A register-based study of health equity in Swedish stroke and diabetes care delivery

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A register-based study of health equity in Swedish stroke and diabetes care delivery

Thesis for doctoral degree (PhD)

by

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I sprickorna kommer ljuset in,
jag tror man kan kalla det gryning.

- Håkan Hellström

Be kind; everyone you meet is fighting a hard battle.

- Ian Maclaren

Research never sleeps.

- Okänd
Abstract
Stroke and diabetes are relatively common conditions and have a huge impact on society’s burden of illness; over 400 million people around the world live with diabetes and 15 million have a stroke every year. Estimates on the disability-adjusted life years lost amount to 68 million due to diabetes and 120 million due to stroke annually. This burden to the individual and to society is neither ignorable nor possible to let escalate.

With a very long history of diagnosis, continuous development of treatments, and extensive research on their effects (>287 thousand articles in PubMed with stroke and/or diabetes in the title), it could be expected that the highest quality of stroke and diabetes care delivery have spread across all groups of patients, no matter demographic profile, socioeconomic situation, or geographical area of residence. The aim of this thesis is to explore whether Swedish healthcare, which is universal and tax-funded, is characterized by health inequities or not, with regards to stroke and diabetes care delivery.

To enable extensive analysis on what patient characteristics that may play a role in regaining health after diagnosis and to what extent, registry data from several local, regional and national sources were linked on patient level. Data included administrative data (from regional databases), disease-specific outcome and process markers on the entire chain of care (the Swedish Stroke Register and the National Diabetes Register respectively), demographic, socioeconomic and geographic information (Statistics Sweden), data on social insurance (the Swedish Social Insurance Agency), and data on municipal care such as special housing and home-help services (the National Board of Health and Welfare). These data were all part of the Sveus databases. All studies comprised analysis via multivariate regressions on health outcomes, resource use, and/or care process.

There are differences in health regained and healthcare received. Women with ischemic stroke were found to have lower function (approximated modified Rankin Scale) one year after stroke whilst a larger proportion of women survived the first year compared to men. Inpatient care received (regional financing) was lower for female stroke patients whilst proportion of patients staying in special housing (municipal financing) was higher during the year prior to and the year after stroke. Women with Type 1 Diabetes had worse blood glucose control compared to men. For Type 2 Diabetes, women had better blood glucose control compared to men, but higher levels of LDL cholesterol. Younger individuals typically showed worse blood glucose control than older for both Type 1 Diabetes and Type 2 Diabetes.

The socioeconomic situation of individuals afflicted with stroke and/or diabetes also seems to play a role regarding health outcomes achieved as well as care process and healthcare resources received; high educational level (>12 years) was a significant predictor for better blood glucose control in both Type 1 and Type 2 Diabetes. High educational level was also a significant positive predictor for survival first year after stroke and functional status first year after ischemic stroke (data not presented in research papers).

There is also a geographic gradient in Swedish stroke care, where a few hospitals achieve significantly better health outcomes than others and a few achieve significantly worse (adjusted for differences in patient characteristics). Some hospitals showed significantly higher levels of resource use whilst other showed significantly lower levels. No clear pattern emerged regarding the included hospitals’ relationship between health outcomes achieved and resources invested.

Studying health equity in Swedish stroke and diabetes care delivery, within the five studies included in this thesis, demonstrates that there are health inequities. Stroke and diabetes have been known and diagnosed in medicine for a long time and still, different groups of people receive different
amount of support for their condition relative to their needs, leading to significant differences in health and health-related quality of life.

To change the situation, there is work that needs to be done by the policy makers, the payers and the care providing organizations. Policy makers need to integrate health equity as part of all relevant policy development, as it is also a prioritized goal according to Swedish law. Payers (of hospital care, special housing, pharmaceutical drugs) can start adjusting their incentive models at hand towards providers, based on dimensions of health equity. Providers must then act to raise awareness on which patients are at particularly high risk of low health outcomes.
List of scientific papers

The thesis is based on the following scientific papers which will be referred to by their Roman numerals:


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<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
</tr>
<tr>
<td>AF</td>
<td>Atrial Fibrillation</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>EU</td>
<td>European Union</td>
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<tr>
<td>DALY</td>
<td>Disability-Adjusted Life Year</td>
</tr>
<tr>
<td>ICD-10</td>
<td>10th revision of the International Classification of Diseases and Related Health Problems</td>
</tr>
<tr>
<td>ICH</td>
<td>Intracerebral Hemorrhage</td>
</tr>
<tr>
<td>IS</td>
<td>Ischemic Stroke</td>
</tr>
<tr>
<td>LDL</td>
<td>Low Density Lipoprotein</td>
</tr>
<tr>
<td>LISA</td>
<td>Longitudinal integration database for health insurance and labour market studies</td>
</tr>
<tr>
<td>LtD</td>
<td>Dalarna County Council</td>
</tr>
<tr>
<td>LUL</td>
<td>Uppsala County Council</td>
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<tr>
<td>mRS</td>
<td>modified Rankin Scale</td>
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<tr>
<td>NCD</td>
<td>Non-communicable disease</td>
</tr>
<tr>
<td>NIHSS</td>
<td>National Institutes of Health Stroke Scale</td>
</tr>
<tr>
<td>PAS</td>
<td>Patient Administrative System</td>
</tr>
<tr>
<td>PREM</td>
<td>Patient Reported Experience Measure</td>
</tr>
<tr>
<td>PROM</td>
<td>Patient Reported Outcome Measure</td>
</tr>
<tr>
<td>RJH</td>
<td>Region Jämtland Härjedalen</td>
</tr>
<tr>
<td>RS</td>
<td>Region Skåne</td>
</tr>
<tr>
<td>RTB</td>
<td>Total Population Register</td>
</tr>
<tr>
<td>RÖ</td>
<td>Region Östergötland</td>
</tr>
<tr>
<td>SAH</td>
<td>Subarachnoid Hemorrhage</td>
</tr>
<tr>
<td>SKL</td>
<td>Swedish Association of Local Authorities and Regions</td>
</tr>
<tr>
<td>SLL</td>
<td>Stockholm County Council</td>
</tr>
<tr>
<td>SoL</td>
<td>Register for care and social services for the elderly and for persons with impairments</td>
</tr>
<tr>
<td>SoS</td>
<td>The National Board of Health and Welfare</td>
</tr>
<tr>
<td>TIA</td>
<td>Transient Ischemic Attack</td>
</tr>
<tr>
<td>UN</td>
<td>United Nations</td>
</tr>
<tr>
<td>VGR</td>
<td>Region Västra Götaland</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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1. Introduction

The United Nations (UN), the World Health Organization (WHO) and the European Union (EU) declare that equity in healthcare is key [1, 2]. The UN declaration of human rights states that a state is obliged to ensure that healthcare is accessible to all, and especially for marginalized and vulnerable groups [3]. Equity in Swedish healthcare is regulated by the Healthcare Act [4], which, together with the universal, tax-subsidized, access to healthcare make health equity expected in the Swedish context.

Reading the first paragraph above might give the impression that health equity or equity in general is a straightforward topic, which would be a significant exaggeration. And perhaps that is a reason for this thesis’ existence; health inequity is a complex concept and comprises multiple perspectives, widely different and sometimes contradictory, depending on the dimension studied. Extensive research has been performed on the topic (see Table 1 and Table 2). Linking the studies to the theoretical foundation of health equity is however somewhat rare.

The WHO has highlighted four non-communicable diseases (NCD) that are particularly heavy burdens to society (cardiovascular diseases including stroke, diabetes mellitus, pulmonary disease and cancer), paired with four risk factors that are modifiable and hence possible for the individual person to impact (tobacco use, unhealthy diet, physical inactivity and harmful alcohol consumption) [5]. Actions against these NCDs are core parts of the WHO Global Action Plan on NCDs [6].

This thesis is a study of health equity with two conditions out of the four mentioned above as examples; stroke (ischemic and intracerebral hemorrhage) and diabetes mellitus (Type 1 and Type 2). Stroke and diabetes are both important comorbidities to one another, and diabetes is also a risk factor for stroke. They can both end up being chronic conditions depending on how well the stroke patient is rehabilitated and how well her activity abilities and functions are recovered. To be able to study health equity in Swedish healthcare on a more general level it is advantageous to investigate pathways regarding both the stroke patient and the diabetes patient. Studying care related to stroke and diabetes enlightens us on different aspects of care; the two conditions afflict patients with different baseline characteristics and health profile, treatment of the two conditions demand resources in separate domains of the healthcare system, and different types of resources and procedures are required during treatment. Thus, studying health equity in the healthcare system is more probable to be valid if evaluating equity within both stroke care and diabetes care (which may sometimes overlap) than one of them alone.

It has not been possible to discuss more general features of health equity concerning stroke and diabetes care delivery within each separate research paper included in the thesis. The thesis’ sections treating health equity is my chance to dig deeper and connect empirical evidence to previously developed theories, and to initiate a discussion on today’s situation as well as on desired policy implications.
Figure 1. Stroke and diabetes incidences in Sweden 2013-2017 according to the national quality registries. Data from the Swedish Stroke Register [7], the National Diabetes Register [7] and Statistics Sweden [8].

Figure 2. Number of new studies per year treating health equity, from 1970 until today. Based on availability on PubMed using search query including equity/equality/inequity/inequality in the abstract and/or title. Total refers to all articles available with "study" or "studying" in title and/or abstract.
1.1 Health equity – what, why and how?

There might be concerns regarding the reasons for assessing the degree of health equity in society. This is probably not the case for readers with a fundamentally egalitarian point of view, i.e. who believe that all individuals – no matter what origin, social status, sex, education or income – are equal in terms of the value of their needs [9]. Some may however think that health equity is not a prioritized goal in itself. Still, these readers probably have an interest in understanding how the distribution of health and healthcare appears across society’s population. But as Sen argues [10], all people – no matter their philosophical or political view – do have some particular dimensions which they think should be equal to everyone, such as equal rights or equal access, or equal opportunities.

In our modern society, the distribution of health would probably be practically possible to control, with highly sophisticated methods to track and map, to ease and to heal. The distribution of health is not to be confused with the distribution of wealth; redistribution of health may not actually require redistributing wealth but could instead be more a question of what the optimal allocation of resources is (e.g. preventative measures rather than reactive measures) or what a more efficient organization of care could look like.

It is worth highlighting the difference between equality and equity in this context. Equality is a descriptive concept with objective facts relating to a certain situation e.g. the amount of outpatient visits per capita for different groups. Equity, on the other hand, adds the perspective of potential justification or absence of justification for such objective facts; is the difference in outpatient visits per capita adequate or not? Health equity can be defined as the absence of systematic disparities in health between different groups defined by their differing social advantages in society, as proposed by Braveman and Gruskin [11], or the absence of unwarranted and avoidable gaps in health between groups with different levels of privilege, e.g. demographic, socioeconomic or geographic [12]. The purpose of this thesis is to, as transparent as possible based on the research performed, show how today’s situation appear with regards to the distribution of health and healthcare after stroke and/or diabetes diagnosis for different groups in society.

In this thesis, health equity in Swedish stroke and diabetes care delivery is studied in terms of the presence of sociodemographic determinants and to what extent these may be related to achieved health outcomes and received care. As Harvard professor and Nobel laureate Amartya Sen points out, the classification of individuals into groups can be made to point out different diversification, which will enlighten us regarding certain inequities but not others [10]. In this thesis I have used traditional ways of classifying individuals into groups to study equity between these groups, for example based on sex or educational level. Indicators used for assessing health equity and comparing results after stroke or diabetes care include health outcomes, levels of resources and degree of different processes received, and can be found in Table 6.

1.1.1 Health equity and its definition(s) within this thesis

World Health Organization presents four overarching dimensions to equity in terms of differences between groups; demographic, social, economic, and geographic [13]. Several attempts to define health equity have been made in the scientific literature; as the subject has a philosophical nature rather than an objective, e.g. medical or physiological one, one needs to understand the rationale behind equity to be able to judge whether there are inequities and whether these are unjust.

Equal opportunities to good health among the general population implicitly assume the same opportunities and access to care in order to achieve health outcomes in line with the rest of the
population, regardless of differences in e.g. sex, origin and socioeconomic status. Consequently, any unwarranted health difference related to such factors should be considered unjust. Whitehead [14] argues that health inequity is the same as avoidable and unjust health differences, i.e. the individual’s belonging to a certain subgroup of the population (e.g. sex) rendering a lower outcome with statistical significance when adjusting for other selected explanatory factors of relevance, is to be seen as a health inequity. Braveman [15] follows that line and states that health equity should be defined as the absence of systematic disparities between the groups (defined by differences in social advantages), and that the level of health within the most privileged group in society could be observed as the minimum level of health for the whole population at a later point in time. However, health inequities within some European countries (e.g. England and Wales) have not only been present for quite a while; they have also widened during the last decades [16].

If health equity is the absence of systematic differences in health between groups of different advantages, then health equity must also be equivalent to absence of systematic differences in social determinants of health (systematic differences in social determinants of health imply differences in health, given the fact that they are “determinants”), i.e. there should be no social determinants of health in a society characterized by true health equity. In free societies, inhabitants tend to specialize within different tasks which demand varying levels of theoretical education. Hence, it is natural with varying levels of education, and the fact that people have different levels of theoretical education cannot possibly be a warranted, just, or fair explanation to differences in achieved health outcomes. Health equity could in that sense also be considered a matter of social justice.

Given that achieved health outcomes to a certain extent depend on the amount and type of resources invested in treatment, it is necessary to also highlight the resource consumption when evaluating health equity in a population. Furthermore, as some explanatory factors can be considered to have a motivated (warranted) clinical effect on the health outcome studied (e.g. reduced consciousness upon arrival at emergency unit could be considered justified to affect the likelihood of survival and return to daily activities) and some explanatory factors cannot be considered a justifiable effect on the health outcome studied (e.g. the patient’s sex as the reason for increased likelihood of good activity ability after stroke), it is important to distinguish them in the discussion on equity and its influencing factors. To complicate things, the reduced consciousness at arrival may be due to the actual stroke severity at onset, but it may as well be due to modifiable factors dependent on e.g. the patient’s living situation.

Within this thesis, stroke and diabetes care delivery is studied from the perspective of health outcomes achieved and the resources invested as well as the care processes leveraged to achieve these outcomes. The outcomes of a patient’s treatment have its base in several separate elements regarding what is generally denominated the determinants of health (see Figure 3). I have tried to distinguish between gradients within health equity on three different dimensions: demography, socioeconomic and geography.

The demographic gradient includes the effect that may come from a patient’s sex or age on the treatment pathways or treatment results. The socioeconomic gradient relates to differences in health outcomes or healthcare consumption that are associated with the belonging in a group with similar characteristics in terms of e.g. educational level or income level. The geographic gradient refers to whether a patient’s geographical residence correlate with the health achieved or healthcare

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1 Given that the studies within this thesis are retrospective, observational registry studies, it is hard to tell whether a causality or only a correlation is at hand.
received. Previous research on these dimensions of health equity in a Swedish setting, regarding stroke and diabetes care delivery, is presented in Table 1 and Table 2 respectively.

1.1.2 Theoretical foundation
There are several theories developed to understand and assess equity or equality. In general, the literature on the subject treats inequity or inequality, i.e. the difference between groups, rather than treating how equal the levels relating to a given indicator are. To better understand the distribution of health in society, it can be valuable to have a look at the distribution of other parameters that in general have a close association with health levels and development of health, such as social and economic welfare.

Theories for understanding and assessing inequity in general
Many of the theories published include health under a broader welfare category. It makes sense to do so, but to understand how health inequity arises and is reinforced, methods focused on assessing inequity in health are needed. The reason for this is merely that health does not have the same properties as welfare in terms of e.g. possibility to redistribute. Temkin [17] discusses several aspects of inequity of which I have selected those I find best suited for discussing inequities in health;

1. Relative versus absolute differences. In the context of treatment outcomes, the relative comparison is generally the most common, e.g. comparisons versus the average or versus other individuals or units. One exception to this would be e.g. adherence to guidelines which often refer to absolute levels in terms of blood glucose or systolic blood pressure. If the comparison is relative, it is still a question whether the individual level for a patient (of body function, of specialized rehabilitation, or of an expensive but effective treatment intervention) should be compared to the average or to the level of the best-off patient/group of patients.

2. The individual’s responsibility of her own health. The discussion on genomic heritage, social effects and the informed choice of the individual is complex. The (assumed to be) informed decision on e.g. smoking or physical activity may have significant consequences for the individual patient’s prognosis to live a well-functioning, healthy and perhaps long life.

3. Maximin principle of justice or equality. Defined by Rawls [18] (as the difference principle) and developed by Temkin [17], the maximin principle of justice states that how well a system delivers depends on how well the worst-off group fares “with respect to inequality” [17]. Applied in practice, this principle would imply that a healthcare system with the apparent mission to deliver welfare to all, including the best off and the worst off, is at its best (and relatively better than other systems, e.g. other regions’ or countries’) when the worst-off group is well taken care of.
**Selected framework focused on health equity**

There is extensive research literature on the topic of health equity and determinants of health. Several elements influence the existence of any (systematic) differences in health outcomes or healthcare consumption; based on a conceptual framework developed by Burström [19], the pathway can be divided into six high-level steps. These are, with some modification, presented in Figure 3.

![Conceptual framework for the arising of inequity in health and healthcare](image)

**Figure 3. Conceptual framework for the arising of inequity in health and healthcare.** Adopted from Burström [19].

There are several dimensions to the emergence of health equity, and the degree of change over each of these steps – possibly to be regarded as a multiplier – determines the different levels that can be observed in the final steps; healthcare delivery and consumption, and health outcomes. Where in this chain of events an individual’s health is especially affected may also vary on individual level. The scope of this thesis includes primarily assessments of the last two steps and aims at illustrating how the determinants of health – the first step – can explain the gradients of any differences to be observed regarding healthcare delivery and consumption (resource use as well as care process) and health outcomes. There is also a dimension of quality of care in the link between healthcare delivery and health outcome, i.e. how much good is done with the resources at hand.

In addition to understanding the key output – health outcomes – it is of importance to also understand and quantify the resource side of it; different groups of patients demand different levels of resources to achieve the same levels of health as the “healthiest” group. It may however be considered challenging, if not impossible, to point out where to draw the line on when the marginal effect per invested Swedish krona is no longer feasible to pay for.

**General indicators of inequity**

There are some general indicators extensively used in the literature to measure the distribution of welfare in a society. These indicators are not often applied to specific cases such as stroke or diabetes care delivery.

The Gini index (introduced by statistician and sociologist Corrado Gini in 1914 [20] and to a broader English speaking audience in 1921 [21]) is a measure of dispersion and relative inequality, initially developed to study the inequality of income and welfare. Its constitution is illustrated in Figure 4, where the y-axis shows the cumulative share of the good or service – e.g. health-related quality of life – whereas the x-axis shows the cumulative share of individuals with a given attribute – e.g. income – ranked from lowest to highest (lowest x is the individual with the lowest income). The 45-degree line represents a situation where health-related quality of life is equally distributed across the population, i.e. all individuals, no matter their income, contribute with an equal share of health-
related quality of life. The grey line – the Lorenz curve – represents an example situation where health-related quality of life is unequally distributed among the individuals studied. The area under the line of perfect equality and above the Lorenz curve (the area of concentration) tells us that individuals with relatively lower income have generally lower health-related quality of life. If the Lorenz curve was situated above the line of perfect equality the relationship would have been the opposite, i.e. the individuals with relatively lower income would be generally better off with regards to health-related quality of life.

Figure 4. Illustration of the Gini index; the line of perfect equality and the Lorenz curve.

This general measure is often used for high-level comparisons, e.g. between countries. However, comparisons have also been performed on other dimensions and on more regional level, e.g. to study healthcare access across different geographical areas [22]. There are also examples on putting the Gini index in relation to disease-specific indicators; Burns and colleagues found that there was a significant positive relationship between the Gini index and the incidence rate of schizophrenia [23], i.e. higher inequality was associated with higher risk of schizophrenia.

There are additional measures such as the decile dispersion ratio (indicates relative inequality, calculated by best-off decile relative to worst-off decile [24]), the Hoover index (also known as the Robin Hood index, Schutz index or Pietra ratio; shows the proportion of distributed wealth to be redistributed in order to achieve perfect equality [25]) and the Atkinson index (presents the proportion of a society’s income that needs to be given up to reach a state of higher income equality, and depends on a given input value on society’s aversion of inequality [25]). These indicators will not be further discussed in this thesis but could potentially be applied to received care or achieved health outcomes after a performed intervention as well as to income and welfare. There are, however, challenges with applying a theory for distribution of wealth to distribution of health, as the latter tend to be somewhat more inert. One notable critique of these general measures is also that they do not account for changes in population volume – e.g. an increase in the absolute number of people in the worst-off group should possibly be viewed as an increase in inequality (at least not a decrease), but according to the Gini index the degree of inequality thereby decreases [26]. The challenge in an international setting is that definitions tend to vary somewhat across borders and therefore one needs to be cautious when performing such comparisons.
1.1.3 Health equity in the Swedish healthcare system

Together with other Nordic countries, Sweden is often referred to as a country with a highly developed welfare system and ability to equalize the distribution of good health among its population [16]. Stated in Swedish law, quality of care shall be independent of a patient’s background, health profile and sociodemographic characteristics, and healthcare delivery should be executed in accordance with individuals’ needs for good health [4]. This statement is in line with the concept of horizontal equity – that equal needs should be reflected in equal healthcare access – as well as with vertical equity – that different needs should be reflected in adequately different healthcare access [27, 28]. Thus, there should be no unwarranted differences in delivered care dependent on differences in e.g. sociodemographic patient characteristics. These explicit law statements are closely related to the overall purpose with the studies within this thesis, which is to determine whether Swedish healthcare (exemplified by stroke and diabetes) could be viewed as characterized by health equity, and whether there are sociodemographic or geographic drivers to differences.

For any welfare-focused state such as Sweden, aspiring to proffer equity across all categories of services offered (including healthcare), the explicit goal is and probably will remain: higher degree of health equity. Notwithstanding the rise of the welfare state, health inequities have not been eradicated and their magnitude do not seem to become smaller over time. The Swedish situation is an illustrating example, anecdotally exemplified by the studies of stroke and diabetes patients included in this thesis. Sweden is generally known as the typical welfare state, with a relatively low Gini index and ranked as being in the higher span in terms of decommodification rates [29] as well as social spending per capita [30]. According to Mackenbach [31], Sweden shows a low relative index of inequality regarding education (for both sexes) and its impact on mortality. Furthermore, Sweden stands out as having low absolute differences in mortality within the population – only the Basque region in Spain beats Sweden regarding lowest inequalities in average rate of death from any cause. Based on e.g. the Gini index in Sweden relative to other countries, it could be suggested that any differences observed between sociodemographic and geographically distributed groups for the Swedish stroke and diabetes patient populations may be of higher proportions when applied to other countries in the world. In other words, if there are significant disparities in equitable Sweden, disparities may be of higher magnitude in other countries. Such a speculative hypothesis would also be an argument to why studying health equity in Sweden should be regarded as highly relevant, as health equity may not be higher in any other country in the world. Interestingly though, Mackenbach [31] did not observe any pattern of systematically smaller differences in health in populations of countries in northern Europe (characterized by more generous welfare policies) compared to other European countries [31]. These findings were based on self-assessed health and the results were not stratified on single conditions such as stroke or diabetes. Whether there is no pattern of systematically smaller differences in e.g. Sweden for the patient populations with these specific conditions is possible but yet to be assessed.
1.2 Stroke

Stroke is an acute condition with risk of severe sequels, particularly if not treated. It is the third leading cause of death in the world, and the third largest cause of disability, with 6.2 million deaths and 120 million DALYs yearly estimated for 2017 (132 million DALYs if including SAH) [32, 33].

1.2.1 Pathophysiology

Stroke is defined as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting at least 24 hours or leading to death, with no apparent cause other than of vascular origin [34]. A stroke can be due to either an occlusion of a blood vessel due to thrombosis or emboli, hereafter referred to as ischemic stroke (IS), or a rupture of the vessel, i.e. a hemorrhagic stroke (intracerebral or subarachnoid hemorrhage) [35].

1.2.2 Epidemiology

During the last couple of years stroke has afflicted approximately 21,000-26,000 individuals per year in Sweden [7, 36], corresponding to an incidence rate of 0.3% of the Swedish population above the age of 18 years [8]. Approximately 75% are first-ever strokes [7]. Of all stroke cases in Sweden, approximately 85% are ischemic, 10% are intracerebral hemorrhages (ICH), and 5% are subarachnoid hemorrhages. More than 80% of stroke cases affect individuals over 65 years of age. Men are predominantly afflicted in younger ages whilst the proportion of women is larger in higher ages [7, 37]. In the study populations for this thesis, only intracerebral hemorrhages and ischemic strokes are included.

Stroke incidence in Sweden has decreased by 15% between 2010 and 2017 overall (although not for all age groups) [7]. There is however concern that the global incidence of and mortality from ischemic stroke will take an upturn for the first time in more than 40 years, possibly due to the increasing prevalence of obesity [32, 38]. There is also evidence that stroke incidence has increased in younger age groups over the last couple of years [39]. Risk factors for stroke include hypertension and atrial fibrillation [40]. For stroke as well as for diabetes, four major lifestyle factors have been raised by the WHO; physical activity, diet, tobacco and alcohol use [5].

Stroke morbidity and mortality is a costly burden to the individual as well as to society. Impairments after stroke include both physical and mental dimensions. In addition to major suffering for patients and their close ones, stroke implies high monetary costs for society, short-term and long-term. Total annual costs due to stroke in Sweden have been estimated to SEK 18 billion [41].

The National Board of Health and Welfare's report on Swedish stroke care states that it could be considered equal on several areas, based on age, sex and geography. At the same time, regional differences in waiting times as well as differences between sexes and socioeconomic groups regarding post-stroke drug treatment are pointed out [42]. Also, regional differences for stroke patients in terms of resource utilization and health outcomes have been described [43].

1.2.3 Treatment of stroke

There are several highly recommended treatment interventions for stroke patients; acute pharmacological and interventional treatments in the acute phase, physical and cognitive rehabilitation in the post-acute phase, and pharmacological preventive treatments in the acute as well as the post-acute phase.
Early acute reperfusion treatment of ischemic stroke includes thrombolysis and thrombectomy. Both have the purpose of removing the thrombosis or emboli causing the ischemia, and thus allow for reperfusion of the brain tissue. Thrombolysis is an intravenous treatment where a pharmaceutical drug is introduced into the blood stream to dissolve the blood clots which would otherwise cause tissue ischemia. It has been proven to be effective under certain time intervals, which have emerged with continuously updated scientific evidence [44-47]. Treatment with thrombolysis also induces risk of side-effects as it has a systemic effect on the entire body’s coagulation process. Thrombectomy is a catheter-based interventional method to remove blood clots from a blood vessel. It has gained an increase in penetration rate as recent scientific evidence has demonstrated its contribution to significantly improved clinical outcomes [48]. A study of thrombectomy in terms of costs and benefits has been performed on Swedish data and deemed the treatment intervention cost-saving from a societal perspective [49]. It is a relatively new treatment intervention and in need of highly competent and experienced neuro interventionists, and so far there is an apparent geographical gradient in the Swedish system’s offering of it [7, 50] (Figure 5).

Hemicraniectomy is a procedure which includes removing parts of the scull bone to release pressure on the brain due to the stroke. It is relatively uncommon, and performed in less than 0.2% of the cases in Sweden [7]. In close relation to having had an ischemic stroke, endarterectomy – removal of stenotic tissue in the carotid arteries – has been shown to be associated with lower risk of stroke recurrence [52, 53].

The National Board of Health and Welfare continuously updates national guidelines for treatment of stroke. These guidelines consider the care process of the stroke patient and include 110 recommendations in the 2018 version. Recommendations include three types; actions to take (graded on a scale 1-10), actions to take if evaluated within a research project, and actions not to take. Actions with the highest degree of priority (“priority 1”) include [54]:

Figure 5. Geography and thrombectomy: number of interventions per 100,000 inhabitants, split by greater healthcare region. Sweden is divided into six greater healthcare regions which shall all be capable of offering advanced care; not to be confused with Sweden’s 21 regions or county councils which tax their inhabitants and fund healthcare for individuals living in their geographic area [51]. Data available via the Swedish Stroke register [7] and the National register for endovascular treatment of stroke [50].
• Structured process for acute care including preparations for thrombolysis and thrombectomy if needed
• Offering thrombolysis within 4.5 hours from stroke onset (first symptom) for patients with acute ischemic stroke
• Offering thrombectomy for patients with acute ischemic stroke and occlusion of the major front vessels of the brain
• Using angiography in direct relation to computed tomography (CT) to identify any occlusion in the major front vessels of the brain in patients with acute ischemic stroke, to prepare for thrombectomy if needed
• Offering treatment at specialized stroke unit in immediate relation to hospital arrival for patients with suspected stroke
• Offering treatment at specialized stroke unit for patients with confirmed stroke
• Offering a doctor’s examination for multimorbidity patients who stay at special housing or receive home care and who are at risk of having a stroke
• Offering ultra sound for patients with ischemic stroke for whom surgical intervention in the carotid(s) (endarterectomy) may be in question
• Offering endarterectomy within 14 days after stroke for patients with carotid stenosis symptoms
• Offering decompressive hemicraniectomy in the acute phase to patients with expansive ischemic stroke
• Examining ability to swallow in patients who have had a stroke
• Using CT to confirm SAH in individuals with severe headache and with less than six hours from onset
• Using lumbar puncture to confirm SAH in individuals with severe headache, with less than six hours from onset, and whom have undergone CT

A significant proportion of the strongly recommended actions (4 out of 13 priority-1 recommendations) relates to treatment with thrombolysis or thrombectomy or preparations to enable such treatment. None of them regards long-term rehabilitation. In addition to the guidelines, the National Board of Health and Welfare has published 35 indicators (including target levels for selected ones), that are designed to reflect adherence to the guidelines over the care process.

Another highly important measure to mitigate risk of stroke recurrence is pharmaceutical drugs, and the pharmacological need depends on stroke subtype, i.e. ischemic versus hemorrhagic. After ischemic stroke, the risk of stroke recurrence is reduced with antithrombotic drugs that impact the coagulation process and risk of blood clotting. If no atrial fibrillation is present, an antiplatelet such as aspirin and/or clopidogrel is used. In patients with embolic stroke anticoagulants are used. Antivitamin K used to be the major secondary prophylactic treatment option but there are now several non-vitamin K anticoagulant drugs available which have increased in penetration during the last couple of years. In addition, statins, antihypertensive medication and, if needed, antiarrhythmic treatment are strongly associated with outcomes in terms of stroke recurrence and vascular death of other origin [40]. In hemorrhagic stroke, antihypertensive treatment is recommended [55].

Stroke unit care has been shown to improve outcome. Patients treated in stroke units are more likely to be alive, independent, and living at home one year after the stroke, regardless of age, sex, or type of stroke [56-59]. Major parts of available literature and results from clinical trials are focused on the acute phase. The long-term outcomes for the individual as well as for society are however dependent also on specialized rehabilitation.
1.2.4 Stroke and mental comorbidity

One percent of the global population receives a formal diagnosis of psychosis or schizophrenia, and the prevalence in Sweden is equivalent; the actual number of afflicted individuals is however expected to be significantly higher [60, 61]. These individuals generally consume more of healthcare resources than other patients; with worse somatic health, they are also more likely to develop comorbidity [62-65]. Somatic comorbidity also seems to be more common in women than in men for this group [66, 67], and the risk of cardiovascular disease increases after treatment with antipsychotic drugs [68, 69].

![Number of PubMed hits concerning stroke and mental comorbidity](image)

**Figure 6. Number of new studies per year treating stroke and mental comorbidity, from 1990 until today.** Based on availability on PubMed using search query including stroke and mental health/mental illness/mental comorbidity/mental ill health in the abstract and/or title.

As seen in Figure 6 there seems to be an increasing awareness in the scientific community, but still unexpectedly low. The group of stroke patients with pre-stroke psychosis and/or schizophrenia – how they are treated in comparison to other stroke patients, and to what extent they regain health after stroke – is relatively unstudied. It has been shown that these patients have lower access to care and to some procedures, [70, 71] also within a universal healthcare system [72, 73]. Furthermore, these individuals receive less stroke rehabilitation [74]. Diagnosis of psychosis or schizophrenia may be considered as having higher specificity compared to other states of mental ill-health and has been shown to be associated with cerebrovascular disease [75]. The subgroup of stroke patients with previous psychosis and/or schizophrenia diagnosis was hence considered an adequate group of individuals to study in terms of comorbidity compared to other stroke patients.
1.3 Diabetes

Diabetes mellitus is a group of chronic metabolic conditions with the common property of inability to maintain consistent blood glucose levels without treatment, which may lead to acute as well as chronic complications. To fulfill the WHO’s diagnostic criteria of diabetes mellitus, there has to be either a fasting glucose of >7.0 mmol/L or a blood glucose of >11.1 mmol/L at 2 hours after ingestion of 75 g of oral glucose (glucose tolerance test), or a level of glycated hemoglobin (HbA1c) of >6.5% [76].

Diabetes is the eighth leading cause of death from non-communicable disease (NCD) in the world (number 15 overall) and the ninth leading cause of disability (number six of NCDs), causing 1.4 million deaths and 68 million DALYs annually [32, 33]. It has been estimated that over 400 million individuals around the world live with diabetes [77]. Between 2007 and 2017 Type 2 Diabetes showed the largest relative increase in DALYs of all conditions defined by the WHO. In addition, rates of complication due to diabetes are on the rise; chronic kidney disease due to Type 2 Diabetes showed the second largest relative increase of all conditions defined by the WHO in terms of DALYs during 2007-2017 [33].

1.3.1 Pathophysiology

The main differentiation of diabetes mellitus is based on the pathologic process leading up to the inability to self-maintain consistent blood glucose levels, and the most common types are Type 1 Diabetes (T1D) and Type 2 Diabetes (T2D). Both types result from several gene mutations in combination with environmental factors, and T2D is considered hereditary to a larger extent than T1D [78]. There are light variants of the condition, with impaired ability to keep blood glucose in the normal interval, referred to as impaired fasting glycemia and impaired glucose tolerance. These conditions can be an intermediary stage (“prediabetes”) prior to a clinical diagnosis of diabetes, and individuals with such a condition are at increased risk of complications compared to individuals with normal levels of fasting glucose [78, 79].

T1D arises when the pancreas fails to produce insulin needed to lower blood glucose by enabling glucose to enter the body’s cells, and it is due to an autoimmune reaction against the insulin-producing beta cells of the pancreas. T2D originates from a combination of higher tolerance and lower secretion of insulin, and an increased hepatic production of glucose [79].

1.3.2 Epidemiology

The prevalence of diabetes in Sweden has been estimated to a total of 4-5% for the two main types, and approximately 85-90% of diabetes patients suffer from T2D [80, 81]. The prevalence of impaired glucose intolerance, an indicator of developing T2D, is estimated to be twice the diabetes prevalence, i.e. 8-10%. For diabetes as well as for stroke, four lifestyle factors have been raised by the WHO as particularly important to address; physical inactivity, unhealthy diet, tobacco and alcohol consumption [5].

Increased rates of short-term and/or long-term complications of diabetes lead to increased need of care and resource utilization. Socioeconomics have been shown to play a role in the development of diabetes and diabetes care; low level of education or low income is associated with increased risk of T2D, and it is more common for low-income individuals not to reach treatment goals for HbA1c and/or blood lipids [81, 82].
1.3.3 Treatment of diabetes

Treatment of diabetes aims at keeping blood glucose homeostasis and thereby minimizing the risk of complications. Complications include vascular — microvascular (nephropathy, neuropathy and retinopathy) and macrovascular (cerebrovascular disease such as stroke and peripheral artery disease) — as well as nonvascular ones including skin changes and infections [79]. A key to successful treatment is continuous monitoring of the patient’s blood glucose levels, but also to monitor his/her health status in terms of risk factors for associated morbidity and to manage any complications.

Individuals with T1D are dependent on continuous treatment with insulin injections, as about one third of individuals with T2D [78]. These are in general manually managed, but the penetration rates of automatic support with injections via insulin pumps are increasing [7]. T2D patients use other pharmaceutical agents such as metformin to lower the insulin resistance. Maintaining a healthy diet and physical activity are main components of a diabetes patient’s self-treatment.

The National Board of Health and Welfare continuously updates national guidelines for treatment of diabetes. These guidelines include recommendations (approximately 140 in the 2018 version) of three types; actions to take (graded on a scale 1-10), actions to take if evaluated within a research project, and actions not to take. Actions with the highest degree of priority (“priority 1”) include [83]:

- Offering intense statin treatment for individuals with diabetes at high risk of CVD
- Offering antihypertensive treatment for individuals with diabetes and hypertension
- Offering support to stop smoking for individuals with diabetes who smoke
- Offering support to increase physical activity for individuals with T2D
- Offering intense treatment for individuals with T1D to reach best blood glucose levels possible with regards to risk of hypoglycemia, reduced quality of life or other negative influences on the individual’s well-being
- Offering intense treatment for individuals with recently diagnosed T2D and no known CVD to reach best blood glucose levels possible with regards to risk of hypoglycemia, significant weight gain, reduced quality of life, expected remaining life span and other morbidity
- Offering annual examination of the urine concentration of albumin in individuals with diabetes
- Offering fundus photography every third year for individuals with T2D who are not diagnosed with fundus disease
- Offering systematic self-assessment of blood glucose levels for individuals treated with insulin injections
- Offering metformin monotherapy for individuals with T2D given no intolerances or contraindications
- Offering care from a multidisciplinary foot team for individuals with severe foot complications (e.g. wounds, infections or deformities)

There are 21 indicators, with target levels for selected ones, that are designed to reflect adherence to the guidelines over the care process.
2. Perspectives on health equity in Swedish stroke and diabetes care delivery

2.1 Previous research: Overview – scope, search and findings

Previous research on the topic of health equity within stroke and diabetes care in a Swedish context has been reviewed. The search was performed in accordance with PRISMA guidelines [84]. Eligibility criteria for inclusion in the systematic review were: evaluation of health equity in stroke or diabetes patients with regards to health outcomes (e.g. mortality), resource use (e.g. inpatient care) or process (e.g. treatment intervention such as thrombolysis) as study outcome, based on Swedish registry data, published during 2000-2018 in a peer-reviewed journal available on PubMed. For inclusion in the final review, studies had to treat health equity based on differences in either demography (e.g. sex, age), social context (e.g. education, immigration, marital status), economics (income) or geography (regional variation). Studies regarding differences in incidence of the conditions only were excluded. Furthermore, international comparisons of outcomes have been excluded as the focus has been regional variations in Sweden specifically. The search string is specified in Appendix A.

Health equity, as being a broad topic, was divided into categories based on what aspect of equity or inequity that was part of each study’s objective. The studies have been divided into three categories based on dimension of equity used, in line with the WHO [13]; demography, socioeconomics (merge of the WHO’s “social” and “economic” dimensions), and geography. If not explicitly stated in the article assessed, categorization was based on the perspectives presented in the article’s results section or based on expressed aim of the study. In total, 27 articles were assessed in full-text and 23 of these were included in the qualitative synthesis. All data sources and outcomes studied have been named as stated in each article respectively.
Of the included articles, 13 treated stroke and 10 related to diabetes care delivery. The major part of stroke articles treated either sex differences (five articles) or socioeconomic differences (seven articles), and the most common outcomes studied were survival or fatality/mortality. All articles applied adjustment of results to reflect differences in case mix between the compared groups, to a varying degree. Studies focused on either ischemic stroke only (five articles) or both ischemic and hemorrhagic stroke (eight articles). None of the retrieved full-text articles focused on hemorrhagic stroke only.

Of the diabetes articles included in the review, six treated T1D, three articles treated T2D and one article treated diabetes as a general condition. The studies assessed association between outcomes and socioeconomic factors (seven articles) or sex (three articles). Most common outcomes studied were mortality (three articles) and glycemic control (three articles). Reviewing previous research on diabetes, it became clear that long-term follow-up is needed to study hard endpoints (e.g. mortality) or long-term disease impact (e.g. end-stage renal disease) as was the case in one of the articles (follow-up time in this study amounted to 19-36 years). The more common approach was to study intermediate outcomes such as glycemic control (HbA1c levels).
Table 1. Previous research on health equity in Swedish stroke care delivery.

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
<th>Year</th>
<th>Registry source(s)</th>
<th>Primary outcome(s) (equity indicators)</th>
<th>Health equity perspective</th>
<th>Covariates / stratification</th>
<th>Study population (incl sex distr and information on case/control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex differences in stroke care and outcome in the Swedish national quality register for stroke care</td>
<td>Eriksson et al [85]</td>
<td>2009</td>
<td>Swedish Stroke Register (Riksstroke)</td>
<td>Fatality, living situation, health status including depression, ADL, patient satisfaction</td>
<td>Demography (sex)</td>
<td>Sex, age</td>
<td>24,633 stroke cases (12,350 men, 12,283 women)</td>
</tr>
<tr>
<td>Sex, diastolic blood pressure, and outcome after thrombolysis for ischemic stroke</td>
<td>Nathanson et al [86]</td>
<td>2014</td>
<td>Södersjukhuset local stroke registry</td>
<td>Functional status (modified Rankin Scale), mortality</td>
<td>Demography (sex)</td>
<td>Sex, age, diastolic blood pressure, comorbidity, medication and selected interaction terms</td>
<td>355 patients (193 men, 162 women)</td>
</tr>
<tr>
<td>Education level and inequalities in stroke reperfusion therapy: observations in the Swedish stroke register</td>
<td>Stecksén et al [87]</td>
<td>2014</td>
<td>Swedish Stroke Register (Riksstroke)</td>
<td>Reperfusion treatment (thrombolysis and/or thrombectomy)</td>
<td>Socioeconomics (education)</td>
<td>Sex, age, education, living situation, ADL, comorbidity, smoking, antihypertensive agents. Stratification on hospital specialization.</td>
<td>85,885 patients (50,166 men, 35,719 women)</td>
</tr>
<tr>
<td>Few sex differences in the use of drugs for secondary prevention after stroke: a nationwide observational study</td>
<td>Sjölander et al [88]</td>
<td>2012</td>
<td>Swedish Stroke Register (Riksstroke) and Swedish Prescribed Drug Registry (Läkemedelsregistret)</td>
<td>Prescribing, primary adherence (filling prescription first 4 months after discharge), persistence (first 2 years after discharge)</td>
<td>Demography (sex)</td>
<td>Age, comorbidity, stroke severity, stroke unit care, statin treatment</td>
<td>18,349 patients (9,331 men, 9,018 women)</td>
</tr>
<tr>
<td>Study Title</td>
<td>Authors</td>
<td>Year</td>
<td>Main Outcomes</td>
<td>Data Sources</td>
<td>Variables</td>
<td>Sample Size</td>
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<tr>
<td>Reduced inequality in access to stroke unit care over time: a 15-year follow-up of socioeconomic disparities in Sweden.</td>
<td>Glader et al [89]</td>
<td>2013</td>
<td>Stroke unit care</td>
<td>Swedish Stroke Register (Riksstroke), Statistics Sweden (LISA, SCB)</td>
<td>Sex, age, education, income, living situation, ADL, stroke severity, stroke severity, year of stroke onset</td>
<td>124,173 patients (77,535 men, 46,638 women)</td>
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<tr>
<td>Socioeconomic Inequalities in the Prescription of Oral Anticoagulants in Stroke Patients With Atrial Fibrillation</td>
<td>Sjölander et al [90]</td>
<td>2015</td>
<td>Prescription of any oral anticoagulant at discharge</td>
<td>Swedish Stroke Register (Riksstroke), Statistics Sweden (LISA, SCB), Swedish National Inpatient Register (Patientregistret)</td>
<td>Sex, age, country of birth, education, income, living situation, ADL, stroke severity, comorbidity, smoking</td>
<td>12,033 patients (5,423 men, 6,610 women)</td>
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<tr>
<td>Socioeconomic factors’ effect on return to work after first stroke</td>
<td>Glader et al [91]</td>
<td>2016</td>
<td>Return to work (patient-reported)</td>
<td>Swedish Stroke Register (Riksstroke), Statistics Sweden (LISA, SCB)</td>
<td>Sex, age, functional status (low mood, pain, ADL), income/education/living situation/country of birth, answering of questionnaire</td>
<td>2,539 patients (1,594 men, 945 women)</td>
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<tr>
<td>Socioeconomic disparities in stroke case fatality - Observations from Riks-Stroke, the Swedish stroke register</td>
<td>Lindmark et al [92]</td>
<td>2013</td>
<td>Case fatality (8-28 days, 29 days-1 year after stroke respectively)</td>
<td>Swedish Stroke Register (Riksstroke), Statistics Sweden (LISA, SCB), Swedish Cause of Death Register</td>
<td>Sex, age, education, income, country of birth, living situation, stroke severity, comorbidty, smoking, stroke subtype, medication, year of stroke onset</td>
<td>60,105 patients (37,074 men, 23,031 women)</td>
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<tr>
<td>Topic</td>
<td>Authors</td>
<td>Year</td>
<td>Database</td>
<td>Outcome Measures</td>
<td>Study Population</td>
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<tr>
<td>Differences in cardiovascular risk factors and socioeconomic status</td>
<td>Eriksson et al [93]</td>
<td>2013</td>
<td>Swedish Stroke Register (Riksstroke), Statistics Sweden (LISA, SCB)</td>
<td>Survival, cause of death, Socioeconomics (education, income)</td>
<td>155,806 stroke patients (77,544 men, 78,262 women); diabetes subcohort consisted of 29,580 stroke patients (19.0% of study population)</td>
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<tr>
<td>Life satisfaction in younger individuals after stroke: different predisposing factors among men and women</td>
<td>Röding et al [94]</td>
<td>2010</td>
<td>Swedish Stroke Register (Riksstroke)</td>
<td>Life satisfaction, Demography (sex)</td>
<td>1,068 stroke patients (609 men, 411 women)</td>
<td></td>
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</tr>
<tr>
<td>Sex differences in management and outcome after stroke: a Swedish national perspective</td>
<td>Glader et al [95]</td>
<td>2003</td>
<td>Swedish Stroke Register (Riksstroke)</td>
<td>Case fatality, functional status, dependence on help, living situation, Demography (sex)</td>
<td>19,547 stroke patients (9,881 men, 9,666 women)</td>
<td></td>
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</tr>
<tr>
<td>Large variations in the use of oral anticoagulants in stroke patients with atrial fibrillation: a Swedish national perspective</td>
<td>Glader et al [96]</td>
<td>2004</td>
<td>Swedish Stroke Register (Riksstroke)</td>
<td>Prescription of oral anticoagulants, Geography (regional variation)</td>
<td>18,276 stroke patients (the two subcohorts presented consisted of approximately 53% women each)</td>
<td></td>
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</tr>
<tr>
<td>Sociodemographic factors are associated with utilization of statins after ischemic stroke/TIA - a cross sectional retrospective study</td>
<td>Geary et al [97]</td>
<td>2017</td>
<td>National Swedish Prescribed Drug Register, Statistics Sweden national registers</td>
<td>Dispensation of statins, dispensation of antihypertensive agents</td>
<td>Socioeconomics (education, income, country of birth)</td>
<td>Sex, age, education, income, country of birth</td>
<td>24,312 stroke patients (the subcohort presented, alive 12 months after stroke, consisted of 9,801 men, 9,443 women)</td>
</tr>
</tbody>
</table>
Table 2. Previous research on health equity in Swedish diabetes care delivery.

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
<th>Year</th>
<th>Registry source(s)</th>
<th>Primary outcome(s) (equity indicators)</th>
<th>Health equity perspective</th>
<th>Covariates / stratification</th>
<th>Study population (incl sex distr and information on case/control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Swedish study of immigrant children with type 1 diabetes showed impaired metabolic control after three years of treatment.</td>
<td>Söderström et al [98]</td>
<td>2016</td>
<td>Swedish National Quality Registry for Paediatric Diabetes in Sweden, Statistics Sweden national registers</td>
<td>Glycaemic control (HbA1c), frequency of hypoglycemia or ketoacidosis</td>
<td>Socioeconomics (immigration)</td>
<td>Sex, BMI, insulin method and units, maternal marital status, maternal education level, maternal employment, maternal social welfare, housing</td>
<td>2,627 diabetes patients; each patient born to immigrant parents matched by three children born to Swedish parents on sex, age and year of diabetes onset (diagnosis)</td>
</tr>
<tr>
<td>Risk of hospitalization for type 2 diabetes in first- and second-generation immigrants in Sweden: a nationwide follow-up study.</td>
<td>Li et al [99]</td>
<td>2013</td>
<td>Swedish Hospital Discharge Register, Statistics Sweden national registers</td>
<td>Risk of hospitalization for type 2 diabetes (T2D)</td>
<td>Socioeconomics (immigration)</td>
<td>Immigrant status (first or second generation), sex, age, geographical region (one of Sweden’s three major cities, Southern Sweden, Northern Sweden), employment, comorbidity, family history of T2D hospitalization</td>
<td>Entire national population 1964-2007</td>
</tr>
<tr>
<td>Long-term detrimental consequences of the onset of type 1 diabetes on annual earnings—evidence from annual registry data in 1990-2005</td>
<td>Steen Carlsson et al [100]</td>
<td>2010</td>
<td>Econ-DISS (Diabetes Incidence Study in Sweden) research database, Statistics Sweden national registers</td>
<td>Annual earnings (after diabetes onset)</td>
<td>Socioeconomics (impact on income)</td>
<td>Sex, age, living in urban area, employment, own and parental education</td>
<td>3,650 diabetes cases, 14,629 controls</td>
</tr>
<tr>
<td>Study Title</td>
<td>Authors</td>
<td>Year</td>
<td>Database/Source</td>
<td>Outcome</td>
<td>Covariates</td>
<td>Cases/Subjects</td>
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<tr>
<td>Age and gender differences in the impact of diabetes on the prevalence of ischemic heart disease: a population-based register study.</td>
<td>Wiréhn et al [101]</td>
<td>2008</td>
<td>Care Data Warehouse in Östergötland (regional administrative database), Cause of Death Registry</td>
<td>Ischemic heart disease</td>
<td>Demography (age, sex)</td>
<td>Sex, age, comorbidity</td>
<td>10,364 diabetes cases, 11,311 ischemic heart disease cases</td>
</tr>
<tr>
<td>Marginal structural model to evaluate the joint effect of socioeconomic exposures on the risk of developing end-stage renal disease in patients with type 1 diabetes: a longitudinal study based on data from the Swedish Childhood Diabetes Study Group</td>
<td>Pazzagli et al [102]</td>
<td>2017</td>
<td>Swedish Childhood Diabetes Register, Swedish Renal Register, National Inpatient Register, Statistics Sweden and National Board of Health and Welfare national registers</td>
<td>Risk of end-stage renal disease</td>
<td>Socioeconomics (unemployment, income support)</td>
<td>Sex, age, own and parental education level, birth cohort</td>
<td>4,034 diabetes patients</td>
</tr>
<tr>
<td>Study Title</td>
<td>Authors</td>
<td>Year</td>
<td>Dataset/Registers</td>
<td>Outcomes/Variables</td>
<td>Participants/Events</td>
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<tr>
<td>Impact of ethnicity on progress of glycaemic control in 131,935 newly</td>
<td>Rawshani et al [103]</td>
<td>2015</td>
<td>National Diabetes Register, National Board of Health and Welfare national registers</td>
<td>Progress of glycaemic control</td>
<td>131,935 diabetes</td>
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<tr>
<td>diagnosed patients with type 2 diabetes: a nationwide observational study</td>
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<td>Socioeconomics (country of birth)</td>
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<td>from the Swedish National Diabetes Register</td>
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<td>Sex, age, diabetes duration, BMI, smoking, previous CVD, physical activity,</td>
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<td>medication, income, education, eGFR</td>
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<tr>
<td>Mortality in childhood-onset type 1 diabetes: a population-based study.</td>
<td>Dahlquist et al [104]</td>
<td>2005</td>
<td>Swedish Childhood Diabetes Register, Cause of Death Register</td>
<td>Mortality (included but not limited to diabetes-related events)</td>
<td>78 cases of fatal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Demography (sex, age)</td>
<td>events in diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Association Between Socioeconomic Status and Mortality, Cardiovascular</td>
<td>Rawshani et al [105]</td>
<td>2016</td>
<td>National Diabetes Register, National Inpatient Register, Cause of Death Register,</td>
<td>Mortality (all-cause, cardiovascular, diabetes-related, cancer)</td>
<td>217,364 diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease, and Cancer in Patients With Type 2 Diabetes</td>
<td></td>
<td></td>
<td>Statistics Sweden national registers</td>
<td>Socioeconomics (income, educational level, marital status, country of birth)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sex, age, diabetes duration, smoking, HbA1c, eGFR, treatment, BMI, albuminuria,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>comorbidity, income, education, marital status, country of birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teenage girls with type 1 diabetes have poorer metabolic control than</td>
<td>Samuelsson et al [106]</td>
<td>2016</td>
<td>Swediabkids (National quality registry for paediatric diabetes in Sweden), National</td>
<td>Glycaemic control (HbA1c)</td>
<td>4,239 diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>boys and face more complications in early adulthood.</td>
<td></td>
<td></td>
<td>Diabetes Registry</td>
<td>Demographic (sex)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sex, age, diabetes duration, smoking, BMI, physical activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impact of Socioeconomic Status on Cardiovascular Disease and Mortality in 24,947 Individuals With Type 1 Diabetes</td>
<td>Rawshani et al [107]</td>
<td>National Diabetes Register, Swedish Inpatient Registry, Causes of Death Registry, Statistics Sweden national registers</td>
<td>Mortality, cardiovascular event</td>
<td>Socioeconomics (marital status, income, education, country of birth) and demography (sex)</td>
<td>Sex, age, diabetes duration, immigrant status, smoking, HbA1c, eGFR, physical activity, comorbidity, albuminuria, blood status, systolic blood pressure, marital status, income, education, country of birth</td>
<td>24,947 diabetes patients</td>
<td></td>
</tr>
</tbody>
</table>
2.1.1 Demography
Sex differences were studied in five of the articles treating stroke. In these articles, outcomes after stroke were either adjusted for sex as a covariate in multivariable regression or outcomes were stratified by sex.

According to the stroke studies included in this review, sex differences in outcomes after stroke care in Sweden exist to some extent. Lower functional status after stroke in women compared to men stands out as a general finding [85, 86, 95]. Differences in survival have also been studied in the same three articles but with somewhat different conclusions. Eriksson 2009 [85] found that women survived the first three months after stroke to a significantly lower degree than men (OR 1.080, 95% CI 1.008-1.158). Regression models within this study were adjusted for sex and age. However, assessing survival in men and women stratified by level of consciousness at arrival to hospital showed that women survived the first three months to a larger extent than men (OR 0.899, 95% CI 0.831-0.974). No significant difference in three-month survival was found by Nathanson 2014 [86] although the authors comment that this may depend on a relatively small study sample. Glader 2003 [95], with a larger study sample (19,547 stroke patients evenly distributed between sexes) and multiple adjustments simultaneously performed, did however also conclude that there were no significant differences in case fatality at three months after stroke between men and women. Eriksson 2013 [93] found that the risk of death after stroke in diabetes patients was significantly higher in women than in men (adjusting for several confounders including patient characteristics, functional status, comorbidity, stroke severity, care process measures and socioeconomic factors).

According to Nathanson [86], women gained relatively more than men with thrombolysis treatment – going from a worse state at stroke onset to a similar status after treatment, with a significant difference in functional recovery, although the study sample was relatively small (n=355). Glader 2013 [89] found that women were treated at a specialized stroke unit to a lower degree than men (OR 0.97, 95% CI 0.95-0.99), having adjusted for confounders such as age, living situation, ADL dependency, comorbidity, education and income.

Age differences between men and women at stroke onset were presented in four of the five studies and highlighted as an important reason for differences in how stroke present in women versus men as well as in the treatment process. For example, Eriksson 2009 [85] concluded that men were on average 4.8 years younger than women and presented age and more severe strokes (level of consciousness at hospital arrival) as the major reasons for women’s lower degree of survival at three months after stroke onset. Age differences between men and women at stroke onset amounted to 4.4-7.0 years in the studies included in the review.

Prescription, adherence (four months) and persistence (two years) to prescription were studied by Sjölander 2012 [88]. The authors found that women were prescribed statins (age-adjusted prevalence ratio, PR, 0.86; 95% CI 0.82-0.91) and warfarin (PR 0.88; 95% CI 0.79-0.97) to a lesser extent (adjusted for different patient characteristics in separate models as presented in Table 1). There was no difference in what the authors call primary non-adherence (filled prescriptions first four months), neither regarding persistence (filled prescriptions first two years) except for antihypertensive treatment with better compliance in women. The authors state that poor persistence in general appears to be a great problem in society and that it should receive more attention. Similar results were shown by Geary 2017 [97] who studied a stroke cohort from Stockholm county. Female sex, lower educational level and income were associated to lower utilization of statins after ischemic stroke. Glader 2003 [95] also concluded that female sex was associated with lower degree of oral anticoagulants prescription, after adjusting for patient characteristics, functional status prior to stroke and clinical status at stroke onset.
Life satisfaction after stroke and potential differences between women and men were studied by Röding 2010 [94]. The authors concluded that there are different drivers of life satisfaction in women versus in men. Further, the women included in the study were less satisfied with their vocational and financial situation than the men.

Three of the included articles on diabetes studied sex differences [98, 101, 104]. A common finding for these was that women were worse off regarding the outcome studied (diabetes-related event mortality, HbA1c levels, and progress of ischemic heart disease risk). However one of them, Wiréhn 2008 [101], found that ischemic heart disease (IHD) afflicted men to a larger extent in each age stratum, but the main finding was that progress of IHD risk due to diabetes was significantly more severe in women. The extent of case-mix adjustments made within these studies varied; all adjusted results for age differences, one also included comorbidity, and in one (Samuelsson 2016 [106]) results were also adjusted for diabetes duration, smoking, BMI and physical activity.

2.1.2 Socioeconomics

Education has been put forward as one of the best variables for assessing socioeconomic association with outcomes in a Swedish context and therefore as the most commonly used [39]. It is also relatively standardized over time (standardization on micro-data level performed by Statistics Sweden [108]). Education could be viewed as a determinant of other socioeconomic measures such as income, although this may not always be the case. Income was included as a predictor for differences in health, resource use or process in six of the 13 stroke articles and in three of the 10 diabetes articles. Country of birth and/or immigration and the association of these with outcomes was explicitly the objective in three of the diabetes articles. One of these also studied the extent of association over generations by comparing outcomes in first-generation immigrants and second-generation immigrants.

Most articles included in this review which were not treating sex differences specifically did instead treat socioeconomic differences and/or their potential impact on outcomes. For stroke, the studies treated access to reperfusion therapy dependent on education level [87], access to stroke unit care dependent on education and income [89], prescription of statins and prescriptions of anticoagulants to stroke patients with atrial fibrillation dependent on education, income and country of birth [90, 97], return to work after stroke dependent on education and income [91], and stroke fatality dependent on education, income, country of birth and living situation [92]. Also, differences in risk of death after stroke dependent on cardiovascular risk factors, socioeconomics (education, income and country of birth) and diabetes diagnosis were assessed in one study [93].

In general, for the above-mentioned studies, socioeconomic dimensions were in fact found to be associated with the outcomes studied. University education and secondary education were associated with higher rates of reperfusion therapy (thrombolysis and/or thrombectomy) after ischemic stroke compared to primary education, adjusted for a wide range of patient characteristics as presented in Table 1 [87]. Also, a socioeconomic gradient regarding access to stroke unit care was presented [89]; although diminishing over time, patients with university education or secondary education as highest educational level were treated at stroke unit to a higher degree than patients with primary education as highest educational level. Income was not significantly associated with access to stroke unit care.

Sjölander 2015 [90] assessed prescriptions of oral anticoagulants (OAC) in first-ever ischemic stroke patients with atrial fibrillation and found that OAC prescriptions were less common in patients born outside of Sweden, in patients with primary school education compared to university education, in
patients with highest income compared to lowest income (analysed in tertiles) and that they were less common with higher age. These analyses were also adjusted for patient characteristics such as stroke severity (level of consciousness at hospital arrival), ADL dependency, comorbidity and smoking.

Glader 2016 [91] found return to work to be less common in patients with low income compared to high income (analyzed in tertiles), after adjustment for other relevant factors such as sex, age and functional status. However, when also adjusting for whether the patient answered the questionnaire on his/her own or with help, no significant differences were identified on the socioeconomic dimensions studied (income, education, country of birth).

Lindmark 2013 [92] identified a socioeconomic gradient in stroke case fatality, present already within 8-28 days after stroke onset. Income and cohabitation were factors associated with differences, and the association increased with fatality >28 days. Educational level was associated with fatality >28 days whilst country of birth was not significant for any of the two phases of fatality. Analyses were also adjusted for sex, age, comorbidity, smoking, stroke severity (level of consciousness at hospital arrival), medication and year of stroke onset.

Of the diabetes studies evaluating association with socioeconomics, three studies explicitly focused on immigration [98, 99] or ethnicity [103], one treating T1D and two treating T2D. One diabetes study [100] assessed income specifically – the impact of T1D onset on income. For the remaining three articles on socioeconomic association (one regarding T1D, two regarding T2D), several factors were assessed simultaneously and none of the ones included (education, income, country of birth, marital status) were particularly emphasized according to the study objectives.

According to the articles assessed within this review, there are significant and unwarranted differences between native Swedes and immigrants regarding outcomes in individuals with T1D and T2D. Söderström 2016 [98] assessed glycemic control in children with T1D born to immigrants versus native Swedes. They found that second-generation immigrants with T1D had significantly higher HbA1c after three years of treatment compared to their Swedish peers, whilst the frequency of ketoacidosis and hypoglycemia did not differ between the groups. Li 2013 [99] studied the risk of hospitalization due to T2D in first-generation and second-generation immigrants. They found that differences in the risk of T2D-related hospitalization compared to patients of native Swedish descent were weakened in second-generation immigrants compared to first-generation, and the authors put forward that environmental factors are likely of greater importance than genetic factors in this context. These conclusions stress the significance of personalized, patient-centered lifestyle interventions.

Rawshani 2015 [103] found ethnicity to be a significant predictor of poorer glycemic control in T2D patients (after adjustment for relevant confounders such as sex, age, diabetes duration, BMI, smoking, previous CVD, physical activity, medication, eGFR, income and education) – in spite of that these same groups of immigrants received glucose-lowering therapy earlier than the native Swedish peers and had a higher number of medical consultations.

Steen Carlsson 2010 [100] studied long-term (up to 15 years) consequences of income dependent on T1D onset. The authors found no significant difference before onset. After T1D onset, adjusting for relevant confounders such as employment, own and parental education, they found that individuals with T1D diagnosis earned less (on average 5.3%) and were less likely to be employed. The authors stress the importance of personalized medicine and self-management improvements to increase not only health in T1D individuals but also productivity on today’s labor market. T1D generally afflicts
younger individuals compared to T2D and stroke, and the burden of disease in terms of disability to work may be substantial to society.

The three studies assessing simultaneous association between different socioeconomic factors and health outcomes (cardiovascular disease in T1D, mortality in T1D and T2D, and end-stage renal disease in T2D) found that several factors do influence health in T1D and T2D patients. Rawshani 2015 [107] concluded that marital status (never married compared to married), income level (lowest two quintiles compared to highest quintile), educational level (primary school compared to university degree), country of birth (born in Sweden versus outside Sweden) and sex (men compared to women) have significant (negative) impact on the risk of cardiovascular disease and death in individuals with T1D. Rawshani 2016 [105] found the exact same socioeconomic factors to have significant impact on mortality (all-cause, cardiovascular, cancer) in individuals with T2D. One relationship of particular interest is the so called healthy migrant effect, which is a term for a lower mortality risk in (non-Western) immigrants compared to native Swedes, suggesting that these immigrants “represent a select and stronger subgroup of their native country” [105]. Pazzagl 2017 [102] concluded that unemployment and receiving income support are associated with higher risk of developing end-stage renal disease in individuals with T2D.

2.1.3 Geography

Only one of the studies included in this literature review treated geographic comparison within Sweden; Glader 2004 [96] assessed regional variations in the degree of prescription of oral anticoagulants before and after stroke onset in patients with atrial fibrillation. Regional variations were significant after adjustment for differences in sex, age, functional status and comorbidity, and the authors conclude that region-level factors (and hence not always national evidence-based recommendations and guidelines) determine whether stroke patients receive optimal treatment or not, regarding primary as well as secondary stroke prevention.

In addition, Stecksn 2014 [87] assessed whether differences in hospital specialization, which may be related to geographical situation, seem to have an impact on the probability of receiving reperfusion therapy after ischemic stroke. Differences in treatment dependent on educational level were not significant except for in large non-university hospitals, where university education and secondary education were associated with higher rates of reperfusion therapy compared to primary education. One of the diabetes studies, which were excluded due to studying T2D incidence and not outcomes for already diagnosed diabetes patients, treated geographic differences [109].
2.2. Recent development and initiatives in Sweden

Several Swedish authorities have healthcare analysis as a part of their mission. The National Board of Health and Welfare (Socialstyrelsen) states that the authority works for "access to good health and social care on equal terms" [110]. An example of this continuous work is the online database on selected indicators for several conditions (Vården I Siffror [111]) that are intended to reflect the situation in Swedish healthcare across the different regions. The Swedish Agency for Health and Care Services Analysis (Myndigheten för vård- och omsorgsanalys) states, in the report "Equal care is possible", that patient characteristics such as sex, ethnicity, sexual orientation and socioeconomic conditions should not affect the extent of care and treatment that the patient receives, and neither should place of residence or region of care [112]. Initiatives on health equity have been established at different levels within Swedish healthcare. One example is the Commission for Equal Health (Kommissionen för jämlik hälsa), appointed by the Swedish government in 2015. The Commission's main focus was around health differences between socioeconomic groups and disparities between sexes [113]. For Swedish stroke and diabetes care specifically, national programs have been established with the objective to collect and enhance availability of knowledge on the conditions and their treatment. The programs are financed by the Swedish Association of Local Authorities and Regions (Sveriges Kommuner och Landsting) [114].
3. Aims and contributions

3.1 Aims of the thesis

Equity in health and healthcare has several dimensions. Equity can be analyzed based on access, level and content of the care offered as well as based on the level of health, body function and activity achieved after treatment, i.e. health outcomes. The collective aim of the studies included within this thesis was to evaluate the extent of health equity in Swedish healthcare today with stroke and diabetes care delivery as examples, based on data for seven of Sweden’s regions (approximately 65% of Sweden’s population). More specifically, to assess and describe possible differences in health outcomes, resource use and care process between subgroups of patients undergoing stroke and diabetes care respectively, and to analyze what factors that may impact such differences.

Subgroups selection has been done to reflect a couple of different perspectives on health equity; the demographic, socioeconomic and geographic perspectives. Each study was performed to test the hypothesis of whether the groups studied had equal health outcomes, resources and/or processes. In a case where such a hypothesis can be rejected, there are health inequities. The purposes for the individual research papers (I-V) included in the thesis were:

I. To explore the relationship between patients’ sex and post-stroke health outcomes and received care in a Swedish setting.

II. To estimate the level of health outcomes and resource use at a hospital level during the first year after a stroke, and to identify any potential differences between Swedish hospitals after adjusting for patient characteristics.

III. To investigate whether Type 1 Diabetes Mellitus care showed absence of systematic disparities and unwarranted differences between groups defined by differences in sociodemographic situation in a setting with universal, tax-funded healthcare.

IV. To investigate the association between sociodemographic factors and diabetes-related health outcomes in individuals with Type 2 Diabetes Mellitus in a setting with universal, tax-funded healthcare.

V. To explore potential differences in health, resource use, and treatment process after stroke for patients with pre-stroke psychosis or schizophrenia, compared to other stroke patients, in a setting with universal, tax-funded healthcare.

3.2 Possible contributions

Conclusions from each separate study reveal potential differences between the subgroups and render knowledge regarding which groups that may require additional efforts (i.e. what factors drive differences and whether such differences are unwarranted or not). Conclusions could enhance identification and spreading of best practices, which could hopefully provide an opportunity to increase equity in Swedish stroke and diabetes care delivery and ensure the best possible health outcomes and effective use of society’s resources.

As equity is and has been a prioritized topic in the Swedish context, the public debate on how to further increase and sustain health equity in society is a continuous discussion on several levels in the community. The studies included in this thesis contribute to the research literature with an update on the health equity situation for two example conditions, each with a significant contribution to society’s total burden of illness. The thesis is supposed to be a timely update regarding the situation in Sweden, to deepen the understanding of how health equity can be viewed and measured, and to highlight some possible policy implications with regards to the results presented.
Decentralization of the decision making within Swedish healthcare to the 21 regional administrative regions also renders a continuous urgency to understand how the situation has evolved nationally during the last couple of years. The thesis will also show to what extent available registries can be used for evaluating health equity. Given the multiple data sources included in the research databases and the ability to adjust results for systematic differences between subgroups, conclusions from the studies have a possibility to become important knowledge contributions on health equity for stroke and diabetes patients in Sweden today. Consequently, the thesis and its studies should be able to further enrich the decision base for e.g. prioritization and resource allocation in healthcare systems with universal and tax-subsidized healthcare.
4. Participants and methods

For all research papers included in this thesis, the study material consisted of patient-level data from regional and national registries. The Sveus databases, which were built from data collected from several sources during the thesis project, were leveraged for the five studies performed. Linking of data was performed on patient level to enable analysis on outcome drivers on individual level. As the data sources cover most of all available research registries in Sweden on the subject, the coverage in terms of indicators could be considered high. Table 3 presents an overview of the five studies.
Table 3. Study overview for research papers I-V

<table>
<thead>
<tr>
<th>Study</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data sources</td>
<td>Patient administrative systems, the Swedish stroke register, LISA, RTB, SoL, MiDAS</td>
<td>Patient administrative systems, the Swedish stroke register, LISA, RTB, SoL, MiDAS</td>
<td>Patient administrative systems, the National diabetes register, LISA, LMR, MiDAS</td>
<td>Patient administrative systems, the National diabetes register, LISA, LMR</td>
<td>Patient administrative systems, the Swedish stroke register, LISA, RTB, SoL, LMR</td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>Main diagnosis inpatient of intracerebral hemorrhage (I61*) or ischemic stroke (I63*) and registration in the Swedish stroke register</td>
<td>Main diagnosis inpatient of intracerebral hemorrhage (I61*) or ischemic stroke (I63*) and registration in the Swedish stroke register</td>
<td>Main or secondary diagnosis of T1D (E10*) in PAS and registration in the National Diabetes Register and/or use of insulin according to the Prescribed Drug Registry</td>
<td>Main or secondary diagnosis of T2D (E11*) in PAS and/or registration in the National Diabetes Register</td>
<td>Main diagnosis inpatient of ischemic stroke (I63*) in PAS and registration in the Swedish stroke register</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>Patients younger than 18 years of age</td>
<td>Patients younger than 18 years of age</td>
<td>First diabetes diagnosis during last year, patients younger than 18 years of age</td>
<td>First diabetes diagnosis during last year, patients younger than 18 years of age</td>
<td>Patients younger than 18 years of age</td>
</tr>
<tr>
<td>Number of episodes</td>
<td>27,691</td>
<td>14,125</td>
<td>16,367</td>
<td>416,228</td>
<td>46,350</td>
</tr>
</tbody>
</table>
4.1 Process setup – the Sveus research and development project

The Sveus project was initiated in 2013 by the Swedish Ministry of Health and Social Affairs (Socialdepartementet) together with seven Swedish regions (Jämtland Härjedalen, Östergötland, Dalarna, Uppsala, Skåne, Stockholm and Västra Götaland). Funding was provided by the collaborating parties, and seven conditions with different properties were included (hip/knee osteoarthritis, spine surgery, maternity care, bariatric surgery, stroke, diabetes and breast cancer).

The overarching purpose of the project was to enable healthcare-providing caregiving units and healthcare-financing regions to analyze and monitor healthcare in a more sophisticated way than previously, to enhance patient-centered and equitable healthcare as well as to enhance a stimulating workplace environment for healthcare personnel. One main activity to achieve this purpose was to develop a set of key performance indicators per condition and to reach consensus within assigned expert groups on what indicators to analyze in order to assess patient-centered performance (levels of health outcomes, resource use and care process), how to define these indicators and select factors of high relevance to adjust for when assessing performance.

4.1.1 Gathering of expertise

To enable alignment and receive expert input from the Swedish scientific and clinical community, multi-disciplinary expert groups were gathered with representatives from several clinical and scientific expert bodies as well as all regions participating in the research project. For each condition covered, experts in the field were asked to join. The expert group involved in the Sveus stroke project is presented in Table 4 and the Sveus diabetes expert group is presented in Table 5, including representative affiliations.
Table 4. Sveus stroke expert group. Participants and co-authors of the final project report.

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation/Representation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sven Andreasson</td>
<td>The Swedish Stroke Association (patient representative)</td>
</tr>
<tr>
<td>Elisabeth Ekstrand</td>
<td>Swedish Association of Physiotherapists</td>
</tr>
<tr>
<td>Lena Eriksson</td>
<td>Region Skåne</td>
</tr>
<tr>
<td>Mia von Euler</td>
<td>Karolinska Institutet</td>
</tr>
<tr>
<td>Birgitta Fagervall-Yttling</td>
<td>Swedish Association of Occupational Therapists</td>
</tr>
<tr>
<td>Lena Henrikson</td>
<td>Swedish Association of Speech Therapists</td>
</tr>
<tr>
<td>Konstantin Kostulas</td>
<td>SLL/ The Swedish Neurological Society</td>
</tr>
<tr>
<td>Ingrid Lekander</td>
<td>Employed at Ivbar, affiliated to Karolinska Institutet</td>
</tr>
<tr>
<td>Mikael Lilja</td>
<td>Region Jämtland Härjedalen</td>
</tr>
<tr>
<td>Stefan Olsson-Hau</td>
<td>Region Skåne</td>
</tr>
<tr>
<td>Hélène Pessah-Rasmussen</td>
<td>Skåne University hospital</td>
</tr>
<tr>
<td>Katharina Stibrant Sunnerhagen</td>
<td>Swedish Association for Rehabilitation Medicine/WebRehab</td>
</tr>
<tr>
<td>Jörg Teichert</td>
<td>Dalarna county council</td>
</tr>
<tr>
<td>Patrick Vigren</td>
<td>Region Östergötland</td>
</tr>
<tr>
<td>Christina Wikman-Lundbom</td>
<td>Region Västra Götaland/Swedish Geriatric Society</td>
</tr>
<tr>
<td>Carl Willers</td>
<td>Employed at Ivbar, affiliated to Karolinska Institutet</td>
</tr>
</tbody>
</table>

Table 5. Sveus diabetes expert group. Participants and co-authors of the final project report.

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation/Representation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gudrun Andersson</td>
<td>Swedish Association for Nurses in Diabetes Care</td>
</tr>
<tr>
<td>Ingalena Andersson</td>
<td>Swedish Association of Clinical Dietitians, Diabetes section</td>
</tr>
<tr>
<td>Mette Axelsen</td>
<td>Swedish Association of Clinical Dietitians, Diabetes section</td>
</tr>
<tr>
<td>Tobias Dahlström</td>
<td>Dalarna county council</td>
</tr>
<tr>
<td>Mats Ek</td>
<td>Stockholm county council</td>
</tr>
<tr>
<td>Bettina Julin</td>
<td>Employed at Ivbar, affiliated to Karolinska Institutet</td>
</tr>
<tr>
<td>Robert Kristiansson</td>
<td>Region Uppsala</td>
</tr>
<tr>
<td>Janeth Leksell</td>
<td>Swedish Association for Nurses in Diabetes Care</td>
</tr>
<tr>
<td>Mikael Lilja</td>
<td>Region Jämtland Härjedalen</td>
</tr>
<tr>
<td>Ågneta Lindberg</td>
<td>Region Skåne</td>
</tr>
<tr>
<td>Peter Lindgren</td>
<td>Employed at Ivbar, affiliated to Karolinska Institutet</td>
</tr>
<tr>
<td>Karin Loostrom Muth</td>
<td>Region Västra Götaland</td>
</tr>
<tr>
<td>Fredrik Lönndahl</td>
<td>Swedish Diabetes Society (patient representative)</td>
</tr>
<tr>
<td>Ann-Marie Svensson</td>
<td>National Diabetes Register</td>
</tr>
</tbody>
</table>

4.1.2 Joint development of definitions and methodology

The definitions and methodology regarding identification of the study populations, appropriate study outcomes, relevant comorbidity and other factors for case-mix adjustments of results were developed in consensus with the expert groups within Sveus stroke and Sveus diabetes. Parts of the work performed by the expert groups have been published in reports [43, 115]. Sources and definitions regarding outcomes and case-mix factors can be found in Table 6 and Table 7.
4.2 Data sources

The study populations for the five studies included in this thesis are based on two original cohorts, from one stroke dataset and one diabetes dataset which have been entirely separated throughout the project. The data sources leveraged for the two datasets are presented below.

4.2.1 Regional administrative systems

All Swedish regions and county councils have patient administrative systems (PAS) which contain data related to care contacts registered within their geographical area. These data include care contact date, diagnosis and procedure codes (ICD-10, KVÅ) and meta data regarding the caregiving unit. The systems generally have very high coverage, and they also include information on care contacts within primary care. The density of diagnosis and procedure codes varies across regions.

For the stroke population, data were retrieved from the seven regions on all adult patients (aged ≥18 years) who were registered with an acute stroke diagnosis, ICD-10 code I61* (ICH), I63* (IS) and/or I64* (unspecified) as main diagnosis anytime from 2006 to 2012. Information on all care contacts registered for these individuals were extracted for the same time period. Data for patients with only unspecified stroke (ICD-10 code I64*) registered were extracted but excluded (approximately 2% of the total sample) due to the obvious uncertainty related to the specificity in the stroke diagnosis which may significantly impact the relevance of being part of the study population.

For the diabetes population, data were retrieved from the seven regions on all adult patients (aged ≥18 years) who were registered with a diabetes diagnosis (ICD-10 codes E10*, E11* and E14*) sometime during 2007-2012. Information on all care contacts registered for these individuals were extracted for the same time period. Unspecified diabetes (ICD-10 code E14*) was excluded due to the obvious uncertainty related to the specificity in the diagnosis which may significantly impact the relevance of being part of the study population.

These patient-level data were linked to patient-level information from other registries as described below. Regional administrative systems data were used for all research papers.

4.2.2 The Swedish Stroke Register (Riksstroke)

The Swedish Stroke Register is one of the national quality registries and the single one relating to the entire chain of stroke care. Patients with acute stroke (intracerebral hemorrhage or ischemic stroke) are included and, during the last years, also patients who have had a transitory ischemic attack (TIA). Patients with subarachnoid hemorrhage (SAH) were not included at the time of the studies [116].

The register includes information on acute treatment, admission to hospital, secondary prevention, patient reported outcomes and experience measures. Data are collected at admission for acute stroke care, at three months and at twelve months after the stroke event. Hospitals admitting patients with acute stroke are expected to collect and report data, and the coverage rate has been estimated to be as high as 97% based on validation with the National Patient Register (Patientregistret) [41]. The equivalent coverage rate for the follow-up forms at three months were estimated to be 86% [41]. The three-months form can be filled out by the caregiving unit or by the patient him-/herself whilst the twelve-months form is sent out to patients via physical mail [7].

Data from the Swedish Stroke Register were used in research papers I, II and V; to select the relevant study population (confirming stroke cases) as well as for information on patient characteristics and health outcomes. Patient-level data were retrieved for all patients with an acute stroke (IS or ICH) registered during 2006-2012 in any of the seven regions collaborating within the Sveus research project (Jämtland Härjedalen, Östergötland, Dalarna, Uppsala, Skåne, Stockholm, and Västra Götaland).
4.2.3 National Diabetes Register (NDR)
The National Diabetes Register is the national quality register for adult diabetes care. It gathers information on patient characteristics and risk factors, care process and interventions, laboratory results and health outcomes. The coverage rate has been estimated to be 96.5% for all individuals diagnosed with diabetes [7].

Data from the NDR were used in research papers III and IV; to select the relevant study population (confirming cases) as well as for information on patient characteristics and health outcomes. Patient-level data were retrieved for all patients with a diabetes diagnosis registered during 2007-2012 in any of the seven regions collaborating within the Sveus research project (Jämtland Härjedalen, Östergötland, Dalarna, Uppsala, Skåne, Stockholm, and Västra Götaland).

4.2.4 Longitudinal integration database for health insurance and labour market studies (LISA)
The LISA database, held by Statistics Sweden, covers individual-level information for a broad range of socioeconomic parameters. It includes data on all individuals from the age of 16 years and integrates information from the educational sector and the labour market on an annual basis. Data from LISA were used in all five research papers included in the thesis, and enabled stratification and case-mix adjustments with regards to socioeconomic variables.

4.2.5 Total population register (RTB)
Statistics Sweden keeps and updates information on individuals’ date of death which is part of the Total population register (Registret över totalbefolkningen). This information was used in research papers I, II and V.

4.2.6 Care and social services for the elderly and for persons with impairments (SoL)
The register is administered by the National Board of Health and Welfare (Socialstyrelsen). It contains individual-level information on municipal services provided for elderly and individuals with functional variations. Data on housing via the local municipality as well as home-help services were used in research papers I, II and V.

4.2.7 Prescribed drugs registry (LMR)
All prescriptions that are filled in an outpatient setting are included in a research database held by the National Board of Health and Welfare. The database contains information on ATC code level, date for filling the prescription, and the attributable amount.

This data source was leveraged in research paper V (filled prescriptions of antihypertensive and anticoagulant medication) as well as in research papers III (confirming Type 1 Diabetes cases) and IV (filled statin prescriptions).

4.2.8 MiDAS database
Individual-level information on leave due to illness or disability, short-term and long-term with a minimum level of two weeks’ absence, is collected in the Swedish Social Insurance Agency’s MiDAS database.

Data from MiDAS were used in research papers I, II and III, to estimate the proportion of stroke patients having formally regained full-time work ability and to estimate the proportion of individuals with Type 1 Diabetes with formal sick leave or disability pension during two years prior to the study baseline.
4. 3 Data management, process mapping and study outcomes

4.3.1 Data management process

A significant share of the time spent on performing the studies included in this thesis consisted of management of data. As described above, data were extracted from 14 different sources, and two separate research databases were built on 11 (diabetes) or 13 (stroke) of these data extracts. Formal data controller of the databases included was Ivbar. Below, a short description of each step within the data management process is presented.

**Ordering of data from the data owners.** After having received ethical approval, data specifications were compiled based on the registries’ existing variable lists and sent to each registry. Data were pseudonymized (de-identified but kept on individual level) by Statistics Sweden to minimize the risk that individual patients would be possible to identify in the research database (information flow process presented in Figure 9).

**Validation of received data.** To secure that all data included in the data extracts received were stored in a structured, readable format and to secure that all data extracts were complete, all data extracts were explored, and counts and values of the data for the different variables were assessed. If needed, which was the case at a few occasions, the registry was contacted to validate the shared data extract, to double-check its contents, and possibly to re-send it. In at least one case, a new data extract was created and shared by the registry in order to complete the dataset according to the original data order.

**Harmonization of definitions across registries.** The different data sources have their own variable lists with different scope and somewhat different denominations. For example, different ways of assigning a care contact to specialized outpatient care versus primary care needed harmonization across regional administrative data. Some activities are possible to register in the health record as well as in the quality registry, and the selection of which variable to use was done on a case-by-case basis (e.g. assessing thrombectomy via the Swedish Stroke Register instead of using the patient administrative data), dependent on the variable’s coverage rate.

**Identification of study populations.** Based on joint discussions in the expert groups, definitions of the study populations within data extracts from the regional administrative systems were set based on diagnosis (ICD-10) codes. These definitions were re-used in all research papers included in the thesis. Based on the definitions of eligibility within other registries, data from these registries were linked on patient level.

**Definition of outcomes.** The study outcomes were defined together with the expert groups. The definitions were based on existing guidelines and the clinical experience of the expert group members. Definitions were designed to include any variants in coding routines within the different regions. These definitions were re-used in all research papers included in the thesis.

**Definition of patient characteristics.** After having selected which patient characteristics to include in the datasets, these were defined and reviewed in open discussions within the expert groups. Definitions were designed to include any variants in coding routines within the different regions. These definitions were re-used in all research papers included in the thesis.

**Validation of the study population, its characteristics and outcomes.** The patient volumes of the study populations, and its levels of indicators concerning both patient characteristics and outcomes were validated via cross-checking with previous research and public reports during open discussions within the expert groups.
4.3.2 Care process mapping

In order to decide on relevant indicators for measurement and analysis, mapping of the care processes was performed. Input from representatives for the seven Swedish regions (Table 4 and Table 5) was leveraged to include the different existing variants.

4.3.2.1 Stroke

Securing high-quality care for the individual stroke patient is dependent on a broad range of competencies within the healthcare sector and possibly over a long period of time. Activities need to be coordinated across departments at the caregiving unit, and sometimes at several caregiving units. Study populations for the studies included in this thesis are defined based upon the stroke diagnosis and, hence, the mapped care process includes activities after stroke onset. When mapping the care process, it was divided into three phases over time, starting at stroke onset; the first phase includes pre-hospital activities and measures taken to limit the damage of the stroke, the second phase includes acute interventions, and the third phase includes post-acute and long-term activities such as rehabilitation.

Figure 9. Process for enabling pseudonymized global patient-level ID with support from Statistics Sweden. Adopted from reports published under the Sveus research and development project [43, 115]
Figure 10. First phase of the stroke care process. Adopted from report published under the Sveus research and development project [43].

The first phase, the pre-hospital phase, is defined by the time from the stroke event to hospital arrival, including patient delay in contact with healthcare, triage and initial assessment of the patient. The shorter the amount of time spent in the first phase, the better, as time of brain tissue ischemia is a strong predictor for outcomes after stroke [117]. The eligibility of some potentially crucial treatment interventions is also dependent on the time window from stroke (symptom) onset to start of intervention.

Pre-hospital conditions for the individual stroke patient are potentially important factors in terms of treatment initiation: living conditions such as living at home or at a facility (e.g. sheltered or special housing) as well as living alone impact the ability to alert the changed state of health and body function; level of understanding of the symptoms and implied sense of urgency impact approach for seeking care (what care level) and with what urgency; living in a rural area impacts options regarding available transporting arrangements, to mention a few.
The second phase, or the acute phase, includes detailed examination, preparation for intervention, intervention as well as monitoring before, during and after the intervention. Generally, the stroke patient undergoes radiological examination, usually computed tomography (CT), to determine whether the stroke is ischemic or hemorrhagic. A CT-angiography determines whether there is a large-vessel occlusion, and thus an indication for thrombectomy. Furthermore, hemorrhagic stroke aneurysms and other vessel malformations are visualized.

If the stroke is confirmed as ischemic, dependent on the amount of time spent in the pre-hospital phase and given no contraindications, the patient may be eligible for thrombolysis and/or thrombectomy. Also, hemicraniectomy may be applicable for patients with a very large ischemic stroke in the media artery of the frontal brain lobe. Patients with hemorrhagic stroke may in selected cases undergo treatment with evacuation of hematoma.
The third phase, including post-acute and long-term activities, is of varying length but in many cases life-long. Main activities include rehabilitation – to enable rebuilding of functions to pre-stroke levels or adaptation to a new situation with lower level of body function – and secondary prevention, to reduce the risk of stroke recurrence.

The amount of resources put into rehabilitation and secondary prevention may have significant impact on long-term outcomes. Several different healthcare professionals are involved during rehabilitation, e.g. physiotherapists, occupational therapists, speech therapists, and psychologists. The probability of receiving inpatient rehabilitation offered before discharge versus less intense rehabilitation activities outpatient or at special housing may play an important role in how well the patient regains health.
4.3.2.2 Diabetes

The individual’s path to diagnosis with diabetes can look very different. There is a significant difference between the patient journey leading up to T1D and that leading up to a T2D diagnosis. These two groups of patients are also generally different in terms of age as well as health profile at diagnosis. Diabetes care is managed at primary care facilities (primarily Type 2 Diabetes) or at hospitals. The care process concisely described below varies somewhat depending on regional and local routines.

Guidelines published by the National Board of Health and Welfare state that it is desirable to maintain HbA1c levels beneath 52 mmol/mol, although the risk-benefit ratio for a treatment intensity needed to reach that level is individual and ought to be assessed on a case-by-case basis. HbA1c levels should however not exceed 70 mmol/mol as the risk of diabetes-related complications increases significantly above this level [83].

![Diabetes care process diagram](image)

**Figure 13. Overview of the care process for an individual with Type 1 Diabetes.** Adopted from report published under the Sveus research and development project [115].

Individuals with Type 1 Diabetes are generally treated inpatient during the first few days after diagnosis (length of stay may vary dependent on initial health state and regional/local routines). As these individuals are dependent on insulin injections, it is of great importance for the individual to – in addition to initiate a good balance of the hormone as soon as possible – learn how to manage these injections and how to perform self-testing to enable adequate dosage. After the initial inpatient stay, follow-up is performed within specialized outpatient care. The standard process includes appointment with dietitian and fundus photography which is also performed with regular intervals over time.

The first year after diagnosis is usually more intense in terms of follow-up visits for patient education and maintaining a good level of self-care than subsequent years. Follow-up visits include injection techniques, selection of insulin and laboratory tests.
Figure 14. Overview of the care process for an individual with Type 2 Diabetes. Adopted from report published under the Sveus research and development project [115].

Healthcare for individuals diagnosed with Type 2 Diabetes is typically managed in primary care. After initial diagnosis and initiation of pharmacological treatment (possibly including insulin injections), patient education can be managed individually or in a larger group. Early appointment with foot therapist and performance of fundoscopy are desirable. Follow-up is somewhat more intense during the first year after diagnosis than subsequent years with diabetes nurse visit after six months, laboratory tests and a doctor’s visit after one year. From that point on it is desirable to have at least one follow-up per year including laboratory tests, to ensure appropriate treatment.
### 4.3.3 Study outcomes, sources and definitions

Assessment of health equity was carried out based on a broad set of outcomes, to reflect the main elements and results from the care processes illustrated in Figure 10-Figure 14.

**Table 6. Study outcomes, sources and definitions.** Overview of the study outcomes for research papers I-V, their sources and definitions.

<table>
<thead>
<tr>
<th>Study outcome</th>
<th>Research paper I</th>
<th>Research paper II</th>
<th>Research paper III</th>
<th>Research paper IV</th>
<th>Research paper V</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival</td>
<td>Date of death (SCB) vs. date of stroke (PAS)</td>
<td>Date of death (SCB) vs. date of stroke (PAS)</td>
<td>-</td>
<td>-</td>
<td>Date of death (SCB) vs. date of stroke (PAS)</td>
</tr>
<tr>
<td>Disease recurrence</td>
<td>Date of new main diagnosis &gt;28 days after index event (PAS)</td>
<td>Date of new main diagnosis &gt;28 days after index event (PAS)</td>
<td>-</td>
<td>-</td>
<td>Date of new main diagnosis &gt;28 days after index event (PAS)</td>
</tr>
<tr>
<td>Functional status</td>
<td>Approximated based on Eriksson et al [118], at twelve months after stroke</td>
<td>Approximated based on Eriksson et al [118], at twelve months after stroke</td>
<td>-</td>
<td>-</td>
<td>Approximated based on Eriksson et al [118], at three months and twelve months after stroke</td>
</tr>
<tr>
<td>General health</td>
<td>Patient-reported on an ordinal scale one year after stroke (Riksstroke)</td>
<td>Patient-reported on an ordinal scale one year after stroke (Riksstroke)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Formal complete work ability</td>
<td>Not registered for sick leave part-/full-time or disability pension (SoS)</td>
<td>Not registered for sick leave part-/full-time or disability pension (SoS)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HbA1c level</td>
<td>-</td>
<td>-</td>
<td>Absolute level (NDR)</td>
<td>Absolute level (NDR)</td>
<td>-</td>
</tr>
<tr>
<td>eGFR</td>
<td>-</td>
<td>-</td>
<td>One-year change (NDR)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Predicted 5-year risk of CVD</td>
<td>-</td>
<td>-</td>
<td>One-year change (NDR)</td>
<td>Absolute level (NDR)</td>
<td>-</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Absolute level (NDR)</td>
<td>-</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>-</td>
<td>-</td>
<td>Absolute level (NDR)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

57
<table>
<thead>
<tr>
<th><strong>Resource use</strong></th>
<th><strong>Inpatient care</strong></th>
<th><strong>Outpatient care</strong></th>
<th><strong>Home-help services</strong></th>
<th><strong>Care process</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial inpatient stay (PAS), total first-year inpatient stay (PAS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total initial inpatient stay (PAS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td><strong>First-year (PAS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Specialty care first-year (PAS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Primary care first-year (PAS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Added hours, i.e. first year vs. prior to stroke (SoS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Added hours, i.e. first year vs. prior to stroke (SoS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Transfer to (SoS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Transfer to (SoS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Net days (FK)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Yes/No (Riksstroke)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Yes/No (Riksstroke)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Yes/No (Riksstroke)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Yes/No within 14 days after index event (PAS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Patient-reported on an ordinal scale three months after stroke (Riksstroke)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Filled prescription after one-year follow-up (SoS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Filled prescription after one-year follow-up (SoS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Filled prescription after one-year follow-up (SoS)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
4.4 Statistical methods and case-mix factors

Throughout the five studies, analysis has included descriptive statistics of the study sample’s baseline characteristics and the study outcomes, as well as results of the study outcomes adjusted based on these baseline characteristics. Multivariate regression analysis was performed using selected relevant confounders as independent explanatory variables. Continuous data (e.g. absolute HbA1c levels, number of home-help services hours) were analyzed using ordinary least squares (OLS) regression, count data (e.g. care days, outpatient visits) were analyzed using negative binomial regression, and binary data (e.g. survival, presence of a specified comorbidity) were analyzed using logistic regression. Regression coefficients were presented in the main document or in supplemental material of each research paper except for research paper II. For the results to be considered statistically significant, two-sided P values less than 0.05 were needed. The software STATA 13.0 was used for statistical analyses.

In order to separate the correct effect attributable to demographic, socioeconomic or geographic factors, it is of importance to adjust for other relevant factors. These factors are different depending on the condition studied (e.g. disease-specific factors for stroke or diabetes) and can in theory differ systematically between the sociodemographic and geographic groups. The set of case-mix factors used in multivariate regression analysis within each research paper is presented in Table 7 and was subject to discussions together with clinical expertise. The demographic characteristics included sex (woman/man) and age in years from administrative data. Highest educational level (from LISA, SCB) was stratified in three levels as according to common practice [108], and origin (LISA, SCB) was stratified in four categories: born in a Nordic country, born in the EU, born in non-EU Europe and born outside Europe. Marital status (LISA, SCB) was used in four categories (never married, married, divorced, widowed). Highest educational level was selected as case-mix factor instead of income level, as previous research points to education as being of higher explanatory value [119]. Patient characteristics with low coverage were excluded as explanatory variables in order not to lose a significant share of the study material (e.g. NIHSS which had a coverage rate of less than 50% for the stroke populations).

Diagnosis (ICD-10) and procedure (KVÅ) codes from the regional patient administrative systems were used to collect patient-level information on medical history during two years prior to baseline. Prescription (ATC) codes were used for collecting information on filled prescriptions from the Prescribed Drugs Registry, previously shown to be appropriate for studying drug utilization patterns [120]. Data from the Swedish Stroke Register were used for identification of several study variables; all patient-reported outcomes and physician-reported prescriptions at discharge, identification of reperfusion treatment, as well as to approximate functional status (the modified Rankin Scale, mRS) at three months and one year after the stroke event based on a previously developed algorithm [118]. Data from the National Diabetes Register were used for study outcomes, information on diabetes duration, BMI and smoking status. In addition, NDR data were used for computation of eGFR and five-year risk of CVD [121, 122]. Additional information regarding data sources used can be found under section 4.2 Data sources.

Output from the regression analyses has been used to make predictions based on pre-specified patient characteristics, e.g. for the different healthcare providers performance assessed in research paper II (in part presented in reports [43, 115]). These predictions are not presented within this thesis.
Table 7. Case-mix factors applied, per research paper.

<table>
<thead>
<tr>
<th>Research paper</th>
<th>Demographic</th>
<th>Socioeconomic</th>
<th>Geographic</th>
<th>Disease-specific factors including comorbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Sex, age (categorical)</td>
<td>Educational level, region of birth, marital status, single household, living arrangements</td>
<td>-</td>
<td>Level of consciousness at hospital arrival, ADL dependency, prior stroke, inpatient care year (-1), atrial fibrillation, hypertension (stroke subtypes analyzed separately)</td>
</tr>
<tr>
<td>II</td>
<td>Sex, age (categorical)</td>
<td>Educational level, region of birth, marital status, single household, living arrangements</td>
<td>Hospital</td>
<td>Level of consciousness at hospital arrival, ADL dependency, prior stroke, inpatient care year (-1), atrial fibrillation, hypertension, stroke subtype</td>
</tr>
<tr>
<td>III</td>
<td>Sex, age (categorical)</td>
<td>Educational level, region of birth, marital status, disability pension/sick leave</td>
<td>-</td>
<td>BMI, diabetes duration, smoking, disease history, prescribed insulin pump</td>
</tr>
<tr>
<td>IV</td>
<td>Sex, age (categorical)</td>
<td>Educational level, region of birth, marital status</td>
<td>-</td>
<td>BMI, diabetes duration, smoking, disease history, HbA1c at baseline, eGFR at baseline, systolic blood pressure at baseline, LDL level at baseline</td>
</tr>
<tr>
<td>V</td>
<td>Sex, age (categorical)</td>
<td>Educational level, region of birth, marital status, single household, living arrangements</td>
<td>-</td>
<td>Level of consciousness at hospital arrival, ADL dependency, prior stroke, inpatient care year (-1), atrial fibrillation, hypertension, stroke subtype, and pre-stroke psychosis/schizophrenia diagnosis</td>
</tr>
</tbody>
</table>

4.4.1 Research paper I
The study population was divided in two, to analyze the two stroke subtypes (IS and ICH) separately. In addition to assessing crude values of study outcomes between sexes, sex was used as case-mix factor in univariate regression analysis of all outcomes.

Multivariate regression analysis was performed with the independent variables (case-mix factors) presented in the above table. Analysis of study outcomes other than survival was based on patients that had survived at the time points studied (e.g. patient-reported outcomes at three and 12 months). Hypertension and atrial fibrillation were included for the analysis of stroke recurrence.
4.4.2 Research paper II
The multivariate model was adjusted for clustering of patients within clinics in addition to case-mix factors presented in the above table, and the case-mix adjusted results were presented per caregiving unit to illustrate the hospital effect on each dependent outcome. Stroke subtype was used as case-mix factor to take the different pathways of IS versus ICH care into account. Hypertension and atrial fibrillation were included for the analysis of stroke recurrence.

Caregiving units were classified as significantly better or significantly worse, as shown in Figure 16 and Figure 17, based on significant deviations in one direction (formal full-time work ability was not included under these criteria as it is not to be considered the equivalence to actual work ability). Analysis of study outcomes other than survival was based on patients that had survived at the time points studied (e.g. patient-reported outcomes at three and 12 months).

4.4.3 Research paper III
The multivariate model was adjusted for clustering of health outcomes within individual patients, as some patients contributed to the study material with more than one one-year episode. The result of this was somewhat more robust standard deviations and confidence intervals of the case-mix factors’ effect on outcome. The association between age groups and outcome was also modelled using restricted cubic splines in accordance with previous research [107, 123] but did not show higher degree of determination. Previous sick-leave or disability pension was added as case-mix factor for all three study outcomes.

Levels of eGFR were estimated with the revised Malmö-Lund formula [121] on patient level. Annual development of eGFR was computed through subtracting eGFR at the end of the year with eGFR at baseline. To compute the five-year risk for CVD on patient level, an algorithm developed on NDR real-life data was used. It is based on eight input variables including age, duration of diabetes, ratio of total cholesterol versus HDL–cholesterol, HbA1c level, systolic blood pressure, smoking status, macro albuminuria status and history of heart conditions [122]. Risk predictions were computed for patients with all input values registered within ±3 months from baseline.

4.4.4 Research paper IV
The multivariate model was adjusted for clustering of health outcomes within individual patients, as some patients contributed to the study material with more than one one-year episode. The result of this was somewhat more robust standard deviations and confidence intervals of the case-mix factors’ effect on outcome. Multiplicative interactions were also tested using the likelihood ratio test.

To compute the five-year risk for CVD on patient level, the algorithm developed on NDR real-life data was used including eight input variables; age, duration of diabetes, ratio of total cholesterol versus HDL–cholesterol, HbA1c level, systolic blood pressure, smoking status, macro albuminuria status and history of heart conditions [122]. Risk predictions were computed for patients with all input values registered within ±3 months from baseline. Levels of eGFR were estimated with the revised Malmö-Lund formula [121] on patient level.
4.4.5 Research paper V

The subpopulation of stroke patients with history of pre-stroke psychosis or schizophrenia was identified by having had at least one care contact with main or secondary diagnosis of ICD-10 codes F20-F29. The diagnosis had to be registered during the two years preceding the stroke event, in either inpatient or outpatient care. Only patients with ischemic stroke were included.

Analysis of study outcomes other than survival was based on patients that had survived at the time points studied (e.g. patient-reported outcomes at three and 12 months). For the analysis of stroke recurrence, hypertension and atrial fibrillation were included as case-mix factors, and the analysis of filled prescriptions of oral anticoagulants was performed for patients with a history of atrial fibrillation only.

4.5 Ethical considerations

The studies included in this thesis have been approved by the Regional Ethical Review Board in Stockholm (reference numbers 2013/1541-31/5 and 2016/785-32 for the studies on stroke, reference number 2013/1197-31 for the studies on diabetes). All studies are based on registry data. As registry data include sensitive data for the individuals included, it is of high importance to secure that only data needed are included in the data export from the registries, and to make sure that the data are kept in a secure setting.

The studies were initiated after formal application approved by the Regional Ethical Review Board in Stockholm. Subsequently, each data holder approved use of data for the study. In the studies performed, only pseudonymized data were accessible and the data were kept in a secure setting on a separate server with individual two-factor authentication login. In scientific communication, only aggregated data which are impossible to triangulate or link to any individual have been presented. Potential harm on patients’ lives by including them in the studies was deemed to be minor whilst increased knowledge based on the results may serve as a base for better understanding of health equity today.

As for registry studies performed in Sweden, no formal informed consent from the patient is needed for approval by the ethical boards. Regional administrative systems are examples of data sources used in these studies that register patient information for all patients, whilst data from quality registries such as the Swedish Stroke Register and the National Diabetes Register are possible for the patient to choose not to be part of. The decision mandate for the individual patient is limited regarding information linked to their identity (although it remains pseudonymized), but it enables research and enhances thorough understanding of diseases and their treatments, benefiting patients and society in general.
5. Results and learnings from research papers I-V

Below is a summary of results from each of the five research papers included in the thesis.

5.1 Your sex is associated with your results after stroke – results from research paper I

We analyzed post-stroke levels of health outcomes and healthcare received in relation to sex, for ischemic stroke and intracerebral hemorrhage.

The study population consisted of 27,691 patients whereof 49.7% women and 50.3% men. 88.2% had suffered an ischemic stroke and 11.8% had an intracerebral hemorrhage. Within a year, 23.4% were deceased (26.8% of women and 19.9% of men) in the ischemic stroke subpopulation, and 40.3% (42.0% of women and 38.9% of men) in the hemorrhagic subpopulation. Women were to a larger extent living in special housing at stroke onset compared to men, and women were in general ADL dependent to a larger degree than men. A larger proportion of women than men were unconscious at hospital arrival.

Women were found to have significantly higher one-year survival in multivariate analyses, correcting for factors such as stroke severity, risk factors and age at stroke (men showed higher one-year survival in univariate analyses). The rate of good one-year functioning (approximated mRS≤2) after IS was lower among the women. Women had significantly shorter initial inpatient stay (IS and ICH) and shorter total first-year inpatient stay (IS), potentially due to that more women were living in special housing before and after stroke. High educational level was a significant positive predictor for survival first year after stroke and functional status first year after ischemic stroke (data not presented in the research paper).
**Figure 15. Overview of study outcomes.** Crude, univariate and multivariate analysis. From research paper I [124] with permission from the publisher.
5.2 Where you receive treatment is associated with what stroke care you get – results from research paper II

We investigated whether there was a geographical gradient in Swedish stroke care, based on data from 35 acute hospitals performing stroke care, within seven different regions covering approximately 65% of the Swedish population.

There were significant variations in patient mix between the caregiving units studied; the proportion of patients with ADL dependency prior to stroke varied between 6% and 20%, the proportion living in special housing prior to stroke spanned from 2% to 22%. Socioeconomic and demographic characteristics varied as well; the proportion of patients with university education spanned from 8% to 27%, and mean age at stroke onset varied between 70 and 80 years.

Six caregiving units seemed to perform significantly better in terms of health outcomes (light grey, Figure 16), and seven units performed significantly worse (dark grey, Figure 16) after adjustments. Caregiving units generally seemed to leverage one type of resource in the post-acute phase, e.g. inpatient care versus outpatient care or special housing, with higher levels of one type and lower levels of the other. Five caregiving units showed significantly lower levels of resources overall (light grey, Figure 17) and three caregiving units showed higher levels (dark grey, Figure 17). Adjusted deviations from the mean differed between caregiving units; -8 to +16 days in initial inpatient stay, -7 to +7 visits in specialized outpatient care first year after stroke, and -10 to +21 visits in primary care first year after stroke. Trends were identified within regions regarding the relationship between outpatient visits in specialized versus primary care; e.g. lower number of primary care visits and higher levels of specialized care (Region Skåne) and vice versa (Region Västra Götaland).
Figure 16. Health outcomes after stroke for 35 Swedish caregiving units. Adjusted differences between caregiving units. From research paper II [125] with permission from the publisher.

Figure 17. Resource use after stroke for 35 Swedish caregiving units. Adjusted differences between caregiving units. From research paper II [125] with permission from the publisher.
5.3 Your demographic and socioeconomic profile tells us how well you do with Type 1 Diabetes – results from research paper III

We assessed which sociodemographic factors that potentially drive differences in health outcomes among Swedish T1D patients, regarding levels of HbA1c, and annual change in eGFR and CVD risk.

**Absolute HbA1c level**

Average HbA1c level in the study population amounted to 64.5 mmol/mol. Several demographic and socioeconomic factors were associated with maintaining blood glucose control, after adjustments of other relevant patient characteristics and clinical factors. Women showed higher (worse) levels than men. Younger patients (below 25 years of age) had higher (worse) levels, and patients in the ages of 70-74 years had best blood glucose control.

Patients with university education showed lower levels of HbA1c than patients with high school or comprehensive school education, and patients with high school education had lower levels than patients with comprehensive school as highest educational level. Married patients showed lower levels of HbA1c than never married, divorced and widowed patients. Origin (born in a Nordic country, outside the Nordics but within the EU, non-EU Europe or outside of Europe) was not associated with absolute HbA1c levels. History of sick-leave and/or disability pension was associated with worse blood glucose control, as was smoking.

In addition, several clinical factors were associated with HbA1c levels; e.g. duration of diabetes, BMI and history of diabetes-related complications were associated with worse blood glucose control, as was prescription of insulin pump. Renal failure was associated with lower HbA1c levels.

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**Figure 18. Absolute HbA1c levels in individuals with T1D.** From research paper III [126] with permission from the publisher.
Annual change in eGFR

Average level of eGFR amounted to 82.8 ml/min per 1·73 m2, and the average annual development in eGFR amounted to -0.43 ml/min per 1·73 m2 per year. Marital status was associated with annual development in eGFR; being married was associated with better development than never married. There was no statistically significant association between highest educational level and annual change in eGFR, nor between region of birth and annual change in eGFR.

Figure 19. Annual change in eGFR in individuals with T1D. From research paper III [126] with permission from the publisher.
Annual change in five-year CVD risk

Average five-year risk of cardiovascular disease amounted to 8.5% in the study population, and the average annual change amounted to +0.54 percentage points. Educational level was associated with annual change in CVD risk; comprehensive school or lower as highest educational level was associated with larger increase in CVD risk compared to high school education as well as university education. Smoking at baseline was associated with lower increase in CVD risk although the absolute CVD risk score was significantly higher for smokers at the end of the follow-up period compared to non-smokers.

As the number of observations was significantly reduced for the analysis of five-year CVD risk (978 observations) compared to the above HbA1c analysis (16,367 observations) due to missing data for some of the underlying risk-prediction variables, a comparative analysis of the data sets was performed to estimate the possible impact of missing data. There were no notable differences between this subpopulation and the original study population.

Figure 20. Annual change in CVD risk in individuals with T1D. From research paper III [126] with permission from the publisher.
5.4 Your demographic and socioeconomic profile tells us how well you do with Type 2 Diabetes – results from research paper IV

We investigated the association between sociodemographic factors and the intermediary risk indicators HbA1c, systolic blood pressure, LDL cholesterol, five-year CVD risk and the process indicator statin use, among Swedish individuals with prevalent Type 2 Diabetes. Results regarding blood glucose control, systolic blood pressure and LDL cholesterol level are presented below.

**HbA1c level**

Average level of HbA1c amounted to 55.1 mmol/mol. The demographic and socioeconomic factors studied were associated with blood glucose control also after adjustments for other relevant factors; women had better blood glucose control than men, and the youngest age groups showed the worst blood glucose control. Individuals with university education showed significantly better blood glucose control than individuals with high school education and comprehensive school as highest educational level. Origin was associated with blood glucose control; being born outside the EU was associated with higher HbA1c levels. Smoking at baseline was associated with higher HbA1c.

In addition, several clinical factors were associated with levels of HbA1c; duration of diabetes, BMI and history of diabetes-related complications (CVD, eye disease and extremity complications) were all individually associated with worse blood glucose control.

![Figure 21. HbA1c in individuals with T2D. From research paper IV [127] with permission from the publisher.](image-url)
Systolic blood pressure

Average level of systolic blood pressure amounted to 135.7 mm Hg. Higher age was associated with higher systolic blood pressure whereas sex was not significantly associated with differences in levels of systolic blood pressure.

Higher educational level, i.e. university education, was associated with lower systolic blood pressure compared to high school education and comprehensive school education. Never having been married was associated with higher systolic blood pressure than being married or being divorced. Being born in a Nordic country was associated with lower systolic blood pressure compared to being born in non-EU Europe (EU-27[128]), whereas it was associated with a higher systolic blood pressure compared to being born outside Europe.

Clinical factors including higher LDL, higher BMI, higher eGFR and higher HbA1c were all individually associated with higher systolic blood pressure. Previous diagnosis of atrial fibrillation, a psychiatric condition or a depressive episode was associated with lower systolic blood pressure. Also, risk of having a systolic blood pressure above 140 mm Hg was analyzed as a dichotomous outcome, and the patterns were the same as in the analyses of systolic blood pressure as a continuous variable in terms of association with the case-mix factors included.

Figure 22. Systolic blood pressure in individuals with T2D. From research paper IV [127] with permission from the publisher.
**LDL cholesterol level**

Average level of LDL cholesterol amounted to 2.7 mmol/L. Women showed higher levels of LDL cholesterol than men. The youngest age group showed higher levels of LDL cholesterol compared to the oldest. Longer duration of diabetes and higher BMI were both individually associated with lower levels of LDL cholesterol, as were previous diagnosis of CVD or of atrial fibrillation.

**Figure 23. LDL cholesterol level in individuals with T2D.** From research paper IV [127] with permission from the publisher.
5.5 Pre-stroke mental comorbidity is associated with what stroke care you get – results from research paper V

We assessed whether individuals with a history of psychosis or schizophrenia diagnosis, registered prior to stroke, received different stroke care in terms of resource levels and process compared to other stroke patients, and whether these individuals achieved health outcomes after stroke that differed from other stroke patients. Explanatory variables used in multivariate regression analysis are presented in Table 7, and results per study outcome is presented in Table 8.

### Table 8. Crude and adjusted values of selected indicators for the psychosis and non-psychosis groups. From research paper V [129] with permission from the publisher. Adjusted values account for differences in case-mix factors as stated in Table 7.

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Pre-stroke psychosis</th>
<th>Non-psychosis</th>
<th>Unadjusted OR/coefficient (CI 95%)</th>
<th>Adjusted OR/coefficient (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-day survival (%)</td>
<td>87.7 (84.4; 90.9)</td>
<td>89.6 (89.3; 89.9)</td>
<td>0.82 (0.61; 1.11)</td>
<td>1.07 (0.71; 1.62)</td>
</tr>
<tr>
<td>1-year survival (%)</td>
<td>74.8 (70.5; 79.1)</td>
<td>76.9 (76.6; 77.3)</td>
<td>0.89 (0.71; 1.12)</td>
<td>1.23 (0.90; 1.68)</td>
</tr>
<tr>
<td>1-year recurrent stroke (%)</td>
<td>8.6 (5.4; 11.8)</td>
<td>5.9 (5.6; 6.1)</td>
<td>1.50 (0.99; 2.27)</td>
<td>1.57 (1.01; 2.44)</td>
</tr>
<tr>
<td>Good 3-months functioning (approximated mRS 0-2, %)</td>
<td>22.2 (16.7; 27.7)</td>
<td>50.6 (50.1; 51.1)</td>
<td>0.28 (0.20; 0.38)</td>
<td>0.44 (0.29; 0.66)</td>
</tr>
<tr>
<td>Good 1-year functioning (approximated mRS 0-2, %)</td>
<td>30.0 (22.3; 37.7)</td>
<td>58.1 (57.5; 58.7)</td>
<td>0.31 (0.22; 0.44)</td>
<td>0.40 (0.24; 0.65)</td>
</tr>
<tr>
<td>Reperfusion treatment (thrombolysis or thrombectomy, %)</td>
<td>3.4 (1.6; 5.2)</td>
<td>6.8 (6.5; 7.0)</td>
<td>0.48 (0.28; 0.84)</td>
<td>0.53 (0.29; 0.98)</td>
</tr>
<tr>
<td>Endarterectomy within 14 days (%)</td>
<td>0.3 (0.0; 0.8)</td>
<td>1.4 (1.3; 1.5)</td>
<td>0.18 (0.03; 1.31)</td>
<td>*</td>
</tr>
<tr>
<td>Initial inpatient stay (days)</td>
<td>12.8 (11.8; 13.9)</td>
<td>13.2 (13.1; 13.3)</td>
<td>-0.03 (-0.12; 0.69)</td>
<td>-0.04 (-0.15; 0.06)</td>
</tr>
<tr>
<td>Inpatient care first year (days)</td>
<td>33.7 (28.4; 38.9)</td>
<td>20.9 (20.6; 21.3)</td>
<td>0.48 (0.36; 0.59)</td>
<td>0.32 (0.20; 0.44)</td>
</tr>
<tr>
<td>Inpatient care first year excluding at psychiatric unit (days)</td>
<td>25.1 (21.1; 29.2)</td>
<td>20.5 (20.2; 20.8)</td>
<td>0.20 (0.08; 0.32)</td>
<td>0.06 (-0.06; 0.19)</td>
</tr>
<tr>
<td>Outpatient care first year (visits)</td>
<td>19.7 (16.9; 22.4)</td>
<td>19.2 (19.0; 19.5)</td>
<td>0.02 (-0.09; 0.13)</td>
<td>-0.01 (-0.12; 0.11)</td>
</tr>
<tr>
<td>Added home-help services (hours)</td>
<td>156 (71; 240)</td>
<td>125 (119; 130)</td>
<td>30.8** (-33.0; 94.5)</td>
<td>25.8** (-40.3; 91.9)</td>
</tr>
<tr>
<td>Antihypertensive medication (%)</td>
<td>68.7 (63.4; 74.1)</td>
<td>84.1 (83.7; 84.5)</td>
<td>0.42 (0.32; 0.53)</td>
<td>0.55 (0.42; 0.73)</td>
</tr>
<tr>
<td>Oral anticoagulant*** (%)</td>
<td>40.4 (26.6; 54.2)</td>
<td>55.0 (53.9; 56.1)</td>
<td>0.55 (0.32; 0.97)</td>
<td>0.54 (0.28; 1.03)</td>
</tr>
</tbody>
</table>

*Omitted from regression model due to perfect co-linearity (sample too small)

**Refers to mean number of added hours of home help for the psychosis group (modeled as continuous variable)

***Proportion of subgroup with diagnosis of atrial fibrillation in the past two years
The subgroup of patients with history of psychosis or schizophrenia was less likely to receive reperfusion treatment and was less likely to report good functional outcome (approximated mRS ≤2) at three months as well as one year after stroke. Regarding secondary prevention, these patients showed lower levels of dispensation of drugs (antihypertensives) and had higher risk of stroke recurrence. Inpatient care consumption during the year after stroke was significantly higher in these patients although this difference was not statistically significant after exclusion of care at psychiatric unit. The results emphasize the importance of taking mental comorbidity into account, as it may have a significant impact on stroke care and its results.

![Figure 24](image_url)

**Figure 24.** Distribution (crude) over approximated mRS categories for the two subgroups, at three months and one year. From research paper V [129] with permission from the publisher.
6. Conclusions and discussion

Several health inequity gradients are present within Swedish stroke and diabetes care, and this knowledge is not new. Some Swedish citizens, all with universal access to healthcare, may in fact be worse off depending on their demographic or socioeconomic profile or their geographic residence. Insights are delivered and actions are taken, continuously, but we have not yet been able to adjust the key mechanisms and drivers of this development in a good way.

6.1 Conclusions on Swedish stroke and diabetes care delivery – equitable or not?

Based on registry data available there are inequities in Swedish stroke and diabetes care delivery today regarding health outcomes, resource use or care process. The inequities seem to be determined by demographics such as sex and age, by the patient’s individual socioeconomic starting point, or by geographic location of the treating unit.

6.1.1 Conclusions on health equity in terms of demography, socioeconomics and geography

As according to the perspectives described under section 1.1.1, here is a short summary on the three dimensions; demography, socioeconomics, and geography.

Demography. There are differences in health regained and healthcare received. Women with ischemic stroke were found to have lower function (approximated modified Rankin Scale) one year after stroke whilst a higher proportion of women survived the first year compared to men. Inpatient care received (regional financing) was lower for female stroke patients whilst proportion of patients staying in special housing (municipal financing) was higher during the year prior to and the year after stroke. Women with Type 1 Diabetes had worse blood glucose control compared to men. For Type 2 Diabetes, women had better blood glucose control compared to men, but higher levels of LDL cholesterol. Younger individuals typically showed worse blood glucose control than older for both Type 1 Diabetes and Type 2 Diabetes.

As stroke and diabetes afflict individuals across most age groups and to a similar extent for women and men, there is no obvious reason to why a difference on any of these dimensions should be expected or, even less so, accepted. There are additional characteristics that are often closely related to these demographic attributes, e.g. elderly women are widowed to a larger extent than men in the same age and live alone to a larger extent. Important to note is however that the demographic differences observed was significant also after adjustments for such characteristics.

Socioeconomics. The socioeconomic situation of individuals afflicted with stroke and/or diabetes also seems to play a role regarding health outcomes achieved and care process and healthcare resources received; high educational level (> 12 years) was a significant predictor for better blood glucose control in both Type 1 and Type 2 Diabetes. High educational level was also a significant positive predictor for survival first year after stroke and functional status first year after ischemic stroke (data not presented in research papers).

The attributes related to an individual’s socioeconomic situation are several, and they are complexly interlinked. The effect of an individual’s social and economic context on that individual’s health has a pathway with several checkpoints in which the difference in effect between a “better-off” and a “worse-off” individual may multiply at each checkpoint (as schematically illustrated in Figure 3). Consequently, there are several stages along the individual’s health pathway where improvements can be made. Lowering the barriers for “worse-off” individuals to reduce comorbidity, to understand their need, to express their need (demand) in order to better access healthcare (theoretically speaking; minimizing the multipliers of the differences in effect along the pathway) are all promising ways to lower health inequity. The case with pre-stroke psychosis/schizophrenia also highlights that
such comorbidity along the pathway complicates the situation with regards to elements such as informed consent and effective rehabilitation due to e.g. social manifestations of the comorbidity [71, 129].

**Geography.** There is also a geographic gradient in Swedish stroke care, where a few hospitals achieve significantly better health outcomes than others and a few achieve significantly worse, after adjustments for differences in patient characteristics. Some hospitals showed significantly higher levels of resource use whilst other showed significantly lower levels. No clear pattern emerged regarding the included hospitals’ relationship between health outcomes and resource use.

Sweden’s decentralization of decision making in healthcare to the 21 regions’ own administrations makes health equity a particularly relevant topic to study. Given this decentralization, geographical differences may appear and accelerate over time. Also, the geographical differences may drive differences that we instead observe as demographic or socioeconomic inequities, as the regions may have varying distributions of health, resources and process amongst its inhabitants. This may also skew the overall national distributions in different directions.

### 6.1.2 Degree of health inequity depends on terms for assessment

Given that there are significant differences in outcomes depending on individuals’ sex, age, socioeconomic situation and geographic place of residence, it is relevant to discuss the context of the assessment and its underlying terms. This can be done in accordance with the principles described under section 1.1.2.

**Dependency on relative versus absolute differences, and comparison to the average or best-off group.** If there was a clear cut-off point on a health status scale at which the above levels did not have an impact on anything with regards to life expectancy or future health-related quality of life, a comparison to that absolute level of health would be feasible. If it was hard to reach that level and seldomly done in the population, it would be more feasible to perform comparisons in relation to others, i.e. given that the target level is almost impossible to achieve, it makes sense to compare the level of health with others’. Then, the next question is whether to compare achieved health level to the top performers or to the average.

As within all five research papers (I-V), the assessments have been based on relative differences (between subgroups of patients) and referring to the average. The reason for this approach is to study the healthcare system based on its actual performance and what it appears to be able to achieve for the population it serves. The risk with applying an absolute level of reference is that it may not be possible to achieve for all patients given the system’s current resources. Assessing the relative difference between patients is more a measure to understand how the current resources have been spent and whether this spending seems equitable or not.

**The extent of the individual’s responsibility of her own health** is a complex topic. The dimensions of an individual’s responsibility are implicitly assessed within research paper III and IV (smoking and BMI used as predictors for health outcomes) and to some extent in research paper II (i.e. the choice of living in a particular region and thereby accepting its properties of healthcare organization and quality of care). We are continuously faced with and forced to make health trade-offs in life; the alternatives may sometimes be clear and sometimes not. It is important to understand that the clarity of alternatives may vary depending on your background.

**The maximin principle of justice or equality** could be used as basis for judging whether Swedish stroke and diabetes care delivery is equitable or not. Based on that principle, the system should be
evaluated from the perspective of how well the worst-off group fares “with respect to inequality” [17], i.e. the results of the worst-off group compared to others.

Then, is the worst-off group relatively well taken care of? This question is a matter of vertical equity [27], and something that Sweden by law aims at [4]. Given the assumption that a state’s laws reflect the inhabitants’ wishes on how things should work, one could say that it is the Swedish people’s wish that the worst-off group shall be well taken care of. The worst-off group is apparently not as well taken care of as the intention is and has been expressed. An objective indication of this is that patient characteristics, that should not play a part in determining levels of outcomes, are statistically significant predictors of outcomes when other relevant factors are adjusted for. Outcomes not being completely explained by need (in this context approximated by clinical patient characteristics), but by other factors such as socioeconomic status, are not the result of an equitable system [28].

It is also important to note that we must distinguish need from demand; demand is more easily measured in terms of resource use indicators but may also exceed or fall short of the individual’s actual need. In addition, resource use is a result of not only demand but of access. These dimensions may all play a part in attenuating or reinforcing health inequity gradients.

6.2 Underlying mechanisms and drivers of health inequity

The conclusion that your age, sex, socioeconomic situation or place of residence affects your chances to regain health or even survive may not be new or unique. Unfortunately, this pattern has repeatedly been proven to prevail, and the research papers included in this thesis are additional pieces of evidence pointing this out. It is also interesting to note that this is still the case for Sweden which offers universal and tax-funded care and is assumed to be one of the most equitable countries in the world according to e.g. comparisons of the Gini index [130].

The association of certain patient characteristics – e.g. socioeconomic situation – with levels of healthcare results and resources received has been pointed out extensively in previous research; it has been suggested that inequality of socioeconomic causes differences in health through several pathways, of which the healthcare system is only one and where the others include the social environment and lifestyle patterns [131]. The inequity connected with the healthcare system refers to what has been described as a lower likelihood of being insured and using fewer healthcare services [132]. In the Swedish context, assessed within this thesis, the former argument cannot be deemed relevant whilst the later could possibly be applicable given recent reforms in parts of the Swedish healthcare system [133]. Sen points out that communities can improve health status among its inhabitants by investing in common goods via e.g. taxation [134], and Sweden is only one example within this category. As access to care is universal and tax-funding covers most of the costs, there must be other barriers that apply to the Swedish setting.

Several mediators of health disparities have been assessed in the literature on health inequities, and to enable changing of the situation and pointing out adequate actions it is essential to understand how the drivers of these disparities act. There are a few recurring themes in the scientific literature; lifestyle, e.g. physical activity and diet including alcohol consumption and tobacco use, as well as environmental factors including specific exposures, work situation and the social environment in professional and private life [40, 135]. In addition to understanding the drivers, it is important to apply sophisticated methods to continuously monitor their development. There are still knowledge gaps regarding how to go about that and take appropriate actions in order to achieve a higher degree of health equity.
6.3 Possible policy implications

6.3.1 A theoretical context of health policy

One explanation to the apparent health inequities highlighted in this thesis is that there is a social hierarchy and that the different social positions have access to different levels of resources [16], which lead to different levels of abilities along the treatment pathway and different levels of health outcomes. Consequently, a select group in general gets the advantages of progress in a field, e.g. thrombectomy after having had a stroke care or automated insulin pump after diagnosis with Type 1 Diabetes. If that would be the only way to approach introduction of new interventions and technology, the fact that stroke and diabetes care delivery are inequitable would still possibly be considered fine as it may change over time; if the level of health within the most privileged group could be observed as the minimum level of health for the whole population at a later point in time [15], then systematic differences in the levels of health between groups could be considered less unjust (as they are temporary). During different stages of the epidemiologic transition it may be inevitable with temporarily present systematic disparities between groups when new ways of healthcare – e.g. diagnostics and treatment methods – spread across the population. Regardless, stroke and diabetes are two well-known conditions since many years. The fact that not all should be able to benefit from available treatments and available levels of health outcomes does just not sound right. In addition to that the conditions have been relatively common – across all socioeconomic groups, across all (Swedish) geographies, and for both women and men – introducing new techniques are not bound to such attributes but could be performed across all these categories to the same extent.

The spreading of best practice within healthcare across all sociodemographic and geographic groups is a condition for minimizing health inequities in society. The theories presented above may be relevant in trying to understand the inert process of spreading interventions, resource utilization and health outcomes across all groups until it can be regarded as a “common good” (as it should be according to the UN, the EU and Swedish law). Figure 25 illustrates how the two groups (embodied by the two colors) for each point in time (“0”, “1”, “5”, “20”), e.g. years after introduction of a new intervention, experience different rates of penetration of the new intervention (embodied by the y-axis, e.g. proportion of the diagnosed population that also has gone through the intervention, assuming that all patients are eligible for it and without any contraindications). The two colors could represent different sexes, different age groups, different socioeconomic groups or different geographies. A difference in penetration is then – rationally or not – explained by the time factor. The longer the time period, the less plausible the argument may seem to be.
Figure 25. Schematic overview of a fictive scenario with differing penetration speed of a new intervention in two different groups with the same clinical eligibility for the intervention.

Given that acute care in general have higher degree of follow-ups and development of guidelines, it is not unlikely that the more chronic the condition, the more dependent on self-care, and the higher the number of comorbidities: the higher the degree of health inequity at any given point in time.

6.3.2 Actions to improve the situation
If the government and regions would want to ensure equitable healthcare delivery, there is a need to introduce new ways of managing population health and healthcare.

There is a need for continuous monitoring of general as well as disease-specific indicators to understand how the situation of health equity is evolving. General indicators are needed to motivate decision makers by conveying the bigger picture, i.e. what is the actual burden to society in terms of health inequities and their implications now and over time. Disease-specific indicators are needed to understand what actions are most relevant and prioritized for the caregiving units and professional groups treating patients with the different conditions. Ongoing digitalization efforts should be designed to enhance this development.

There is a need to translate recommendations that come out of assessment initiatives to reduce health inequities, into concrete action programs across regions. The key to success is probably to be as concrete as possible regarding identified drivers and actions needed – e.g. how to raise awareness of best self-treatment in Type 2 Diabetes – and to use all available and justifiable techniques for implementation.

There are multiple initiatives and ongoing work by different organizational bodies that impact the situation of health inequities in a positive direction. Without such initiatives, the situation in terms of health inequity would probably be much worse. For example, the quality registries continuously (annually in most cases) report the development of the case mix of the patient population and the development of health over time. Furthermore, the National Board of Health and Welfare publishes clinical data that are possible to evaluate for healthcare professionals as well as the general public [111]. During 2018, the Swedish regions have initiated a joint system for knowledge sharing and steering, with support from the Swedish Association of Local Authorities and Regions (SKL). The purpose of this system is to enable development and spreading of best practices, with the long-term goal to contribute to better and more equitable healthcare [114]. These efforts altogether highlight the situation and makes the room for improvement publicly known.
6.4 Limitations, strengths and validity

As the study populations assessed within this thesis are based on the Swedish population only, and as healthcare systems differ significantly between countries with regards to financing, organization and access for the individual, general conclusions can be applied to the Swedish setting but for other contexts only with caution. All five studies included within this thesis are based on registry data, and consequently they have several features in common.

6.4.1 Selection bias
Selection bias concerns the risk that the sample of the study material is not representative for the population intended to be studied [136]. Consequently, there would be selection bias present if the sources of data were not representative for stroke patients and diabetes patients in the Swedish population.

The registries used in the studies of this thesis have high coverage rates with regards to the Swedish population; the Swedish Stroke Register and the National Diabetes Register both have a coverage rate estimated to more than 90% for the time periods studied [7, 80], and the regional administrative systems are supposed to be a complete reflection of care delivered to the inhabitants. The overall degree of selection bias is estimated to be small as the coverage rates of the registries used for inclusion of subjects are high. It is however important to note that there may be certain groups of patients that are systematically lost in follow-up and who for that reason are not subject to inclusion within the quality registries. If the extent of such systematic error is not negligibly low, the study populations would not reflect the general population.

6.4.2 Information bias
Given that the studies included are registry studies, we are dependent on that the interpretation of variables at registration are the same across different caregiving units and regions who report data on baseline characteristics and outcomes. Otherwise, there may be systematic errors in terms of what information is included in the reported data. The quality registries included continuously follow up on reporting to the registry and publishes support for registration and interpretation which are continuously updated [137, 138]. Such efforts should minimize the risk of significant deviations regarding interpretation and misunderstanding of variables from the quality registries.

6.4.2.1 Reporting routines
Reporting routines may vary between regions as well as between care levels. Given the national approach from quality registries versus the regions’ – by nature – regional routines, the risk of information bias is probably higher concerning regional administrative data even though the underlying logic is supposed to be the same, using the same versions of diagnosis (ICD-10) and procedure (KVÅ) codes.

In the case of diagnosis and/or procedure registrations within primary care, it was apparent that a significant proportion of visits missed information on main diagnosis or procedure, which may imply that the correct levels of comorbidity are underestimated. This risk is probably more applicable to the Type 2 diabetes population (research paper IV) as these patients are cared for within primary care to a larger extent than individuals with T1D or stroke.

Bias due to reporting routines is also particularly relevant regarding research paper II in which stroke care at different hospitals within different regions is assessed. Systematic errors and ways of registering and reporting may be assumed to be equally distributed over several dimensions including sex (research paper I) but not when assessing different caregiving units and regions, as the routines are probably a result of the local or regional culture.
6.4.2.2 Recall bias
Recall bias appears when the reported information on e.g. disease history differs from what was actually the case, due to recollection back in time [136]. This applies to all research papers (I-V) in terms of patient-reported baseline characteristics and outcomes, and the degree of recall bias is probably related to the time interval between the activity and the reporting/filling out the form, as well as to the cognitive state of the patient (e.g. dementia in stroke patients).

6.4.2.3 Validity of indicators selected and their underlying data
Indicators used within the studies included in this thesis generally have high coverage rates and have been subject to validation in scientific studies (e.g. the acute form for registration in the Swedish Stroke Register [139]). There are a few indicators that pose higher risk of bias;

- Patient-reported outcomes – these are to some extent subject to be filled in by a next of kin (especially for the stroke populations) rather than the patient in case the patient have challenges with doing it on his or her own (research papers I, II, V).
- Approximation of modified Rankin Scale (mRS) – there is no specific mRS information in the Swedish Stroke Register, but a previous study [118] has validated the method of approximating mRS based on a number of different variables collected by the registry (research papers I, II, V).
- Comorbidity – instead of selected diagnoses, inpatient care the year prior to the stroke event was used as a proxy and independent variable (research papers I, II, V). Comorbidity reported by the diabetes cohorts (research papers III, IV) may to some extent be subject to recall bias described above.
- Stroke recurrence – its registration is uncertain as the routines for registering new or recurrent stroke may differ between caregiving units and regions. Therefore, only recurrent strokes registered at clinics managing acute stroke care were included (research papers I, II, V).

6.4.3 Confounding
With the various data sources available, there was a strong ability to adjust for a broad range of possible confounders in the analysis. In order to ensure that all possible confounders were accounted for, care processes for the two conditions were mapped and the data sources available were leveraged to identify all relevant indicators. However, there may still be residual confounding present that have not been accounted for during this process. Furthermore, not all relevant factors identified were available, including;

- Stroke severity (NIHSS). As the coverage rate of NIHSS amounted to below 50% for included subjects, the variable was not used in order not to significantly reduce the size of the study sample. Instead, level of consciousness at arrival to hospital was used as proxy, as this indicator has been shown to be associated with outcomes (e.g. survival and functional status after discharge) [140] and as it has very high coverage in the Swedish Stroke Register.
- Metabolic factors such as diet, physical activity and smoking. It is possible to register smoking in both the Swedish Stroke Register and in the National Diabetes Register, but the coverage rate for this variable varied in relation to the other quality registry variables used; for the stroke cohorts the coverage rate was significantly lower than the other case-mix factors included, which was not the case for the diabetes cohorts. The variable was hence not used for the stroke cohorts but included in adjustments for the diabetes cohorts.
- Environmental factors such as air pollution and exposure to dangerous materials (e.g. lead), shown to be associated with outcomes [135].
• Information on informal care such as support at home from family or spouse which would have added an important perspective in terms of actual resource use.
• Data on municipality-financed healthcare (data on region-financed healthcare and municipality-financed home-help services were available).

Post-hoc corrections to account for the multiple tests performed within the studies were not consistently done. Such corrections can be of value in order to adjust the level of statistical significance for the results when the number of study outcomes is high (research papers I, II, V). In research paper I, the results from a Bonferroni correction was presented and showed that all differences found after multivariate adjustments were still significant except for one (initial inpatient stay in ICH patients). In the diabetes studies (research papers III and IV) the need for post-hoc correction is not considered warranted given the lower number of study outcomes (three in research paper III and five in research paper IV).

6.5 Topics for future research

**Personalization of diabetes care.** As many sociodemographic determinants are associated with health outcomes in diabetes patients, it should be highly prioritized to assess different ways of reducing that gradient with variants of personalized treatment regimes, evaluated in a controlled research setting.

**Randomized clinical trial of an updated care process and its impact on health equity**, e.g. stroke patients with history of psychosis or schizophrenia, to enable evaluation of new ways of working to reduce inequities along the treatment pathway.

**Studying the age at disease onset as a determinant for health** (e.g. time after stroke event, duration of diabetes). To deepen the understanding of the value of primary prevention, it would be interesting to study the association of long-term health outcomes and the individuals’ age at disease onset.

**Compliance to pharmaceutical treatment in stroke patients with history of mental comorbidity.** Patients with pre-stroke psychosis seem to need additional support for enhancing compliance to pharmaceutical treatment, regardless of the cause of its lower levels compared to other stroke patients (i.e. a lower frequency of prescriptions, a lower compliance in filling the prescriptions, or a combination of both). The drivers of these differences need further assessment and was not addressed in research paper V as Prescribed Drug Registry data extracts do not cover prescriptions that have not been filled.

**Distribution of somatic illness between sexes in patient populations with mental illness.** As concluded within research paper V, an inverse relationship in the sex distribution of stroke patients with previous diagnosis of psychosis or schizophrenia was found; psychosis and schizophrenia are more common in men, but women were overrepresented in the sample of stroke patients studied [60] [129]. This pattern needs to be better understood.
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8. References


78. WHO fact sheet 138: Diabetes Mellitus.


Appendix A

Search string for previous research on health equity and stroke on PubMed

\[
\text{stroke[Title/Abstract]} \\
\text{AND} \\
\text{(((((equity[Title/Abstract]) OR equality[Title/Abstract]) OR disparity[Title/Abstract]) OR disparities[Title/Abstract]) OR difference[Title/Abstract])) OR variation[Title/Abstract])} \text{ OR} \\
\text{determinant[Title/Abstract]} \text{ OR predictor[Title/Abstract]} \\
\text{AND} \\
\text{register[Title/Abstract] OR registry[Title/Abstract]} \\
\text{AND} \\
\text{Sweden [Title/Abstract] OR Swedish [Title/Abstract]}
\]

Search string for previous research on health equity and diabetes on PubMed

\[
\text{diabetes[Title/Abstract]} \\
\text{AND} \\
\text{(((((equity[Title/Abstract]) OR equality[Title/Abstract]) OR disparity[Title/Abstract]) OR disparities[Title/Abstract]) OR difference[Title/Abstract])) OR variation[Title/Abstract])} \text{ OR} \\
\text{determinant[Title/Abstract]} \text{ OR predictor[Title/Abstract]} \\
\text{AND} \\
\text{register[Title/Abstract] OR registry[Title/Abstract]} \\
\text{AND} \\
\text{Sweden [Title/Abstract] OR Swedish [Title/Abstract]}
\]