15 to 84 years in the period of 1988-95. The burden of 18 disease groups were analyzed; alcohol addiction, asthma and chronic obstructive pulmonary disease, blood malignancies, bronchial and lung cancer, colorectal cancer, dementia, depression and neurosis, diabetes, falls, hearing disorder, ischemic heart disease, neck and back disease, psychosis (excluding schizophrenia), respiratory infection, self-inflicted injuries, stroke, traffic accidents, and breast cancer in women only. We excluded congenital malformations and perinatal diseases together with prostate cancer in men.

Table 1. The 20 disease and injury groups that contribute the most to the burden of disease in Sweden. Total number of DALYs and the percentage of the total for a mean year in the period 1988-1995. (From Peterson et al 1998,⁹⁹ also table 1 in Paper I)

<i>Men</i>			<i>Women</i>		
<i>Disease group</i>	<i>DALY</i>	<i>%</i>	<i>Disease group</i>	<i>DALY</i>	<i>%</i>
1. Ischemic heart disease	200 277	19.2	1. Ischemic heart disease	133 985	13.7
2. Depression and neurosis	69 046	6.6	2. Depression and neurosis	106 527	10.9
3. Stroke	60 975	5.8	3. Stroke	67 767	6.9
4. Alcohol addiction	46 693	4.5	4. Dementia	61 188	6.3
5. Self-inflicted injuries	44 217	4.2	5. Breast cancer	29 851	3.1
6. Dementia	32 801	3.1	6. Asthma and COPD	27 769	2.8
7. Asthma and COPD	29 242	2.8	7. Psychosis exc. schizophrenia	24 931	2.6
8. Bronchial and lung cancer	28 197	2.7	8. Neck and back diseases	22 876	2.3
9. Traffic accidents	24 266	2.3	9. Respiratory infections	20 136	2.1
10. Psychosis exc. schizophrenia	24 140	2.3	10. Gynecological cancer	20 014	2.0
11. Prostate cancer	23 734	2.3	11. Self-inflicted injuries	19 334	2.0
12. Hearing disorder	22 132	2.1	12. Colon and rectum cancer	17 926	1.8
13. Respiratory infections	21 059	2.0	13. Congenital malformations	17 324	1.8
14. Neck and back disease	20 085	1.9	14. Bronchial and lung cancer	16 689	1.7
15. Congenital malformations	18 696	1.8	15. Hearing disorder	16 040	1.6
16. Colon and rectum cancer	17 886	1.7	16. Diabetes	16 037	1.6
17. Diabetes	16 339	1.6	17. Alcohol addiction	13 427	1.4
18. Falls	14 010	1.3	18. Falls	12 385	1.3
19. Blood malignancies	13 901	1.3	19. Traffic accidents	11 828	1.2
20. Perinatal disease and SIDS	13 502	1.3	20. Perinatal disease and SIDS	11 526	1.2
<i>sum</i>	741 198	71	<i>sum</i>	667 560	68
<i>Others</i>	305 692	29	<i>Others</i>	309 834	32
TOTAL	1 046 890	100	TOTAL	977 394	100

Disability-Adjusted Life Years (DALY)

Burden of disease calculations measure the total levels of ill-health due to premature mortality and non-fatal health outcomes, and which diseases that contribute to these levels of ill-health.^{88-92,188} The Disability-Adjusted Life Year (DALY) measure combines the burden of premature mortality with the burden of disability of a disease. The burden of different diseases can be aggregated to reflect the burden of disease groups and, thus, also compared with the burden of other disease groups. The DALY measure is composed of YLL (Years of Life Lost) and YLD (Years Lived with Disability). Each disease and disease specific stage has been valued on severity and assigned disability weights. The disability weights are valued on a scale from 0 (full health) to 1 (death), see table 2 for some examples of disability weights. Health and research professionals did the initial valuation of disability weights. Person-trade-off (PTO) and time-trade-off (TTO) methods have been used to derive disability weights. In PTO subjects are asked to make tradeoffs between treating different groups of patients. In TTO subjects are asked to imagine themselves in a disease, but they can tradeoff the disease by living shorter time in full health.¹⁸⁹ Disability weights have been shown to be valued similar between countries in a European setting.^{93,94} Each year lost due to premature mortality has been assigned the disability weight of 1 and will give rise to 1 YLL. Each year lost due to morbidity has been assigned the disease and severity stage specific disability weight. The total DALYs for a specific disease is the sum of the total YLLs and YLDs for that specific disease. The DALY measure is usually expressed as a quotient of person years (number of DALYs / 100 000 person years).

Table 2 Examples of average disability weights for some diseases, regardless of disease stage. The weights are set to describe the severity of disease, note that the high weight of appendicitis is only applicable to one or two weeks during a year whereas vision impairment and schizophrenia have longer duration.

Disease	Disability weight
Schizophrenia	0.379
Lung cancer	0.146
Vision impairment	0.098
Appendicitis	0.463
Common cold	0.070

To calculate DALYs the disability weight is multiplied by the duration of disease and the number of persons affected:

- 10 persons sick for a whole year with a disease with the disability weight of 0.3 result in $10 \times 0.3 = 3$ YLDs.
- One person sick for half a year with a disease with the disability weight of 0.46 result in $1 \times 0.46 / 2 = 0.23$ YLDs
- One person dying at the age of 50 with a remaining life expectancy of 34 years (assuming that if one is alive at 50 then one is expected to live until 84) result in $1 \times 34 = 34$ YLLs

The Swedish Burden of Disease Study used the WHO global disability weights, but not discounting or age weighting. Discounting values burden in the future less than burden today, align with the economic concept of discount rate. Age weighting values burden of disease in productive age groups more than burden in the young and old.

The life expectancy at birth was set to 80 years for men and 82.5 years for women, align with the WHO Global Burden of Disease calculations. The burden of disease was calculated for a mean year during the period 1988-1995.

Attributing DALYs to socioeconomic groups

DALYs per 100 000 person years by sex and age group were taken for each disease group from the Swedish Burden of Disease Study and attributed to the different socioeconomic groups according to group size and relative risk of disease. To determine age, sex and disease specific relative risks by socioeconomic group two databases were used.

The Social Database (Socialmedicinska databasen)

The Social Database is managed by the Swedish National Board of Health and Welfare. The database contains information on all deaths and patients being treated in hospital as well as information on socioeconomic and demographic data linked together by personal identification number. The Social Database was used to calculate mortality rates by socioeconomic groups for all studied disease groups.

Swedish Survey of Living Conditions (ULF)

The Swedish Survey of Living Conditions is a national representative sample conducted yearly by Statistics Sweden (SCB).¹⁹⁰ The database contains information on self-reported health, health-care utilization and socioeconomic factors. From this database the prevalence ratio by socioeconomic group was derived from self-reports on long-standing illness for neck and back disease, asthma and chronic obstructive pulmonary disease, depression and neurosis, hearing disorder, and diabetes. For the remaining disease groups the morbidity rates were derived from the Social Database.

Stockholm Heart Epidemiology Program (SHEEP)

The Stockholm Heart Epidemiology Program (SHEEP) is a population based case-control study of risk factors for incident first event of MI with detailed information on various exposures, socioeconomic and demographic data and has also been described in detail earlier.¹⁹¹⁻¹⁹⁵ Previous analyses of the SHEEP study have studied the risk of MI and exposure to a wide range of risk factors, for example; decision latitude and job strain,¹⁹⁶ interleukin-6,¹⁹⁷ work related stressful life events,¹⁹⁸ moist snuff,¹⁹⁹ urban air pollution,²⁰⁰ alcohol consumption,²⁰¹ previous hospitalization for depression,²⁰² short stature,²⁰³ social context,¹² physical activity,²⁰⁴ and being a professional driver.²⁰⁵ The SHEEP study is used in Paper II – IV.

Study base SHEEP

The study base included all Swedish citizens aged 45-70 years with no prior clinically diagnosed MI event living in Stockholm County during 1992-1994. Men were

included in 1992-93 and women in 1992-94. From January to October 1992 the upper age limit was set at 65 years but from November 1992 and onwards it was 70.

Case definition

Cases were identified through a special organization set up at the coronary and intensive care units of ten emergency hospitals, and from computerized hospital discharge records for Stockholm County and death certificates from the National Cause-of-Death Register maintained by Statistics Sweden (SCB). Cases were diagnosed according to standard criteria specified by the Swedish Association of Cardiologists.²⁰⁶ To be included cases had to fulfill two of the three criteria; symptoms, ECG and enzymes. To ensure that only individuals with first-time MI were included, each case was checked for earlier MI in the Hospital Discharge Register. Cases were included at the time of disease onset. The sampling fraction for cases is close to 1. In total 761 female and 1,485 male cases were included.

Sampling of controls

One control per case was randomly selected at the time of case incidence from the study base after stratification for age, sex and hospital catchment area. Controls were sampled from a computerized register of the Stockholm population. The sampling fraction by sex, age and hospital catchment area is known. More controls than cases were finally included, because sometimes the control was already included when the case chose not to participate. In addition, if a control did not participate a substitute was sampled, but sometimes they both ended up participating. In total 1,118 female and 2,088 male controls were included.

Collection of individual information

All study subjects received a postal questionnaire covering a large set of potential risk factors and were invited to a physical examination and blood sampling. In case of missing answers a supplementary telephone interview was done. For fatal cases a relative answered the questionnaire 6 to 12 months after the event. The questionnaire response rate among cases was 72 percent for women and 81 percent for men, and corresponding figures among controls were 70 percent and 75 percent respectively. Subjects were equally inclined to participate regardless of age or catchment area. In 2003 record linkage of register-based information on income, wealth and family structure was carried out.

Socioeconomic classification

An occupation-based measure of socioeconomic position is used in this thesis as the measure of the social stratification process in society. The classification is based on the occupation-based socioeconomic classification of Statistics Sweden.²⁰⁷ It divides the working force into self-employed persons and employees. The employees are divided into manual workers who are normally affiliated to the Swedish Confederation of Trade Unions (LO) and sell their time for collectively negotiated wages and into non-manuals who sell their competence for salary. The manuals are further subdivided in unskilled and skilled manuals and the non-manuals into lower, intermediate and higher non-manuals based on the average educational requirements of each occupation.

In an aggregated form the classification consists of six groups:

- *Unskilled manual workers*: occupations normally requiring less than 2 years of post-comprehensive school education. (e.g. drivers, shop assistants)
- *Skilled manual workers*: occupations normally requiring 2 years or more of post-comprehensive school education. (e.g. bakers, mechanics, nursing assistants)
- *Lower non-manual workers (assistant non-manuals)*: occupations normally requiring 2, but not 3, years of post-comprehensive school education. (e.g. pharmacy assistants)
- *Intermediate non-manual workers*: occupations normally requiring 3, but not 6, years of post-comprehensive school education. (e.g. registered nurses, mechanical engineers,)
- *Higher non-manual workers (employed and self-employed professionals)*: occupations normally requiring at least 6 years of post-comprehensive school education. (e.g. teachers, government administrators)
- *Self-employed (other than professionals)*: Self-employed and farmers

Nordic occupational classification

In Paper II all subjects have been categorized according to the Nordic Occupational Classification (NYK) in addition to the socioeconomic classification. In NYK the subjects have been categorized into branches of business and within these into subgroups of more distinct occupational categories.²⁰⁸ This classification is originally based on the International Standard Classification of Occupation from 1958 managed by the International Labour Organization (ILO).²⁰⁹ The coding and grouping of occupations is based on similarities in the result of the work. The classification generally does not take into account how the work was done, or the educational requirements or job position.

Confounders and potential mediating factors

As Paper I analyzed the burden of disease for the whole Swedish population by socioeconomic group and Paper II analyzed the misclassification of socioeconomic position no further information on confounders or potential mediators was used. The confounders and potential mediators presented below apply to Papers III and IV.

Confounders

- Cohabiting status was defined as either being married or cohabiting at inclusion or not.
- The highest self-reported educational level was defined as college or higher education including university, the middle group being an educational level equivalent to high school or other intermediate level education, and the lowest group the compulsory level.
- Family income was measured as the individual's disposable post-tax income in the year prior to inclusion after transfers of social benefits, taking into account, where applicable, the income of both spouses and the number and weights, according to an equivalent scale, of adults and children in the household. Family income was categorized into tertiles based on the distribution among the controls.
- Job strain was defined as combined exposure to self-reported lack of control and high psychological demands at work, with the worst quartiles for each entity as exposed.
- Outside the working market was defined as being unemployed, on sick leave, early retired, or pensioners at inclusion.
- Social network was calculated as a summary index of questionnaire data on network structure, social support and social activities similar to earlier studies.²¹⁰ Experience of self-perceived lack of control over excessive demands in life was measured by a short version of the perceived stress scale from Cohen et al.²¹¹

Health behaviors

- Alcohol consumption in the year prior to inclusion was divided into four categories; abstainers, 0.1 to less than 5 grams of alcohol per day (reference category), 5 to 70 g/d (men), and more than 70 g/d (men), 5 to 30 g/d (women) and more than 30 g/d (women).
- Obesity was defined as body mass index (BMI) $\geq 30\text{kg/m}^2$.
- Subjects who reported inactive leisure time, including only occasional walks, during the last 5-10 years were categorized as 'exposed' to physical inactivity.
- Subjects who had never smoked regularly for at least 1 year were considered non-smokers. Subjects who smoked daily when included or had stopped smoking within the last year were classified as current smokers. Subjects, who had stopped smoking for more than 1 year before inclusion, were classified as ex-smokers.

Biomedical risk factors

- Subjects were classified as diabetics if information from the questionnaire stated diabetes with insulin, drug treatment, or diet control at the time of inclusion.
- Familiarity of cardiovascular disease was defined as at least one first relative with previous coronary heart disease before the age of 65.
- Hypertension was defined as on antihypertensive drug therapy for the reason of hypertension or a systolic blood pressure ≥ 170 mmHg or a diastolic blood pressure ≥ 95 mmHg.
- Small for gestational age was defined as the smallest 25 percent based on information from birth records.

STATISTICAL ANALYSES

Effect measures

Logistic regression

In Paper I unconditional logistic regression was used to calculate incidence rate ratio and in Paper II-IV to calculate odds ratios (OR) as estimates of incidence rate ratios.

Attributable fraction

Attributable fraction (AF) was used to calculate the counterfactual burden of disease choosing a feasible minimum risk approach (all socioeconomic groups having the same risk as the least adverse group). Attributable fraction was calculated according to Rothman.²¹²

$$AF = \sum_i P_i \left(\frac{RR_i - 1}{RR_i} \right)$$

AF is the sum of each exposure specific attributable fractions, where i represents exposure level for category i and P_i represents the proportion of all cases that falls in exposure category i .

Slope index of inequality (SII)

The effect measures used in Paper I to study the socioeconomic dimension to inequalities in health were the slope index of inequality (SII), and the relative index of inequality (RII).^{145,146,213} The SII is the slope of the regression line showing the relationship between a group's health and its relative rank in the socioeconomic distribution.

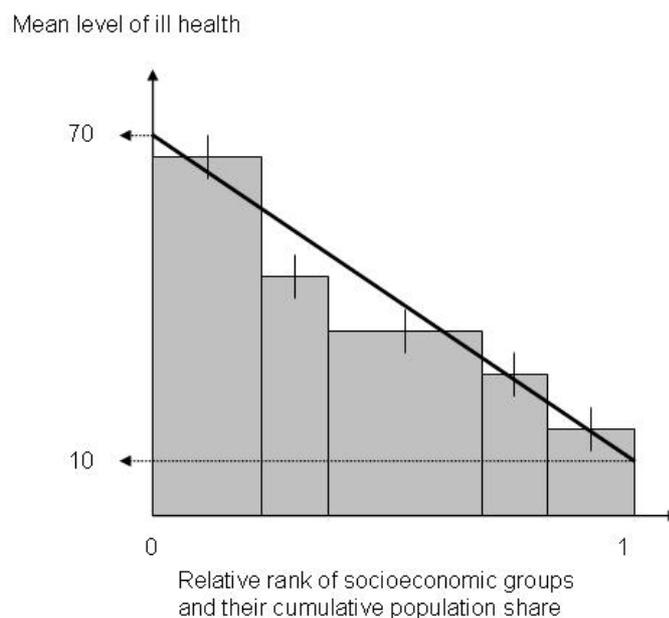


Fig 2. Slope index of inequality (SII) and Relative index of inequality (RII)

It is calculated by weighted least square linear regression using the mean health status of each socioeconomic group and the midpoint of the groups ranked by their socioeconomic position. The height of the bin is the mean health of that socioeconomic group and the width the proportion of the total population in that group.

The SII evaluates the distribution of health over the whole population and is sensitive to group size but dependent on the (socioeconomic) ranking of groups. The SII can be interpreted as the absolute difference in health between those at the bottom of the social hierarchy compared to those at the top, taken the health status of all in-between groups into account. In figure 2 the SII equals -60 (10-70= -60) and can be interpreted as those at the top of the socioeconomic hierarchy having 60 units less of ill health per population unit than those at the bottom. Confidence intervals were calculated according to Kakwani et al.²¹⁴

Relative index of inequality (RII)

The RII was initially defined as the SII divided by the mean level of health.¹⁴⁵ A by Mackenbach and Kunst modified RII has been presented, where the RII is the ratio of the estimated health problems, calculated by the slope index of inequality, of those at the bottom and those at the top of the social hierarchy.^{146,213} In figure 2 the RII equals 7 (70/10=7) and can be interpreted as those at the bottom of the hierarchy having 7 times greater risk of ill health than those at the top of the hierarchy.

Observed-to-expected ratio

In Paper IV age standardized observed-to-expected ratios are presented, where no difference in the observed and expected frequencies is notated by a ratio equal to 100.

Measures of interaction on an additive scale

Synergy Index and Relative Excess Risk due to Interaction

The synergy index (SI) measures the biological or public health interaction between two risk factors expressed as the ratio of the relative excess risk for the combined effect of the risk factors and the sum of the relative excess risks for each separate effect of the two risk factors.²¹⁵ The interpretation is that a SI greater than 1 indicates that the absolute excess risk for those exposed to both risk factors is greater than the sum of the absolute excess risks for those exposed to each separate risk factor.

$$SI = \frac{RR_{11} - 1}{[RR_{10} - 1] + [RR_{01} - 1]}$$

Where RR_{00} are the jointly unexposed ($RR=1$); RR_{11} is the rate ratio for those exposed to both risk factors; RR_{10} and RR_{01} are the rate ratios for those exposed to one of the risk factors, respectively.

The relative excess risk due to interaction (RERI) is:

$$RERI = RR_{11} - RR_{10} - RR_{01} + 1$$

A RERI equal to zero indicates that the effect of being exposed to both risk factors A and B is the same as the sum of the independent effects of the two exposures. If the RERI is greater than zero the effect of joint exposure exceeds that of the sum of the two independent effects, i.e the effect of joint exposure is greater than additivity. SI and RERI were calculated according to Rothman.²¹⁶

Specificity and sensitivity

In Paper II a hypothetical scenario with varying specificity in the classification of socioeconomic position is analyzed. The concept of specificity and sensitivity, and for completeness predictive value positive and predictive value negative, is presented in table 3.

Table 3. Definition of specificity, sensitivity, predictive value positive and predictive value negative.²¹²

Test result	Disease	No disease	Total
Positive	a	b	a + b
Negative	c	d	c + d
Total	a + c	b + d	a + b + c + d
Sensitivity of test	a / a + c		
Specificity of test	d / b + d		
Predictive value positive of test		a / a + b	
Predictive value negative of test		d / c + d	

RESULTS

Paper I: Socioeconomic differences in the burden of disease in Sweden

Objective: To analyze how much of the total burden of disease in Sweden, measured in disability-adjusted life years (DALYs) is a result of inequalities in health between socioeconomic groups and how this burden is distributed across different disease groups and socioeconomic groups.

Ischemic heart disease, depression and neurosis, and stroke are the three diseases with the largest contribution of DALYs to the burden of disease in Sweden for both men and women, accounting for about 30% of the total burden (table 1, p.12). The rank order of the largest disease groups contributing to the burden of disease is similar for men and women, except for breast cancer which is number five in women and alcohol addiction and self-inflicted injuries which rank in fourth and fifth place in men.

Applying the slope index of inequality and the relative index of inequality as effect measures enables evaluation of inequalities in health taking the distribution of health over all socioeconomic groups into account. In table 4 the diseases are ranked according to the absolute contribution of DALYs to the socioeconomic inequalities in health.

Applying a counterfactual exposure of feasible minimum risk, i.e. all socioeconomic groups having the same burden as the least adverse group, we have calculated the proportion of the excess burden of the total burden. About one third of the burden is unequally distributed across socioeconomic groups. In women ischemic heart disease, depression and neurosis, and stroke account for more than half of the unequally distributed burden of which most falls on the unskilled manual workers. Breast cancer accounts for 1% of the unequally distributed burden in women, but this burden affects those in higher non-manual positions more, thereby reducing the socioeconomic inequalities in the burden of disease. In men ischemic heart disease, alcohol addiction, and self-inflicted injuries account for half of the unequally distributed burden largely affecting the unskilled manual workers.

The composition of the burden due to mortality and morbidity differs between disease groups. For ischemic heart disease and self-inflicted injuries more than 90% of the burden is composed of burden from mortality. For two other large contributors, depression and neurosis and neck and back disease almost the entire burden is from morbidity. The composition of mortality and morbidity in the equally and unequally distributed burden is similar. Half of the burden among women is due to mortality, whereas among men 60% is due to mortality. Taken together this implies that those in socioeconomic adversity not only die at younger ages they are also more ill during their lifetime.

Table 4. Slope Index of Inequality (SII), Relative Index of Inequality (RII), Years of Life Lost (YLL) and Years Lived with Disability (YLD) per 100 000 person years, by disease group, sorted by falling SII (DALY per 100 000 person years). Men and women 15-84 years. A mean year in Sweden 1988-1995.

Men					Women				
Disease group	SII	RII	YLL	YLD	Disease group	SII	RII	YLL	YLD
Ischemic heart disease	3616	2.03	4940	373	Ischemic heart disease	1997	2.50	1933	400
Alcohol addiction	1549	11.26	267	659	Depression and neurosis	1502	1.72	12	2818
Self-inflicted injuries	1306	2.85	1355	4	Stroke	721	1.80	870	387
Depression and neurosis	1031	1.76	7	1859	Neck and back disease	698	2.90	2	714
Neck and back diseases	765	4.07	2	630	Dementia	486	2.43	142	441
Stroke	763	1.65	1101	462	Psychosis excluding Schizophrenia	334	1.90	11	526
Bronchial and lung cancer	534	1.94	818	16	Alcohol addiction	328	4.25	55	210
Asthma and COPD	471	1.98	331	386	Self-inflicted injuries	310	1.68	600	7
Dementia	470	2.39	120	454	Diabetes	302	2.48	165	191
Hearing disorder	457	2.09	0	647	Asthma and COPD	279	2.40	229	380
Psychosis excluding Schizophrenia	394	2.48	15	450	Bronchial and lung cancer	265	1.66	523	9
Diabetes	391	2.43	278	191	Hearing disorder	259	1.88	0	424
Respiratory infections	381	2.78	361	44	Respiratory infections	158	1.98	192	49
Traffic accidents	320	2.16	364	72	Falls	58	1.34	73	129
Falls	201	2.23	160	104	Blood malignancies	49	1.19	273	9
Blood malignancies	34	1.09	373	11	Colon and rectum cancer	33	1.07	429	39
Colon and rectum cancer	8	1.02	480	41	Traffic accidents	6	1.03	144	50
					Breast cancer	-338	0.70	900	59

Paper II: Misclassification of occupation-based socioeconomic position and gender comparisons of socioeconomic risk

Objective: To analyze to what extent gender comparisons of socioeconomic inequalities in health are influenced by the use of an occupational classification system, which tends to be less precise in the female sector of the labor market, to define empirical indicators of socioeconomic position.

We show that half of the men belong to the 24 largest branches of business for men in the Nordic Occupational Classification whereas half of the women belong to the 10

largest branches for women. Also 17 percent of women and only 8 percent of men are found in unclassified subgroups. In women 85 percent of those classified as “office secretary”, “typist”, or “stenographer” are classified as lower non-manuals and the remaining 15 percent as intermediate non-manuals. We assigned each individual a socioeconomic position based on the most common socioeconomic position in the corresponding occupational category. The result was that 67 percent of men and 77 percent of women classified in this way were classified in the same socioeconomic position as when socioeconomic position was based on more detailed information on the individual’s job title and work tasks.

We find that women are found in fewer occupational categories than men and more often in unclassified subgroups, and that the socioeconomic classification of women within occupational categories is heterogeneous. However, male occupational groups are nevertheless socioeconomically more heterogeneous. We have varied the specificity, from 80 to 100 percent, in classifying men and women to a socioeconomic position and studied the effect on the synergy index. The change in the synergy index was never greater than 10 percent from the actual true value. This empirical simulation of varying degrees of misclassification of men and women show that socioeconomic misclassification among women is often compensated for by less socioeconomic misclassification among men.

Paper III: Accumulation of adverse socioeconomic position over the entire life course and the risk of myocardial infarction among men and women

Objective: To analyze the accumulation of adverse socioeconomic position over the life course in detail, with help of yearly information from birth to disease onset on individual socioeconomic position, and the risk of myocardial infarction.

The accumulation model in life course epidemiology hypothesizes that the longer time spent in socioeconomic adversity the greater is the risk of disease.

The SHEEP study has extensive information on socioeconomic position and it has been possible to assign a socioeconomic position to each individual yearly from birth till inclusion. Each year in manual position for men and women has been defined as in socioeconomic adversity. The number of years in adversity has been used to calculate the share in life spent in adversity. Approximately one third of both male and female controls are in the category of never in socioeconomic adversity (reference group) and about 10 per cent are in the most exposed group of those always in adversity. Men always in adversity have a relative risk of 2.36 (95% CI: 1.79 –3.11) for MI and women in always adversity have a relative risk of 2.54 (95% CI: 1.70 – 3.78) compared to the reference groups of those never in adversity (table 5). Adjustment for unhealthy behavior, and for social factors decreases the accumulation effect. Adjustment for social trajectories during the life course also decreases the accumulation effect. The increased risk of myocardial infarction is present even just after a few years in socioeconomic adversity.

Table 5. Relative risk (RR) of myocardial infarction, with 95% confidence intervals (95% CI), and exposure to increasing proportion (%) of life in adverse socioeconomic position among men and women aged 45-70, Stockholm Heart Epidemiology Program (SHEEP) 1992-94.

% of life in adverse socioeconomic position		Men					Women				
		Never	0<=33	33<67	67=<100	Always	Never	0<=33	33<67	67=<100	Always
Crude*	RR	1	1.55	1.65	1.82	2.36	1	1.29	1.49	1.52	2.54
	95%CI		1.23, 1.96	1.32, 2.06	1.39, 2.39	1.79, 3.11		0.92, 1.79	1.06, 2.09	1.04, 2.22	1.70, 3.78
Behavioural†	RR	1	1.53	1.49	1.48	1.84	1	1.02	1.15	0.99	1.52
	95%CI		1.20, 1.95	1.18, 1.88	1.12, 1.95	1.38, 2.47		0.71, 1.46	0.80, 1.65	0.65, 1.49	0.98, 2.37
Social‡	RR	1	1.40	1.41	1.38	1.73	1	1.17	1.30	1.21	1.89
	95%CI		1.09, 1.78	1.11, 1.80	1.02, 1.87	1.26, 2.38		0.83, 1.64	0.91, 1.98	0.80, 1.82	1.22, 2.93
Psychosocial§	RR	1	1.53	1.61	1.70	2.09	1	1.22	1.40	1.35	2.18
	95%CI		1.21, 1.94	1.28, 2.02	1.29, 2.23	1.57, 2.78		0.87, 1.72	0.98, 1.98	0.91, 2.01	1.44, 3.31
Biological#	RR	1	1.58	1.66	1.83	2.28	1	1.40	1.47	1.39	2.45
	95%CI		1.24, 2.01	1.32, 2.09	1.39, 2.41	1.71, 3.03		0.99, 1.98	1.03, 2.11	0.93, 2.08	1.61, 3.73
Traject**		1	1.52	1.63	1.46	1.75	1	1.10	0.95	0.78	1.11
			1.16, 2.00	1.14, 2.33	0.95, 2.24	1.05, 2.92		0.70, 1.71	0.56, 1.62	0.39, 1.53	0.46, 2.69

† Adjusted for alcohol consumption, physical activity, smoking, age and catchment area

‡ Adjusted for cohabitation, education, family income, outside working market, age and catchment area

§ Adjusted for social network, life control, job strain, age and catchment area

Adjusted for body mass index, diabetes, hypertension, age and catchment area

** Adjusted for trajectories of social mobility, age and catchment area

Paper IV: Multi-exposure and clustering of risk factors, socioeconomic trajectories and the risk of myocardial infarction in men and women

Objective: To study the prevalence and clustering of risk factors for myocardial infarction between and within socioeconomic groups and whether the risk of myocardial infarction due to exposure to increasing number of risk factors differed between socioeconomic groups.

Men in non-manual socioeconomic position in both childhood and adulthood have the lowest prevalence of seven cardiovascular risk factors, i.e. diabetes, hypertension, low life control, low social network, obesity, physical inactivity, and smoking. For women the pattern is similar, with those with manual experience showing the highest prevalence of risk factors. Men are on average exposed to 1.31 risk factors and women to 1.47 risk factors. Those with adulthood manual experience have the highest prevalence of exposure to three or more risk factors, whereas those with non-manual adult socioeconomic position have the highest prevalence of null-exposed. In the total population we see clustering on the individual level indicated by a higher prevalence than expected of null-exposed and of those exposed to three or more risk factors. Men born in non-manual position but who end up in manual position have a high prevalence of those exposed to three or more risk factors and a strong tendency to cluster risk factors on the individual level, indicated by an observed-to-expected ratio of 138 (table 6). Though it is notable that the largest observed-to-expected ratio for both men and women is in the always non-manual group exposed to three or more risk factors, indicating that individual clustering is most common in this socioeconomic trajectory.

Exposure to increasing number of risk factors increases the risk of myocardial infarction for both men and women. In the total population the relative risk for men exposed to one risk factor is 1.70 (CI 95% 1.34 - 2.17), two risk factors is 2.43 (CI 95% 1.90 - 3.10), three or four risk factors is 4.06 (CI 95% 3.12 - 5.27), five or more is 6.75 (CI 95% 3.50 - 13.01), for women the gradient is similar. In the analyses stratified by socioeconomic position men with no risk factors have similar risks regardless of socio-economic position, but for the exposed there is a tendency for the number of risk factors to play a stronger role if you are in adult manual position.

Table 6. Age-adjusted observed (O) and expected (E) prevalence (%) of exposure to increasing number of risk factors and observed-to-expected ratio by socioeconomic position in childhood and adulthood among the controls.

Men	ALL	Child-hood		Non-manual		Self-Employed*		Farmer		Manual		N=1498												
		Adult	O	E	Non-manual		Non-manual		Manual		Manual													
					O	E	O	E	O	E	O		E											
No of risk factors	O	E	O:E	O	E	O	E	O	E	O	E	O	E	O:E										
0	27	22	122	33	29	115	18	12	154	31	29	106	28	23	119	20	16	128	27	25	108	21	15	146
1	34	39	89	36	41	88	30	32	95	41	41	100	31	39	79	28	36	79	38	40	95	30	34	87
2	24	27	89	20	23	89	20	33	59	18	23	78	32	26	121	34	31	109	25	26	97	26	32	80
3+	15	12	122	11	7.6	138	33	24	138	11	7.7	140	9.4	11	84	18	18	103	11	10	107	24	20	121
p-value			<0.001			0.01			0.01		0.4				0.22			0.51		0.72				<0.001
lambda			32.1			10.6			10.7		2.5				4.4			2.3		1.3				16.3
Women																								
No of risk factors	O	E	O:E	O	E	O	E	O	E	O	E	O	E	O:E										
0	22	18	124	29	23	128	9.9	11	90	40	37	109	29	25	115	16	12	128	17	16	106	16	12	132
1	34	36	92	32	39	82	35	31	113	42	41	103	32	41	80	28	32	88	38	35	108	29	32	90
2	27	30	91	23	27	85	35	34	104	13	18	74	31	25	121	34	33	104	27	31	89	32	33	95
3+	17	16	107	16	12	140	21	25	83	4.8	4.5	107	8.5	9.3	91	22	24	95	18	18	98	24	23	105
p-value			0.01			0.02			0.9		0.8				0.57			0.82		0.74				0.59
lambda			10.8			9.6			0.59		0.8				2.0			0.9		1.2				1.9

* Self-employed in childhood and manual in adulthood are omitted due to small numbers (men 25 controls, women 16 controls)

DISCUSSION

Socioeconomic inequalities in health

Socioeconomic inequalities in burden of disease

In Sweden one third of the burden of disease studied is unequally distributed across socioeconomic groups. The unequally distributed burden of disease is to a large extent put on the unskilled manual workers. A few disease groups account for more than half of the unequally distributed burden, with ischemic heart disease being the largest contributor, a finding also supported by a recent study.²¹⁷ The diseases with the largest contribution of DALYs to the socioeconomic inequalities in health are also the largest contributors to the total burden of disease.

The DALY measure incorporates value judgments, e.g. disability weights, gender issues, and optionally discounting and age-weighting. The manual socioeconomic groups die at younger ages than the non-manual groups. Discounting would put proportionally less burden on long future losses of healthy life lost due to deaths and chronic diseases occurring at younger ages. This would narrow the gap difference in the burden of disease between the manual and higher non-manual socioeconomic groups. Age weighting, where death and disease in older age is valued less than in younger age, could reduce the burden on the higher non-manual socioeconomic groups relatively more than for the manual groups. With age weighting, diseases occurring in younger age like psychiatric disease and traffic accidents would have a relatively larger share of the total burden of disease. Critiques of the DALY argue that preventing the death of a disabled person is valued less than preventing the death of a healthy person, as in the case of the disabled person a life in less than full health would be saved.^{112,115} On the other hand if this is put against the value choice of severity then the person in greatest need should be saved first.¹⁵⁴ Much of the debate about DALYs is related to gender issues. Some argue that the difference in life expectancy between men and women of 2.5 years used today is too short. According to this view, without the social suppression of women, women would be biologically determined to instead live 5 years longer than men.¹¹² One has to keep in mind that the eventual beneficial composition of the female body or the effects of male dominance on health is not as clear cut. Today maybe the most adequate way would be to use the same life table for both men and women. This would increase the burden of disease among men. A recent study of ethical principles among Swedish public health workers demonstrated a rejection of the idea of compensating less health with power and influence, and support of the idea that a biological based difference in health is fair, but rejected the idea of maximizing health over gender equality.²¹⁸ Hence, people were rather inconsistent in their principles.

In Europe, socioeconomic inequalities in health have been targeted as one of the most important issues for public health policy.²¹⁹ The DALY measure makes it possible to quantify the overall differences in burden of disease, and also to analyze which specific disease groups contribute most to the socioeconomic inequalities in health, while taking both mortality and morbidity into account. This helps policy makers understand overall and disease-specific inequalities in health, and subsequently to target measures to address them. E.g. the Swedish Parliament has decided on public

health priorities and goals for the coming ten years.²²⁰ Hence, in the balance between efficiency and equity, there were no conflicting choices: targeting the diseases with the largest contribution of DALYs to the overall burden of disease will also reduce inequalities in health most.

Socioeconomic position

Social stratification is present and a fundamental concept in the distribution of power and influence in society. Hence, if studying socioeconomic inequalities in health, rather than health variation, we should seek for indicators of this social stratification. Occupation, education and income are all in some part indicators of this social stratification. Östlin et al have highlighted that ignoring markers of health inequalities such as socioeconomic class, race and gender leads to biases in the content and process of research.²²¹ The discussion on what indicators of socioeconomic position to use when studying socioeconomic inequalities in health is ongoing.^{123,128,134,135,144,222} There are several proponents of the use of context- and disease-specific indicators. Braveman et al critically examined standard measurements of socioeconomic status (foremost from a US perspective) and recommended being more precise in the consideration of plausible pathways and mechanisms when choosing a measure of social position.¹⁴⁴

Geyer et al have pointed out that education, income and occupation-based measures as indicators of socioeconomic position cannot be used interchangeably as the effects on various health outcomes differ.²²³ Others have showed that education, occupational class and housing standard predict all-cause mortality in a similar way, but when broken down to cause-specific mortality the association differs indicating different causal pathways.²²⁴ Studying the effect of different indicators of socioeconomic position within the same settings results in persons being moved in and out of exposed and unexposed groups with a change in absolute level of risk in each group as a consequence. The group sizes will also change and as a consequence the measures of socioeconomic inequality will differ by what indicators are used. Within a specific setting analyzing the differences in “effect” or “explanatory power” by the use of different indicators of socioeconomic position is influenced by the studied subgroups size and absolute risk, and by whether we are studying effect on the relative or absolute scale.

Socioeconomic differences in the distribution of risk factors together with differences in susceptibility to these risk factors result in socioeconomic inequalities in health, though which these risk factors are or how the causal pathways linking exposure to disease act is not fully understood. Conventional risk factors like smoking, hypertension and cholesterol have been shown to limitedly explain the socioeconomic inequalities in coronary heart disease.²²⁵⁻²²⁷ Lynch et al pointed out that the evaluation of which risk factors contribute to the mechanisms of socioeconomic inequalities in health should not solely be based on reductions in relative risks.¹¹⁹ In their example the RR of least to most educated in the scenario of feasible minimum risk, i.e. when lowering the risk in the least educated to the level of the most educated, is similar to the RR in the scenario of theoretical minimum risk, i.e. when lowering the risk in the least educated to the level of the most educated when both groups are free from conventional risk factors. They concluded that conventional risk factors actually do explain a large part of the population burden of disease and of the absolute socioeconomic inequalities in health, as the RD in the feasible minimum risk scenario was much larger than the RD in the theoretical minimum risk scenario.

The gender paradox states that the explanation of women's higher life expectancy is that women are biologically determined to live longer than men, whereas the gender suppression of women in society causes the higher morbidity among women. Sex is a biological characteristic not equivalent to the social construct of gender. The relevance of gender relations and sex-linked biology is dependent on the studied health outcome.²²⁸ Others have pointed out that the gender paradox might not really be a paradox,²²⁹ i.e. men have both higher mortality and morbidity.¹³⁵ The results in Paper I show that the diseases that account for the socioeconomic inequalities in health among women are very similar to those that account for the inequalities among men. Hence, the socioeconomic suppression of women and men seem to affect similar pathways. In the most affluent suburbs of Stockholm the gender gap in life expectancy is the smallest.⁶⁶ Hence, when socioeconomic suppression is small the risk factor burden of men and women seem similar, indicated by small differences in life expectancy. Whether biological variation can be regarded as unfair or not is difficult to address. In general the causes of biological variation could be exposures acting during pregnancy, or just mutations by "chance". The first scenario could be valued as unfair whereas the second would not. However, these exposures could not be exposure-dependent, i.e. dependent on the sex of the child. Hence, eventual biological variation between sexes might be more difficult to address to the concept of unfairness. Though some extreme forms of fetal diagnostics resulting in the abortion of female fosters in some parts of the world could be regarded as exposure-dependent. Thus, it has been proposed to include sex ratio in measures of gender equality.²³⁰

The aforementioned difficulties in defining socioeconomic positions are greater when also including the concept of gender, i.e. should socioeconomic position on the individual or the household level be used to define men and women? Difficulties in defining and measuring gender have also been addressed.²³¹ It has been proposed to use integrated approaches to women and men's health that consider both socioeconomic inequalities and gender equity.²³² Erikson argues that occupation-based measures of socioeconomic position should take the position of both spouses into account. If we, on the other hand, want to study the effects of the work environment individual measures of occupation are better fit. In their simplest form education, income and occupation can be seen as purely individual characteristics of socioeconomic position. If a potential pathway for education leading to better health is the ability to grasp relevant information then why would not the beneficial effects of a higher education in a spouse spill over to the partner? And, if higher income makes it possible to acquire health-enhancing resources then we should measure the family's total income, as both spouses would benefit. The same idea applies to occupation-based measures of socioeconomic position. Of course, exposure to working hazards and psychosocial working conditions are individual exposures, but health behaviors, health enhancing resources and lifetime opportunities could well be affected by the socioeconomic position of the spouse.¹²⁷ The conclusion drawn from these arguments is that whenever possible occupation, education and income should also be measured in a way that they reflect the socioeconomic position, income level and the educational level of both spouses.

Measures

Decision makers of public health policy are often interested in absolute figures on exposure prevalence, costs, persons needed to treat, number of saved lives or prevented or treated morbidity.^{119,146,152,233} Easily understood and intuitively interpretable measures of group comparison are also to be preferred. As public health research on inequalities in health often deals with the whole population there is a request for measures that will depict the distribution of health of the entire population. The RR and the RD do not seem to fit the desired characteristics of a measure depicting socioeconomic inequalities in population health. Measures that quantify the public health burden due to specific risk factors for specific diseases, for example the DALY, are of interest for public health policy.^{219,233,234} The attributable fraction also serves the purpose of depicting the whole population by estimating the proportion of cases of a disease that would not have occurred if the exposure would not be present.^{234,235} Though, it is important to notice that the attributable fraction is affected not only by the magnitude of the effect but also by the group sizes of the studied exposed groups. In Paper I we used an attributable fraction measure based on the counterfactual distribution of feasible minimum risk, i.e. all socioeconomic groups having the same risk as the higher non-manuals who have the lowest risk. This should not be misinterpreted as the theoretical minimum risk of no socioeconomic exposure. For some specific outcomes higher non-manuals could have a greater risk than those in other socioeconomic groups, e.g. mortality from mountain climbing or as observed in our study the larger burden from breast cancer among higher non-manual women.

Coming back to the previously mentioned different interpretations of the social inequalities among thirteen countries in Europe, not only dependent on whether one's perspective is the absolute or relative scale, but also dependent on the notion of risk assessment from an individual perspective. From this point of view, all alike, a manual worker would choose to live where his absolute risk of disease is the lowest.^{46,150}

As discussed above the difference between absolute and relative measures is important to recognize, as is the difference between measures that compare groups and those that depict the whole population. The RR measures the effect of lower socioeconomic position on health comparing two groups, whereas the RII measures the total impact of lower socioeconomic position on population health, taking rank order and group size into account. The RD and SII express these differences in absolute terms, respectively. The attributable fraction is, as mentioned, also a measure of total impact.

In 1999 WHO presented an approach to measure total inequality in health defined as variation in health between individuals in a population.²³⁶⁻²³⁸ As this way of measuring health inequality is insensitive to the socioeconomic dimension and fails to correspond with the aforementioned recommendations of measures of socioeconomic inequalities it has been widely discussed and criticized.^{1,80,142,239,240} The measures of slope index of inequality, relative index of inequality and attributable fraction fulfill the recommendations by Wagstaff et al, and by Mackenbach and Kunst, though data availability and request for simplicity in presentation of results often also justify the use of the relative risk and risk difference.^{145,146,149}

Life course epidemiology

The accumulation model in life course epidemiology hypothesizes that the longer time spent in socioeconomic adversity the greater is the risk of disease. The results in Paper III support other studies that have shown cumulative time in life spent in adverse socioeconomic position to be associated with cumulatively increased risk of cardiovascular disease.^{39,40,164-166,168-173,182,241} The accumulation effect is just partly explained by behavioral risk factors such as alcohol consumption, physical inactivity, and smoking. In a paper showing cumulative effects on cardiovascular disease of 10 different measures of socioeconomic position and material standards in women the authors could also not fully explain the effect by adult risk factors.¹⁷² Others have pointed out that behavioral and biological risk factors measured at just one point in time does not accurately reflect their cumulative contribution to increase in risk of disease.¹⁶⁸

The early and strong increase in risk of MI after only a few years in adverse socioeconomic positions has not been reported before as it demands detailed information of the kind available in the SHEEP study. The results must be interpreted with caution, but a plausible interpretation is that anyone can spend a year or two in adverse socioeconomic positions in-between studies or jobs or when first entering the labor market regardless of childhood or supposed future socioeconomic position. We may also think of corresponding processes at the end of working life.

Accounting for directions of social mobility can decrease the effect of cumulative exposure to adverse socioeconomic position on the risk of MI.¹⁶⁹ In Paper III, controlling for social trajectories among men diminishes the accumulation gradient, but leaves the early and strong increase in risk of MI unaffected. For women both effects are diminished. This complicates the interpretation of the accumulation hypothesis as a simple dose-response relationship between exposure to socioeconomic adversity and risk of MI. Together with the finding of a rapid increase in risk after a few years of adversity this indicates important selection processes that are complementary to the accumulation of exposure. What matters is not pure accumulation of adversity in itself but also how (social mobility) and when (critical period) the accumulation occurs.

The risk of MI increases with exposure to an increasing number of risk factors. This applies to all social trajectories but there is a tendency for the number of risk factors to play a stronger role if you are in a manual position as adult, indicating possible interaction with unmeasured risk factors more prevalent in these socioeconomic groups. The relative risk of MI for the unexposed is similar between strata of socioeconomic trajectories, especially for men. This indicates that residual confounding is small or that very little of the socioeconomic inequalities, on the relative scale, in MI remains to be explained if all major risk factors were eliminated as proposed recently by Lynch et al.¹¹⁹

In Paper IV we find an increased accumulation of risk factors, for both men and women, in social trajectories including periods in manual position as has been reported by others.^{173,174,180,181,242} Accordingly we find an increased prevalence of multi-exposure considering diabetes, hypertension, low life control, low social network, obesity, physical inactivity, and smoking, among both men and women, compared to the expected level. This is especially apparent among those in a manual position in adulthood. Clustering of risk factors in individuals was seen in the unstratified analyses. Previous studies in adults found that the pattern of clustering of

cardiovascular risk factors neither differed for men nor for women between those with low and high educational attainment,²⁴³ or between women of manual and non-manual socioeconomic position.¹⁷⁴ In adolescence cardiovascular risk factor clustering has been shown to be more extreme in those with low income and those scoring low on cognitive tests.²⁴⁴ There is however in our study no indication of an extra strong clustering in manual trajectories that would contribute to the increased proportion of multi-exposed in manual groups. The results rather point in the opposite direction, as there is some clustering of multi-exposed in the non-manual trajectories.

An individual's health behavior can be simplified as either based on purely individual preferences involving free choice,^{245,246} or based on individual preferences influenced by the social, economic, cultural and political context for that individual.²⁴⁷⁻²⁴⁹ Lynch et al have shown that adult behavior is patterned by childhood socioeconomic circumstances implying that free choice is not totally free.²²⁷ Implications for health policy are profound. The idea of free choice easily ends up in victim blaming whereas the second model implies that changes in society can influence people's life chances from early childhood and as a consequence their health behavior. Discussing the mechanisms of risk factor clustering is closely related to these concepts of free choice and social construct. Have those few persons exposed to risk factors in the least adverse socioeconomic groups made a personal choice to continue being exposed to more health-damaging behaviors? Could this behavior be understood as related to acts of social construct of hedonism in these well-off groups? Conversely, in the always manual group risk factors are clustered on the group level resulting in the individuals being multi-exposed by the social construct of behavior and there is not the same a priori individual decision to take-up unhealthy behavior and thus there is less clustering in these most exposed groups. On the other hand there are more null-exposed than expected and this may in part be related to the tradition of puritanism, enhanced by popular movements among the Swedish farmers and working class in the late nineteenth and early twentieth century.

Understanding the casual chains leading to risk factor clustering is one of the important keys to the understanding of how inequalities in health emerge, be it socioeconomic position, norms in society or culture, biological mechanisms or psychosocial characteristics. However, the presence of clustering in itself is merely a descriptive measure of the risk factor profile in a studied context. The concept of clustering can be seen as occurring on two levels, the individual level (individual clustering) and clustering on the group level (in life course epidemiology usually called socioeconomic differences in risk factor accumulation). It is important to notice that accumulation in itself leads to increased levels of multi-exposure and that clustering as defined may or may not be an important feature. The reasonable interpretation of our results seems to be that social position has a large influence on the risk of becoming exposed but that a large part of the risk factor accumulation within manual trajectories operates through uncorrelated pathways if the classification of causal models proposed by Kuh and Ben-Shlomo is correct.¹²⁰ The important feature of the risk factor clustering model is that it points at a possible common cause of risk factor exposure that we would like to discover. However, it is not for certain that the best way to proceed is to conduct cluster analyses of various kinds. It might be better to develop specific mechanistic hypotheses and to test them in specifically designed studies. The outcome, whether it is a disease or an exposure, should preferably be measured as an incidence and the analyses as little biased as possible. This issue of how to get etiological insights from observations of clusters has been critically discussed before.²⁵⁰

Limitations

Methodological considerations

The occupation-based socioeconomic classification is not in its deepest sense a measure of rank order of socioeconomic groups. The measures used to describe the inequalities in health in Paper I have been the SII and the RII, both requiring rank ordering of socioeconomic groups. We have studied the five major socioeconomic groups and ordered them from unskilled manual to higher non-manual, omitting self-employed and farmers together with the unclassifiable. If the groups of self-employed and farmers and unclassifiable were to be included, and ordered with the unclassifiable as the lowest group and the self-employed and farmers in the middle, the differential burden of disease due to socioeconomic distribution would be even larger, and both the SII and the RII would increase for each of the studied disease groups.

Selection

The SHEEP study is population-based with known sampling fractions for controls and a sampling fraction very close to 1 for cases. There was no systematic difference in response rate across age groups or across hospital catchment areas. Smoking was shown to be more prevalent among non-respondents but even if all had participated the effect on the overall smoking prevalence among controls would be small. The validity of MI diagnosis and the reliability of case definition from the hospital discharge register and cause of death register were high.^{251,252} The control was sampled from the same catchment area as the case. As the catchment areas differed in socioeconomic composition and MI is more common in adverse socioeconomic groups, there could be an over sampling of controls from adverse socioeconomic groups. This would dilute the socioeconomic risk and without this over sampling the observed socioeconomic risk would be even larger.

Misclassification

Non-differential misclassification of exposure influences the effect towards the null. In the SHEEP study both cases and controls gave detailed information on their occupational history and we have no reason to believe that there is any important disease-dependent misclassification of exposure (socioeconomic position). Exposure-dependent misclassification of exposure has been proposed, e.g. women misclassified into lower socioeconomic positions.¹³⁷ In Paper II we studied the eventual misclassification of socioeconomic position and find that women are categorized into fewer occupational categories than men and also that women more often are categorized in unclassifiable subgroups. However, we did not find that this in general leads to a more severe underestimation of the socioeconomic gradient in risk among women than among men as the misclassification of socioeconomic position of women is mostly compensated for by misclassification of men.

Our findings do not support the assumption that misclassification of individual socioeconomic position is greater among women than among men, and further that the dilution of the socioeconomic gradient among women due to random misclassification of exposure may be compensated by even less misclassification among men. In epidemiology we should always consider misclassification but it may not be as crucial for the gender comparisons of socioeconomic gradients as previously proposed.

Confounding

Confounding can lead to either an under or over estimation of the effect. A confounder has an effect by itself and is differently distributed among the exposure groups to be compared.²¹² A mediating factor has an effect by itself and is part of a causal chain from the exposure to outcome, whereas a confounder is not part of that particular causal chain. The SHEEP study has extensive information on potential confounders and mediating factors for both cases and controls from birth till inclusion. In Paper II-IV using SHEEP data socioeconomic position has been the main exposure. Socioeconomic position could be seen as a distal risk factor acting through more proximal mediating factors where the distinction from confounder might not be easy to define. Adjustment in the analysis in Paper III has been done more in the notion of common causal pathways of being potential mediators than being confounders.

Conclusions

A third of the burden of disease in Sweden is unequally distributed

In Sweden approximately one third of the burden of disease studied is unequally distributed across socioeconomic groups. The unequally distributed burden of disease is to a large extent put on the unskilled manual workers. The diseases with the largest contribution of DALYs to the socioeconomic inequalities in health are also the largest contributors to the total burden of disease. Hence, in the balance between efficiency and equity, there were no conflicting choices for public health policy: targeting the diseases with the largest contribution of DALYs to the overall burden of disease will also reduce inequalities in health most.

Misclassification of socioeconomic position is not as great a problem in gender comparisons of socioeconomic risk as has been anticipated

Our findings do not support the assumption that misclassification of individual socioeconomic position is greater among women than among men, and we further conclude that the dilution of the socioeconomic gradient among women due to random misclassification of exposure may be compensated by less misclassification among men.

The higher the share of life spent in socioeconomic adversity the greater the risk of myocardial infarction

The results support the hypothesis that accumulation of time spent in adverse socioeconomic position during the life course increases the risk of myocardial infarction, in part but not fully explained by the acquisition of health-damaging experiences or by how and when the experience of adverse social positions are accumulated. In addition we find a strong effect after only a few years spent in socioeconomic adversity indicating a selection process differentiating between persons in adversity for just a short period and persons determined to stay longer in adverse positions. These findings question an overly simplistic interpretation of the accumulation hypothesis that the longer time spent in socioeconomic adversity the higher the morbidity and they indicate that it also depends on how (social mobility) and when (critical period) the accumulation occurs.

Risk clustering does not seem to play an important role in the accumulation process leading to higher prevalence of multi-exposed in the most adverse socioeconomic groups

Our findings supports the hypothesis that the greater the socioeconomic adversity the greater is the risk factor burden possibly through accumulation of risk factors although we have not included any concept of the timing of risk factor acquisition in these analyses. Different mechanisms of accumulation have been proposed in a classification of life course models of disease etiology. Risk clustering is one possible mechanism leading to more multi-exposure than expected among individuals experiencing the longest periods of socioeconomic adversity, due to socioeconomic, behavioral, psychosocial, cultural or biological factors. In combination with synergetic effects between risk factors this would lead to a greater risk of disease. However we do not find that risk clustering plays an important role in the accumulation process leading to higher prevalence of multi-exposed in the most adverse socioeconomic groups.

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