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## **AS TIME GOES BY**

Diabetes mellitus and the health  
services from short- and long-term  
perspectives – healthcare  
utilisation, costs and health-related  
quality of life

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## ABSTRACT

**Aim:** To analyse how healthcare utilisation, healthcare costs and health-related quality of life (HRQoL) differ for individuals with diabetes compared to control individuals from the general population and how these differences are associated with disease duration and changes in the health care over time. A further aim was to explore diabetes care from an equity perspective.

**Methods:** The research was based on four cohorts with disease durations of 1, 8, 15 or 24 years. These cohorts were selected from the Diabetes Incidence Study in Sweden, which registers all incident cases of diabetes in the age group 15 to 34 years, the majority Type 1 and insulin-treated. Control individuals were selected from the population register matched by age, sex and county of residence. In January 2008, a survey questionnaire was mailed by post to the 1983, 1992 and 1999 cohorts and their matching control groups. In 2009, the same survey questionnaire was quarterly sent to the 2008 cohort and to matching controls. The overall response rates were 54% (n=864) for individuals with diabetes and 51% (n=1616) for control individuals.

**Results:** Higher utilisation of healthcare services by patients with diabetes compared to control individuals, and the necessary medication, led to an annual excess costs of 40 000 to 50 000 Swedish crowns per patient with no significant differences among the four cohorts. The costs of health care for women (in both the diabetes groups and the control groups) were almost double the costs for men in most cohorts.

Living with diabetes had a negative impact on HRQoL and the difference to control individuals increased by disease duration for women with diabetes. However, there were no significant differences between individuals with diabetes 1 year after diagnosis and the control individuals, which may be related to good early management of diabetes care and an early adaptation to the disease.

Compared to a previous study conducted in the early 1990s, excess costs increased mainly due to the greater use of insulin pumps and insulin analogues. Utilisation patterns for patients with diabetes were stable except for a significant decrease in hospital inpatient care 1 year after diagnosis (60% to 13%), and an increase in daycare 8 years after diagnosis (11% to 44%). The excess costs 1 year after diagnosis were similar whereas excess costs 8 years after diagnosis more than doubled, but while the largest proportion of costs in 2009 was for hospital outpatient care, 16 years earlier most costs were for hospital inpatient care. In line with the results from the previous study, the largest proportion of costs 8 years after diagnosis were attributable to insulin treatment and monitoring of blood glucose, followed by the costs for hospital outpatient care.

**Conclusions:** Individuals with diabetes seem to lead rather unrestricted lives with less hospital inpatient care and a higher degree of self-management than 16 years earlier. However, the findings indicate that healthcare utilisation, costs and HRQoL vary by gender and socio-economic background. In addition to having diabetes, being a women, having a low education level or low income, and not being married all had a negative effect on almost all outcome measures addressed in this thesis.

Utilisation patterns, costs and HRQoL can be described and analysed by continued health services research, and may be a valuable complement to more clinically oriented research. Health services research may also provide valuable information in the formulation of future healthcare policies. In contrast to randomised controlled trials, long-term studies of diabetes populations in real-world health systems can shed light on issues of access to the healthcare systems as well as on associated equity issues.

## LIST OF PUBLICATIONS

- I. **Sparring V**, Nyström L, Östman J, Wahlström R, Burström K, Jonsson PM. Changing healthcare utilization patterns in diabetes mellitus: case-control studies 1 year and 8 years after diagnosis. *Diabetic Medicine*, 2011;29(6):784-791.
- II. **Sparring V**, Burström K, Jonsson PM, Nyström L, Wahlström R, Östman J, Zethraeus N. Excess costs of medical care for individuals 1, 8, 15 and 24 years after diagnosis of diabetes: estimates from young and middle-aged incidence cohorts in Sweden. Manuscript.
- III. **Sparring V**, Nyström L, Wahlström R, Jonsson PM, Östman J, Burström K. Diabetes duration and health-related quality of life in individuals with onset of diabetes in the age group 15-34 years – a Swedish population-based study using EQ-5D. *BMC Public Health*, 2013;13:377.
- IV. **Sparring V**, Jonsson PM, Wahlström R, Brown C. Equity in healthcare utilisation, dissatisfaction and self-rated health for individuals with onset of diabetes in the age group 15-34 years compared to the general population. Manuscript.

The articles will in the thesis be referred to by their Roman numerals.

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## ABBREVIATIONS AND DEFINITIONS

CI	Confidence Interval
DCCT	Diabetes Control and Complications Trial
DISS	Diabetes Incidence Study in Sweden
EQ-5D	Euroqol 5 Dimensions
GDP	Gross Domestic Product
HbA1c	Glycated haemoglobin (blood test showing the average level of blood glucose over the previous three months)
HRQoL	Health-Related Quality of Life
HPSR	Health Policy and Systems Research
HSR	Health Services Research
IDF	International Diabetes Foundation
LISA	Longitudinal integration database for health insurance and labour market studies
NDR	National Diabetes Register
OR	Odds Ratio
PIN	Personal Identification Numbers
SF-36	Short Form 36
SRH	Self-Rated Health
SWED-QUAL	Swedish Health-Related Quality of Life Survey
VAS	Visual Analogue Scale





# 1 PROLOGUE

I have had many windows of opportunities in my life. As time went by, these opportunities led me to where I am today with this thesis.

My interest in health care began with the first window. While working temporarily at a staffing company I was sent to the Federation of Swedish County Councils (now the Swedish Association of Local Authorities and Regions). I was surprised to see how useful my background in studies in international management was. In collaboration with thoughtful and creative colleagues and healthcare professionals, I worked to improve Swedish healthcare. When the Federation offered me a job, I gladly accepted because it felt good to work in an area where I could contribute to society.

After a few years of working in other areas, another window opened for me. I was contacted by Professor Mats Brommels, and met with him and Professor Göran Tomson. This meeting led to my employment at the Karolinska Institutet (KI), in the newly established Medical Management Centre (MMC). I was thrilled to be working again in the healthcare sector. My years at MMC have been both joyful and fruitful. I hope they will continue to be so.

At KI, I worked with Dr. Pia Maria Jonsson on projects that investigated gender differences in patient safety and in the National Quality Registers. When Dr. Jonsson received funding from the Swedish Council for Working Life and Social Research for a follow-up of her thesis from 2001, another new window opened. Feeling excited about the possibility of digging deep into a research project, I enrolled as a PhD student and began the studies and research that have resulted in this thesis.

My thesis title, *As time goes by*, has two implications. First, the title refers to the past three decades during which the management of diabetes developed mainly in three areas: advances in medical treatment; changes in level of care; and the increased role of the patient. Second, the title refers to the duration of diabetes that may affect how people with diabetes experience their disease.

## **2 DEVELOPMENTS IN HEALTH CARE AND IN THE MANAGEMENT OF DIABETES**

About 365,000 people in Sweden have diabetes, most of whom have Type 2 diabetes (1). About 15% of these people have Type 1 diabetes, which is the main diabetes examined in this thesis. After Finland, Sweden has the highest incidence rate of Type 1 diabetes in the world (2).

Type 2 diabetes, which is more common and is found in about 85% of people with diabetes, has a low incidence before the age of 30 years and increases markedly by age. Type 1 diabetes is an autoimmune disease in which the ability of the pancreas to produce insulin is low or non-existent. Type 1 diabetes, which usually begins before age 30, is a life-long disease, which is associated with risks of acute and long-term complications. In the following sections, the development of management of diabetes is explored from different health services perspectives. In this way, healthcare utilisation and changing utilisation patterns, the costs of diabetes and health-related quality of life (HRQoL) are explored. The study of diabetes from these perspectives reveals how the changes in the management of diabetes care have affected people with diabetes. The study also reveals how these perspectives are affected by the duration of the disease. This study has contributed to our understanding of how well Swedish diabetes care meets one of its major goals – equitable care for all patients.

### **2.1 LONG-TERM COMPLICATIONS AND MORTALITY**

Diabetes is a chronic disease that may affect people's lifespan and their HRQoL. Individuals who receive a diagnosis of diabetes, especially Type 1 diabetes, often face a major upheaval in their lives. How they react to this diagnosis depends on how they generally react to difficulties in life and to their life situation at the time of diagnosis (3, 4). In the early stages of diabetes, the focus is on achieving metabolic glucose control and teaching patients disease management. Chronic hyperglycaemia is accompanied with long-term microvascular (5) and macrovascular complications (6) both in Type 1 and Type 2 diabetes. Because of these complications, people with diabetes, on average, have a shorter lifespan. Population-based studies in Sweden have found that age- and sex-standardised mortality is more than double in the first decades with the disease, mainly because of ketoacidosis (the shortage of insulin that makes the body burn fatty acids and produce acid ketones). Mortality after 10 years with diabetes is mostly caused by macrovascular disease and diabetic nephropathy (7). In the long-term, complications such as retinopathy, nephropathy, neuropathy and cardiovascular disease (described below) are likely to develop.

Diabetic retinopathy occurs in both Type 1 and Type 2 diabetes and refers to the changes in the retinal vessels due to diabetes. These changes may lead to impaired vision and, in severe cases, to blindness. These risks increase with disease duration. However, through early diagnosis and treatment, the incidence of blindness and visual impairment among patients can be significantly reduced (8, 9).

The most serious complication and leading cause of death among individuals with diabetes is nephropathy. Diabetic nephropathy, which is a pathological change in the kidneys, is the most common reason for dialysis or kidney transplants in Sweden. Prior to modern treatment, the highest incidence (5% per year) occurred after 15 to 20 years or disease duration. Today, the highest incidence (less than 2%) is seen after 25 to 30 years (10).

Neuropathy, defined as pathological changes in the peripheral nerves, may be one of the most common complications resulting from diabetes. Its prevalence is estimated at around 10% in patients at the onset of diabetes and at more than 50% in patients with longer disease duration. Although usually not life-threatening, neuropathy may lead to a significant reduction in the quality of life as many natural functions such as gastrointestinal disturbances and circulation may be affected. Patients may also experience problems with their blood pressure and sex life. There is a correlation between disease duration and the development of polyneuropathy (i.e., neuropathy affecting several nerves simultaneously); the longer someone has had diabetes, the more frequently peripheral polyneuropathy develops (11).

Diabetes also increases the risk of macrovascular complications, which are almost identical with atherosclerosis seen in patients without diabetes. These cardiovascular diseases include ischemic heart disease, stroke and peripheral vascular disease. Individuals with diabetes have a greater likelihood than individuals without diabetes for another heart attack or stroke. Peripheral atherosclerosis is a common reason for amputation when foot ulcers do not heal (12).

The average lifespan is shorter for people with Type 1 diabetes because of both acute and chronic complications associated with the disease. Early mortality is mainly related to ketoacidosis (13). Suicide, caused by psychosocial factors (7), is the primary reason for excess mortality among those with diabetes onset between the ages of 15 and 34 years. Most excess late mortality, after a disease duration of 20 years, has been related to cardiovascular disease and nephropathy (14-16).

## **2.2 DEVELOPMENTS IN THE MANAGEMENT OF DIABETES**

In 1993, researchers at the Stockholm Diabetes Intervention Study (17) and the Diabetes Control and Complications Trial (DCCT) (5) reported for the first time that long-term, intensified conventional insulin treatment could delay the development and the progression of microvascular lesions in Type 1 diabetes mellitus. These fundamental observations resulted in the development of many insulin analogues and also of sophisticated devices for continuous, subcutaneous insulin administration. The goal of these analogues and devices was to mimic the physiological blood insulin profile and thus to produce near-normal glycaemia in patients. Furthermore, the Swedish National Guidelines for diabetes care were formulated, as in other countries, with the aim of achieving good quality of life for patients with diabetes. The Guidelines also included recommendations for the allocation of resources in an equitable way. The Guidelines have been regularly updated since 1993. The most recent Guidelines were published in 2010 (18).

The National Guidelines recommend that patients with Type 1 diabetes be offered the following:

- advice for a healthy life style related to diet, physical exercise and non-smoking,
- assistance in lowering blood pressure and reaching lipid levels that may reduce the risk of cardiovascular disease,
- intensive treatment in order to achieve the best possible blood sugar levels,
- NPH insulin and insulin analogues, and insulin pumps if blood sugar levels are volatile,
- group education that takes cultural background into consideration,
- periodic check-ups for foot problems with foot treatment if the risk for foot ulcers is high, and
- physiotherapeutic treatment for shoulder pain.

In addition to advances in medical treatment, diabetes management has made advances in the changes in the level of care and in the recognition of the benefits of patient involvement. The medical advances include multiple daily injection regimens, the use of insulin pumps, and new insulin analogues (17, 19). In order to use resources more effectively, there has been a shift from hospital inpatient care to daycare, from visits to specialists in hospitals to visits to family doctors, as well as from visits to physicians to visits to diabetes specialists. Another major advance is the increased recognition of the importance of the role of the patient in disease self-management (18).

The National Board of Health and Welfare evaluated Swedish diabetes care in 2011. The evaluation revealed positive results and improved advances, in terms of both process measures and outcome measures. However, the evaluation also stated that there was room for improvement, especially concerning the achievement of HbA1c levels, in particular for individuals with Type 2 diabetes. Another concern was the lack of culturally adapted patient education. The main data source was the National Diabetes Register (NDR), in which the quality of diabetes care is measured by clinical parameters. NDR, which covers approximately 90% of the diabetic population (20), facilitates monitoring individual patient development of certain risk factors. NDR also allows healthcare facilities to compare their results from year to year and to benchmark their results against national averages.

### **2.2.1 Diabetes care in Sweden**

In Sweden, the responsibility for financing and organising health services lies with the 20 county councils, and in some cases, with the municipalities. The Health and Medical Service Act regulates the responsibilities of county councils and municipalities, and gives local governments some freedom. Public providers provide the majority of healthcare services to the public, but the share of such services provided by publicly funded private producers has increased, especially in primary care. In 2011, visits to private physicians in primary care accounted for 40% of all medical visits and visits to private specialists for 24% (21). In this taxpayer-funded, decentralised system, the national government contributes to information distribution, for example, by National Guidelines.

In Sweden, the number of visits to physicians in primary care has increased by 12% from 2007 to 2011. The number of hospital visits has also increased annually whereas the total number of in-hospital patient days has decreased. The average length of hospital stay in 2007 was 5.8 days; in 2011 it was 5.3 days. Because fewer patients require inpatient care, they can be treated in daycare (e.g., day surgery). On average there were 0.41 day-surgery visits for each inpatient visit in 2010. In 2006, there were 0.36 such day-surgery visits (21).

In order for diabetes care to function effectively, well-functioning care routines and cooperation (between diabetes patients and the diabetes team) are needed (3). Type 1 diabetes patients are mostly treated at hospital diabetes clinics whereas most Type 2 diabetes patients are treated at primary care units (unless the cases are complicated) (22). Multiprofessional teams are responsible for most diabetes care in Sweden. These teams have physicians with special responsibility for patients with diabetes, and diabetes nurses as key members, but may also include dietitians, podiatrists, counsellors and physiotherapists. Although almost all hospital diabetes clinics use such multiprofessional teams, only 30% of the primary care units have diabetes teams. However, 90% of the primary care units reported they have a diabetes-educated nurse (22).

Of the diabetes clinics, 70% offer group training for people with Type 1 diabetes and 40% offer group training for people with Type 2 diabetes. Only 3% of the clinics offer training that takes different patient cultural backgrounds into consideration (22).

Patient fees cover only a small percentage of the healthcare costs in Sweden. The patient fee for a hospital stay is 80 Swedish crowns per day for the first ten days and thereafter 60 crowns/day. Fees for primary care, which vary depending on the county councils, range from 100 to 200 crowns per visit. The fee for a specialist visit is an additional 350 crowns. For patients with high utilisation of health care or high costs for prescription medication, there is an annual high-cost ceiling of 900 to 1,100 crowns for medical consultations and 2,200 crowns for prescription medications.

## **2.2.2 Healthcare reforms in Sweden 1983-2008**

There have been several important reforms of the Swedish healthcare system since the early 1990s when Jonsson (23) conducted her study on diabetes care. While most of these reforms were general reforms that did not necessarily affect diabetes care, some reforms were more likely to affect the care of people with diabetes.

With the Patient Choice Reform, initiated in 1991, people were given the right to choose their healthcare providers (24). This reform was expanded in 2001 to include hospital outpatient care. In 1997, the Medical Products Reform was launched which redirected responsibility for medications from the national government to the county councils. The main justification for this reform was the government's need to manage the continual increase in the costs of medications in a more rational and cost effective way. Each county council now has a medication committee that is responsible for a safe, rational and cost-effective pharmacotherapy.

For years, the Swedish public has complained about long waiting times for health care. Several reforms have tried to tackle this problem. In 2000, the National Action Plan for Health Care was introduced (24). Its aim was to strengthen the primary care provided by the county councils and the municipalities in order to, among other things, improve care processes and increase access to care. The concern was that problems with access to elective care could create a serious credibility problem for the entire Swedish healthcare system. In 2002, the national government set aside 1.25 billion crowns to be used to create a sustainable improvement in healthcare access (24). In 2008, another 1 billion crowns, were set aside to strengthen healthcare access, and in 2013, yet another 1 billion crowns were set aside (25). In 2005, the national government introduced a healthcare guarantee that states that patients are entitled to receive an appointment at a community healthcare centre within 8 days of initial contact, an appointment with a specialist within 90 days, and treatment within 90 days (26).

## **2.3 DIABETES CARE FROM A HEALTH SERVICES RESEARCH PERSPECTIVE**

The theoretical perspective of this thesis comes from health services research (HSR), which is applied research aimed at improving the quality, organisation and management of health services (27, 28). HSR can be defined as the examination of *"how people get access to health care, how much care costs, and what happens to patients as a result of this care"* (29). It builds on scientific enquiry involving different disciplines including economics, epidemiology, public health, medicine, operations management and psychology. The underlying aim of HSR is to conduct research that can be applied by physicians, nurses, health managers and administrators, and other decision-makers in the healthcare sector.

HSR overlaps with health policy and systems research (HPSR) (30) in which health systems are often described as six building blocks: health services; health workforce, health information; health financing; medical products and technologies; and leadership and governance (31). These blocks have their own dynamic response to their fluctuating environment. However, while HSR may focus on services and programmes for particular health conditions, HPSR has a broader perspective that considers the health system and policy context (30).

HSR focuses on the *input, process* and *outcome* of health care with the aim of achieving an equitable healthcare system, or satisfactory quality, at an affordable price (27, 28, 32). This perspective implies that the focus of such research is the interaction between people with diabetes and the healthcare system, although it is recognised that individuals with diabetes and their families play a key role in managing the disease. Good health services are defined as services that deliver "effective, safe and quality personal and non-personal health interventions to people in a timely and geographically appropriate manner, and with a minimum waste of resources" (33), p. 3). In recent decades, certain factors have been identified that could affect the *input* of health care such as new medications, new forms of treatment, staff changes (e.g., working in diabetes teams), and more frequent use of diabetes nurses. In terms of *process* in health care, there have been changes in care levels with a shift towards outpatient care and primary care. There have also been changes in the staff-patient interaction where patients, to a larger extent, are more involved in their own care. Data on the *process* of

health care are important for evaluating if health service resources are used efficiently (32). Possible measures could be levels of use by different population groups as well as costs in relation to healthcare utilisation and medical treatment. Health *outcomes* are the effects of health services on patients' health. Appropriate *outcome* measures to study changes in *input* and *process* could be patients' perceptions of outcome in relation to their HRQoL and their satisfaction with the outcome and the mode (*process*) of delivering that care (28). As diabetes care covers various parts of the healthcare system, and collaboration between the different parts are vital for supporting individuals with diabetes, repeated measurement and analysis of healthcare utilisation patterns, costs and HRQoL in a population with a chronic disease may indicate problems in the health system as a whole.

In studying the utilisation and costs of health services, it is of great importance to balance need (what people benefit from), demand (what people ask for), and supply (what is provided). The need for health is related to the overall aim of a healthier population (27). However, need is a relative concept and is very much dependent on socio-economic and cultural factors (28).

In studies on utilisation and costs of health services it is also of importance to apply a longitudinal perspective. One possibility is then to follow cohorts of individuals over time. This is, however, a quite expensive and difficult approach. A more feasible alternative is to use already registered cohorts of individuals with different characteristics as well as existing data from such registers, and adapt these to the research questions at hand. In the context of this thesis research it was possible to use a selection of diabetes incidence cohorts with various disease durations, and design a study, which included cross-sectional analyses and comparisons. The findings and their interpretation could through such an approach be linked to disease duration although the data collected were not directly related to a longitudinal follow-up of the cohorts.

### **2.3.1 Healthcare utilisation**

The excess use of healthcare services by patients with diabetes is partly the reason that diabetes creates a substantial economic burden on society (34, 35). Changes in healthcare utilisation patterns and excess healthcare utilisation are partly a reflection of the effectiveness and efficiency of the healthcare system in treating patients with diabetes (36, 37). Previous studies in other contexts indicate that healthcare utilisation related to diabetes changes over time as a function of disease duration (38-42). The effects of disease duration on excess healthcare use have also been shown in Sweden (34), but not the changes in the utilisation of healthcare services over time.

Parslow et al. (43) found that there are gender differences in the use of healthcare services and that some differences can be explained by women's use of reproductive health services. However, even when women's visits to gynaecology and obstetrics departments are omitted, their use of healthcare services is still higher than men's. Other factors that influence the level of healthcare utilisation are lower self-rated health (SRH), lower incomes and lower education levels. In addition, people with diabetes may have depression symptoms that may account for higher healthcare utilisation (44).

### 2.3.2 Excess costs

In 2007, the International Diabetes Federation (IDF) estimated the direct costs of diabetes to the healthcare sector in various countries. The estimation, which was based on a model that assumed the prevalence of diabetes in each country would be 6%, concluded that the cost of care for a person with diabetes is 2.5 times greater than that of a person without diabetes (35). The IDF's new estimates of healthcare spending due to diabetes show that on average \$5,063 per person is spent in high-income countries compared to \$271 in low- and middle-income countries. The estimate for Sweden was \$5,440 per person (2).

Estimating costs can be done using either a top-down or a bottom-up strategy (45). A top-down strategy uses published data based on aggregate figures on consumption related to diagnosis, e.g., diabetes. The disadvantage of this approach is that it could miss costs of diabetes-related complications, e.g., cardiovascular disease, unless diabetes is registered as the main diagnosis. A bottom-up strategy, which involves cost estimates derived from an investigation of a sample of people with diabetes, permits a more comprehensive inventory of the utilisation and costs of diabetes care than is possible using only data from databases in the healthcare system. In a bottom-up strategy, it is also easier to analyse the relationship between different background characteristics of the people with diabetes and the costs of care.

Cost analyses should preferably be based on opportunity costs (i.e., the value of the forgone benefits because the resource is not available for its best alternative use), the pragmatic approach to costing is to take existing market prices unless there is some particular reason to do otherwise (45), p. 57). Unfortunately, it is often difficult to conduct costing studies if hospital costs are not very detailed. Because of the unavailability of data, it is common that assumptions about costs are made, for example, by using general per diem or average hospital costs (28, 45).

Several studies have shown that the healthcare costs related to diabetes are a substantial burden on society (34, 37, 46-62). The reason is partly due to the high prevalence and increasing incidence of Type 2 diabetes. Healthcare costs have also increased by approximately 20% since 2002 because of the ageing population and because of the development of new and more expensive treatments (21). In Sweden, healthcare costs are approximately 14% of GDP (21). Of these costs, 6-7% are calculated as attributable to diabetes care (54, 63).

The excess costs for diabetes vary considerably with patient age (54). The diabetes/non-diabetes cost ratio was higher among children (7.7) than among people over 75 years of age (1.4). Costs have also been found to increase with diabetes duration (63). The direct costs for diabetes in Sweden have been estimated at around 40% of total costs for diabetes, and the indirect costs (i.e., production losses due to morbidity and premature death) at around 60% (63, 64). Henriksson et al. (63) found that the direct costs were almost 50% higher for patients with longer diabetes duration than ten years compared with patients with a diabetes duration of less than five years. In two Swedish population-based incidence cohorts (from 1983 and 1992; diagnosed at the age of 15-34 years), were investigated one and eight years after diagnosis. The estimated costs for medical care after one year was 5.6 times higher for patients with diabetes than for the age- and sex matched control group, whereas the corresponding figure after eight years was 3.8 (34).



Diabetes costs can be divided into two categories: costs for the prevention and treatment of diabetes and costs for diabetes-related complications (65). The largest impact on costs of diabetes care results from diabetes-related complications rather than direct costs for the actual treatment of diabetes (52, 63, 66-71). Studies conducted in clinical settings have confirmed that intensive management of diabetes can prevent, or at least postpone, the occurrence of long-term complications (5, 17, 72) and can reduce the considerable social and economic consequences of the disease to the individual and to society (23, 73, 74). As a consequence, when costs are shifted to the early years following diabetes diagnosis, the total overall costs of the disease may decrease and the cost-effectiveness of diabetes care may improve. On the other hand, intensive treatment regimens may negatively influence HRQoL in early diabetes care even though the reverse (i.e., improved HRQoL) may be the eventual outcome.

As the treatment of diabetes has changed considerably in the three last decades, it is likely that the costs for diabetes care have risen. Follow-up or repeat studies are therefore important in order to compare excess costs over time and to obtain new cost estimates that reflect current treatment practices. This research was conducted 16 years after Jonsson's (34) study of the 1983 and 1992 cohorts with a disease duration of 8 years and 1 year, respectively. Repeat investigations of these cohorts, now with disease durations of 24 and 15 years, respectively, enabled the analysis of healthcare utilisation and the use of medications over a longer time period. Furthermore, inclusion of two new cohorts from 1999 and 2008, with disease durations of 8 years and 1 year, respectively, enabled direct comparisons with the earlier study.

### **2.3.3 Health-related quality of life**

Because diabetes is associated with both a risk for acute and chronic complications, it is likely to affect HRQoL. HRQoL is a subjective assessment of health status that includes aspects such as general health, physical, emotional, cognitive, and role functioning, as well as social well-being (75).

For individuals with diabetes, HRQoL can be measured with a diabetes-specific instrument that may detect subtle disease and treatment-related effects (76-79), or with generic instruments that enable comparisons to the general population or to other diseases (79-82). The choice of type of instrument depends on the research question and which decisions one wants to make based on the results (83). In order to compare the difference between individuals with varying diabetes duration, and the difference between individuals with diabetes and the general population, a generic instrument is the most appropriate choice. The literature supports the use of generic HRQoL instruments for measuring health status in individuals with diabetes. Examples of such instruments are the Short Form 36 (SF-36), the Health Utility Index (HUI), and the EQ-5D (76, 84, 85). The EQ-5D, which is a short instrument that can be included in any questionnaire, has been used in the general population as well as with a wide range of health conditions and treatments (86).

### **2.3.4 Equity perspective**

Equity in health implies that resources will be distributed and processes will be designed in ways that are fair and just, while recognising that different groups in a population have different needs and power (87, 88). One main goal of Swedish health care is to provide equitable access to high quality care regardless of age, sex, geographic area, social status, or ethnic background (89). However, despite efforts to reduce inequities in health and health care in recent decades, there are few indications that gender and socio-economic inequities have diminished in Sweden (90).

Gender-specific analyses from the study in the early 1990s showed that, 8 years after diagnosis, the excess costs were higher for women than men, mainly due to women's more frequent use of hospital outpatient care and more intensive glucose monitoring (36). SRH was poorer among individuals with diabetes than in population controls both 1 year and 8 years after diagnosis (91). This difference was found in men and women and in the socio-demographic subgroups studied except among individuals from upper social class backgrounds or with academic educations. These findings suggested the interaction between (female) gender and (low) social class are predictors of poor SRH. Gender and socio-demographic factors were more closely associated with SRH 8 years after diagnosis than 1 year after diagnosis, suggesting early socio-demographic stratification in the health of the diabetic population.

## **2.4 JUSTIFICATIONS**

The prevalence of diabetes mellitus in Sweden is increasing (as well as in other countries) and therefore creates a substantial economic burden for society (52, 92). Because the patterns of healthcare utilisation are closely related to the direct costs of diabetes (36), the value of this research is its examination of the changes in healthcare utilisation patterns that may reflect the effectiveness and efficiency of the healthcare system. The trade-offs between early diabetes control and the occurrence and severity of long-term complications can be addressed by comparing diabetes patients' healthcare utilisation and HRQoL with control individuals' healthcare utilisation and HRQoL. In this thesis, it was possible to apply a longitudinal approach using yearly cohorts from the DISS registration of all incident cases of diabetes in the 15 to 34 years age group.

The four cohorts of individuals with diabetes selected for this thesis represent the development of diabetes in different phases and its associations with healthcare utilisation, costs and HRQoL 1, 8, 15 or 24 years after diagnosis. Two cohorts, 1983 and 1992, were studied previously at 8 years and 1 year after diagnosis, respectively (23). This research was conducted 16 years after Jonsson's study of the 1983 and 1992 cohorts. Follow-up of these cohorts, now with disease durations of 24 and 15 years, respectively, will enable the analysis of healthcare utilisation and the use of medications over a longer time period. This longitudinal approach to the examination of patterns and costs may indicate if changes in diabetes treatment and management have had any effect. Furthermore, two new cohorts from 1999 and 2008 were included, also with disease durations of 8 years and 1 year, respectively, which will enable direct comparisons with the previous study. It was hypothesised that the direct costs of diabetes during the first year after diagnosis may have increased since the early 1990s due to more counselling and treatment efforts, while the costs 8 years after diagnosis may not have changed significantly. Furthermore, due to the intensive treatment of

diabetes in the early stages, the HRQoL for the patient with diabetes was likely to be negatively affected whereas HRQoL was expected to improve in the stable stages of the disease. However, with longer disease durations and the possibility of potential diabetes-related complications, a gradual decrease in HRQoL beyond that of the general population was expected. As there are few indications of diminishing gender and socio-economic gradients in health and health care (90), it was expected that there would be no change in the previously observed differences.

### 3 AIMS AND OBJECTIVES

The main aims of this thesis were to analyse how healthcare utilisation, costs and health-related quality of life differ for individuals with diabetes compared to control individuals from the general population and to analyse how these differences are associated with disease duration and changes in the healthcare over time. A further aim was to explore diabetes care from an equity perspective.

The specific objectives were:

- a) To describe healthcare utilisation patterns in young and middle-aged patients 1 year and 8 years after diagnosis and to compare with the general population at two time points 16 years apart, in the early 1990s and in the late 2000s.
- b) To compare the estimated annual excess costs for the treatment and management of diabetes in four cohorts (1, 8, 15 and 24 years after diagnosis), and with estimates of excess costs in two cohorts from the early 1990s (1 year and 8 years after diagnosis).
- c) To describe and analyse HRQoL in individuals with onset of diabetes between 15 and 34 years of age and with a disease duration of 1, 8, 15 and 24 years, and to compare these individuals with the general population.
- d) To explore the role that gender and socio-economic factors play in healthcare utilisation, dissatisfaction with services and SRH in Sweden for individuals with diabetes compared with the general population.

In this thesis, time after diagnosis has been used as a proxy for disease duration.

## 4 METHODS

As was described earlier, health services research focuses on the input, process and outcome of healthcare services. This thesis focuses on the following outcome measures: healthcare utilisation, costs of medical care, and HRQoL. These measures may indicate how the changes in the processes of the healthcare system are associated with providing equitable health care. It is a cross-sectional examination of four diabetes cohorts with elements of case-control analyses in the four studies.

### 4.1 STUDY POPULATION

In 1983, the Diabetes Incidence Study in Sweden (DISS) was initiated with the aim of identifying important factors in the development of diabetes and its complications (93). DISS registers all incident cases of diabetes mellitus in the age group 15 to 34 years based on reports from all departments of medicine and endocrinology and all primary health care units in Sweden. Each year, approximately 400 cases are registered. A standardised form is used to record basic information about patients at the time of diagnosis (personal identification number-PIN, name and address, date and place of diagnosis, basis for diagnosis, height and weight). In addition, the physician's clinical classification of the type of diabetes is reported. Since 1998, blood samples for determination of islet cell antibodies have been delivered to a central laboratory in order to improve the classification of diabetes. The ascertainment level has been estimated at 80% (94). A 20-year follow-up by DISS found that 74% of the individuals in the register were diagnosed with Type 1 diabetes, 15% had Type 2 diabetes, and 10% were difficult to classify at diagnosis (93, 95).

The study population for this thesis consists of cases of diabetes diagnosed in the years 1983, 1992, 1999 and 2008. In this follow-up, conducted about 25 years after DISS was initiated, the patients in the four cohorts had had diabetes for approximately 24 years, 15 years, 8 years or 1 year, respectively. The assumption behind the selection of these four cohorts was that, over this span of years, the patients would have experienced both short- and long-term complications. In addition, these complications would have affected their healthcare use and their HRQoL. One data file for each year cohort in DISS containing PINs was sent to Statistics Sweden for identification of control individuals from the general population register. For each individual in DISS, two control individuals (matched by age, gender and county of residence) were selected at the time of the follow-up. In the general population register, demographic characteristics of Sweden's population are reported by age, sex, marital status, citizenship, country of birth, migration, birth and death (96). Two cohorts, 1983 and 1992, were followed-up in the early 1990s using the same matching procedure for control individuals.

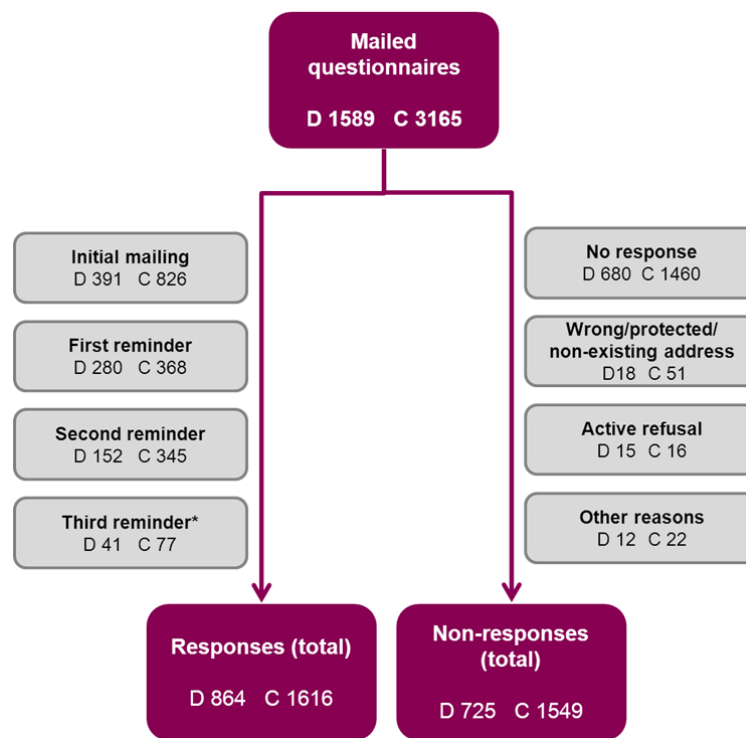
## 4.2 DATA COLLECTION

### 4.2.1 Procedure

A survey questionnaire and explanatory letter were mailed by post to the 1983, 1992 and 1999 cohorts and matching control groups in January 2008, asking for information about the previous year (i.e., approximately 24, 15 or 8 years after the diabetes diagnosis; see Appendix 1). During 2009, the same survey questionnaire was mailed by post quarterly to the 2008 cohort and to another set of matching control group (i.e., 1 year after the individual date of diagnosis of each patient with diabetes). Response envelopes were enclosed with the questionnaire so that the responders could answer by post. Responders could not answer via the Web or by email.

Two weeks after the mailing of the questionnaire, a first reminder was sent to all cohorts. A second reminder was sent to all cohorts, two weeks later, with another copy of the questionnaire. Eight weeks later a third reminder was sent to the 1983, 1992 and 1999 cohorts. This third reminder was not sent to the 2008 cohort because the third reminder sent to the other cohorts had not added much to the final response rates. The questionnaire was in Swedish. However, recipients could request an English version of the questionnaire by contacting the thesis author by mail or telephone.

Statistics Sweden, which administered the questionnaire for the 1983, 1992 and 1999 cohorts, was responsible for both the distribution and the optical reading of the questionnaires. Statistics Sweden also sent the questionnaire to the 2008 cohort but the thesis author registered all responses and managed the data. See Figure 1 for a flowchart of the data related to the mailed questionnaires.



**FIGURE 1.** Data collection: Numbers of individuals with diabetes (D) and control individuals (C), \*a third reminder was not sent to the 2008 cohort.

### **4.2.2 Questionnaire**

The questionnaire had 27 numbered questions. With the 47 sub-questions, the questionnaire had 74 questions in total. Individuals with diabetes were asked to respond to an additional 12 diabetes-related questions with 11 sub-questions. Therefore, these individuals responded to 97 questions in total.

The questionnaire addressed the following aspects of health care: HRQoL; healthcare utilisation; prescription and non-prescription medication use; short- and long-term sick leave; dissatisfaction with health care; and socio-demographic issues. The questionnaire, which also had diabetes-related questions about the use of insulin, devices and test materials, was an updated version of the questionnaire used in earlier studies from 1991 and 1993 by Pia Maria Jonsson (23). For the research for this thesis, minor changes were made to the previous questionnaire. For example a few questions were deleted as no longer relevant. The EQ-5D questionnaire (explained next) was added in order to make comparisons with population studies and studies using EQ-5D in other diabetes populations.

Data on HRQoL were collected using the SWED-QUAL instrument, which is a modified translation of SF-36 that covers physical functioning, role functioning, emotional functioning, well-being, pain, sleep, family functioning and general health perceptions (97). In order to compare different generic methods for the measurement of HRQoL in men and women with diabetes, the questionnaire also included the EQ-5D instrument (86). The EQ-5D, which is less extensive than the SWED-QUAL, provides access to comparison materials both in disease populations (85, 98-104) and in the Swedish general population (81, 105).

Data on healthcare use patterns were gathered from responses to structured questions about the numbers of contacts with different healthcare areas. Some questions requested the number of contacts for hospital outpatient care, hospital emergency room treatment, and clinic visits in the most recent three months. Other questions requested information on the number of days for inpatient care and daycare in the last year. Daycare was defined as visits to hospitals for participation in education or training programmes, for operations, or for other procedures where observation, although not overnight stay, is required. Inpatient care covered hospital admissions as well as total length of stay at different clinics. The questionnaire also requested information on the number of visits to community healthcare centres or private practitioners and the number of house calls by nurses or physicians from community healthcare centres in the most recent three months.

The Swedish Surveys of Living Conditions conducted by Statistics Sweden (106) guided the construction of the questionnaire (e.g., for wording and recall periods).

### **4.2.3 Additional data sources**

Informed consent was requested from all questionnaire responders in order to complete the data set with socio-economic variables available in the Longitudinal integration database for health insurance and labour market studies (LISA by Swedish acronym) hosted by Statistics Sweden (107). Variables included were education level, gainful employment, income level, sick leave days and early retirement as registered in the database 2006 (education level included Spring term 2007).

Data for calculating costs for inpatient and outpatient care were obtained from the Swedish Association of Local Authorities and Regions (108) as well as from various counties' price lists for care for patients from other counties (109-112). Costs for materials, test devices and insulin and other glucose-lowering medications were obtained from the Dental and Pharmaceutical Benefits Agency (113).

#### 4.2.4 Responders and non-responders

The overall response rate for all four cohorts was 54% for individuals with diabetes and 51% for control individuals. The response rate varied between the different cohorts (the rate was especially low in the 2008 cohort) and was generally lower compared to the previous study conducted in the early 1990s. Low response rates are an increasing problem in surveys and have also been experienced by, for example, Statistics Sweden (114, 115). Table 1 shows the response rates for the different cohorts, both for this study and for the previous study.

**TABLE 1.** Response rates for the different cohorts

Incidence cohorts	1983		1992		1999		2008	
	Case n (%)	Control n (%)	Case n (%)	Control n (%)	Case n (%)	Control n (%)	Case n (%)	Control n (%)
Follow-up year	1991		1993					
Disease duration	8 years		1 year					
Total sample	442	865	322	658				
Responses	317 (72)	586 (68)	237 (74)	443 (67)				
Follow-up year	2007		2007		2007		2009	
Disease duration	24 years		15 years		8 years		1 year	
Total sample	422	841	418	828	409	815	340	681
Responses	276 (65)	530 (63)	228 (55)	434 (52)	217 (53)	396 (48)	143 (42)	256 (38)

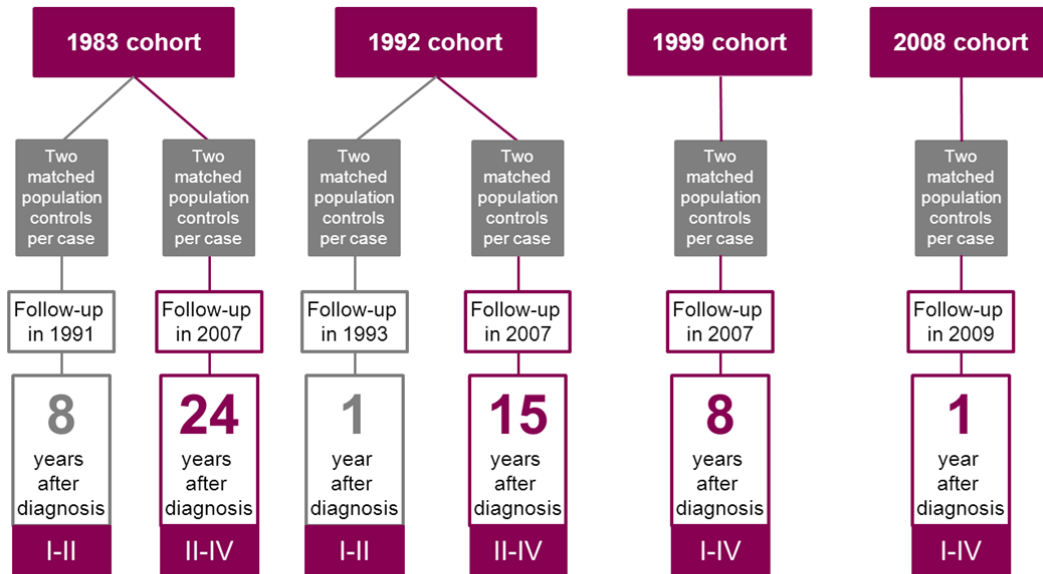
As the response rates were low, we asked Statistics Sweden to contact a random sample of the non-responders by telephone in 2008. In total, 300 individuals were contacted, of whom 150 were reached. Most of the non-responders remembered having received the questionnaire (89% of the individuals with diabetes and 84% of the control individuals). The non-responders gave several reasons for not responding. The most common reasons were lack of time (44%; 36%) and just not wanting to respond (27%; 23%). Another reason was the length of the questionnaire (17%; 16%).

They were also asked the SRH question about their health at that moment on a five-point scale ("In general, would you say your health is: very good; fairly good; fair; rather poor; very poor?"). Among the individuals with diabetes, 32% rated their health as less than good compared to 16% among the control individuals.



### 4.3 OVERVIEW OF THE FOUR STUDIES

The four research studies of this thesis use the data collected in the postal questionnaire. Figure 2 shows the cohorts used in each of the studies. In addition, Figure 2 shows that, for two studies, comparisons were made with studies from the early 1990s.



**Study I:** Changes in healthcare utilisation pattern  
**Study II:** Excess costs of medical care  
**Study III:** Diabetes duration and HRQoL  
**Study IV:** Equity in healthcare utilisation, dissatisfaction and SRH

**FIGURE 2.** Overview of the studies

### 4.4 OUTCOME MEASURES

The main outcome measures for this thesis are healthcare utilisation in hospital and in primary care, costs for healthcare utilisation (and for the individuals with diabetes, costs of treatment and monitoring), and HRQoL as measured by EQ-5D. In addition, equity in terms of how socio-demographic factors influence the first three outcomes was explored.

#### 4.4.1 Healthcare utilisation (Study I)

In this case-control study, the effect of diabetes on healthcare utilisation was analysed using retrospective data from the questionnaire in order to compare utilisation patterns 1 year and 8 years after diagnosis. Comparable data from the early 1990s was used to describe changes in the 16-year period.

Questions about utilisation addressed both outpatient care and inpatient care (Table 2). The questions asked for data on the number of visits to various hospital outpatient clinics and hospital emergency rooms, visits to community health centres and private practitioners, house calls from community healthcare centre personnel, and visits to occupational healthcare offices. The recall period was three months. Inpatient care and

daycare at hospital clinics were surveyed for the most recent year, with questions on the number of stays and days at inpatient clinics and the number of days at daycare clinics.

**TABLE 2.** Specification of which clinics were covered in the questionnaire

	Hospital outpatient clinics (recall period 3 months)	Hospital inpatient clinics (recall period 1 year)	Daycare (recall period 1 year)
Internal medicine/endocrinology	X	X	X
Surgery/orthopaedics/urology	X	X	X
Gynecology	X	X	
Ophthalmology	X	X	
Ear, nose and throat	X	X	
Psychiatry	X	X	
Diabetes	X		X
Other	X		X
Emergency department	X		

#### 4.4.2 Costs of medical care (Study II)

Estimated healthcare costs were divided among the following categories: hospital inpatient care; daycare; hospital outpatient care; non-hospital outpatient care; and glucose-lowering treatment and monitoring. Costs were estimated using the collected data on resource consumption (quantity), which was multiplied by a unit cost (price). The resources consumed were extracted from the questionnaire described above; the reported data were extrapolated to provide an estimate of the annual resource consumption. For example, the number of outpatient visits in the three-month period was annualised (3-month visits x 4) as yearly visits. Similarly, the use of medications and test devices was annualised (two-weeks use x 26) as the yearly use.

The excess costs of medical care for the diabetes patients were calculated as the healthcare cost difference between the diabetes cohorts and the control groups. The excess costs are presented as cost ratios for the diabetes cohorts and the control groups (diabetes/non-diabetes ratio) in order to facilitate comparisons with other studies.

Unit costs for different types of inpatient and outpatient care were collected from data compiled by the Swedish Association for Local Authorities and Regions as well as from price lists used for care of out-of-county patients (108). An average cost for inpatient care, daycare, outpatient hospital care, and non-hospital outpatient care was calculated as the mean of the costs for the different sources. Pharmaceutical prices published by the Dental and Pharmaceutical Benefits Agency were used to calculate costs for insulin, oral hypoglycaemic agents and other glucose-lowering medications and devices (113). The estimated costs were calculated by multiplying the average costs for insulin type with the average use of insulin per day. The costs are expressed in Swedish crowns (SEK) at 2009 prices (mean exchange rates for 2009: 1 USD=7.65 SEK and 1 EUR=10.62 SEK). The results from the previous studies were inflated from 1997 to 2009 year prices using the Swedish Consumer Price Index for Sweden.

#### **4.4.3 Health-related quality of life (Study III)**

EQ-5D is a standardised instrument used to measure health outcomes for a wide range of health conditions and treatments for patients as well as for the general population (81, 86). With the EQ-5D measure, respondents classify their health status in five dimensions (mobility; self-care; usual activities; pain/discomfort; anxiety/depression), and at three levels of severity (no, moderate or severe problems). In this classification, 243 possible unique health states can also be converted into a single index value (EQ-5D<sub>index</sub>) for health status (1=full health; 0=dead). The index value is assigned by adopting the most commonly used value set, the York MVH A1 value set, which derives from valuations of health states representing the average preference of the general UK population (116). The EQ VAS score was recorded on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state), where respondents were asked to identify their present health state.

#### **4.4.4 Equity in healthcare (Study IV)**

Six variables from the questionnaire were used to evaluate the effect of diabetes: case/control, sex, age, marital status, education level and income (sum of income from work, studies, military duty and parental leave). The dependent variables were coded so that the category of interest was use of healthcare, dissatisfaction with care received, or reporting less than good SRH.

Global SRH has been widely used as a reliable indicator of an individual's health. Therefore, SRH was selected as an indicator of the respondent's health status at the time of the survey. The respondents were also asked if they had had any problems receiving the care they needed. If the respondents answered affirmatively, they were asked to describe these problems.

### **4.5 DATA ANALYSIS**

Data were analysed using Statistical Package for Social Sciences (SPSS versions 16-20; IBM Corporation, New York, USA). Table 3 presents an overview of which statistical tests were used to analyse the data in the four studies. Level of significance was determined at  $P < 0.05$ .

**TABLE 3.** Overview of statistical tests in the four studies.

Study	Variables <sup>1</sup>	Pearson's $\chi^2$ -test or Fisher's exact test	Independent samples t-test	Regression	One-way ANOVA
I	DV: visits to different types of healthcare facilities  IV: case/control, sex	Socio-demographic characteristics  Differences in utilisation patterns among patients with diabetes between the respective 1- and 8-year cohorts.		Logistic regression. Case-control comparison using odds ratios and 95% CI	
II	Costs for healthcare utilisation, and monitoring and treatment of diabetes	Socio-demographic characteristics	Differences in mean costs between patients with diabetes and control individuals		Differences in mean costs between patients with various diabetes duration. Post-hoc tests: Bonferroni and Dunnett T3
III	DV: EQ-5D <sub>index</sub> and EQ VAS score  IV: sex, diabetes diagnosis, disease duration, level of education and marital status	Socio-demographic characteristics  Percentage of reported problems in the EQ-5D dimensions	Differences in the mean EQ-5D <sub>index</sub> and EQ VAS score between diabetes individuals with various disease duration.	Multivariate linear regression. Identification of factors predicting variation in mean EQ-5D <sub>index</sub> and EQ VAS score	Differences between diabetes individuals with different disease duration. Post-hoc tests: Bonferroni and Dunnett T3 tests
IV	DV: healthcare utilisation, dissatisfaction and SRH  IV: case/control, sex, age, marital status, level of education and income	Socio-demographic characteristics		Univariate analysis to find IV of interest. Backward conditional (Wald) stepwise logistic regression to examine the strength, using unstandardised coefficients	

<sup>1</sup>DV=dependent variables, IV=independent variables

#### 4.5.1 Study I

The five-category question concerning the level of education was dichotomized in the analysis into short education (secondary school or lower) and long education (college or university). Marital status was dichotomized into married or cohabiting, and single. Visits to clinics were dichotomized into no visits and one or more visits.

The study analysed the impact of diabetes on healthcare utilisation. Patients with diabetes were compared with control individuals in a logistic regression analysis that calculated the odds ratios (ORs) and 95% confidence intervals (CIs). Pearson's  $\chi^2$ -test was used to compare utilisation patterns between the respective 1- and 8-year cohorts of patients with diabetes.

#### 4.5.2 Study II

Pearson's  $\chi^2$ -test, or where appropriate Fisher's exact test, was used to test whether there was a difference in socio-demographic characteristics between patients with diabetes and control individuals in the various cohorts. Independent samples t-test was used to test whether there were differences in the mean healthcare costs between patients with diabetes and control individuals. Comparisons between patients with different diabetes duration were performed using one-way ANOVA. Post-hoc tests were performed with Bonferroni and Dunnett T3 tests.

#### 4.5.3 Study III

The main outcome measures were self-reported health as expressed in the five EQ-5D dimensions, the EQ-5D<sub>index</sub> and the EQ VAS score. Pearson's  $\chi^2$ -test or Fisher's exact test was used to test whether there was a difference in socio-demographic characteristics for patients and control individuals in the various cohorts, and the percentage of reported problems in the EQ-5D dimensions. The categories moderate and severe problems were collapsed before testing, resulting in the following two categories: moderate or severe problems, and no problems. Independent samples t-test was used to test whether there were differences in the mean EQ-5D<sub>index</sub> and EQ VAS score between control individuals and the individuals with diabetes in the four cohorts (1, 8, 15 or 24 years after diagnosis). Comparisons between individuals with different diabetes duration were performed using one-way ANOVA. Post-hoc tests were performed with Bonferroni and Dunnett T3 tests. The same tests were used for the control individuals.

A multivariate linear regression analysis was performed to identify variables that could predict the variation in the dependent variables mean EQ-5D<sub>index</sub> and EQ VAS score. The independent variables included were sex, diabetes diagnosis, disease duration, level of education, and marital status. Level of education was dichotomised into primary school or lower and secondary school or higher, and marital status was dichotomised into married or cohabiting, and not married or cohabiting.

#### 4.5.4 Study IV

Variables were included in multivariate analysis based on significance in univariate analysis ( $p < 0.10$ ). Indicator coding was used to explore, for dichotomous independent variables, whether the effect of one of the independent variables on the chances of falling in the category of interest in the dependent variable is the same for each category of the other independent variable (117).

Backward conditional (Wald) stepwise multiple regression was used to identify the significant predictors of each dependent variable. The probability for variable entry was set at  $p \leq 0.05$  and that for exclusion at  $p \geq 0.10$  to find the most parsimonious model. Backward conditional stepwise logistic regression is regarded as the most sensitive stepwise approach in exploratory research (117) and has been widely used in such research (see, for example: (118-121)).

Interaction variables were used to investigate any equity issues regarding individuals with diabetes' experience of health care and health status. Wherever the case/control

variable was significant in univariate analysis, interaction variables were created with the significant equity independent variable to test whether equity issues operated the same for those with diabetes in comparison to control individuals. In addition, for any dependent variable where both marital status and gender were significant in the univariate analysis, an interaction variable of marital status\*gender was tested with that dependent variable to explore whether any equity issues related to gender were in fact more deeply layered due to different effects of gender for different marital statuses.

#### **4.6 ETHICAL CONSIDERATIONS**

Information about the research purpose, its design and the voluntary participation was explained in a letter included with the questionnaire. The 1983, 1992, and 1999 cohorts were asked to sign an informed consent giving us permission to collect socio-economic data from Statistics Sweden. The letter sent to the 2008 cohort informed them that by responding to the questionnaire they implicitly permitted collection from LISA.

The risk of privacy invasion was considered small. The data requested for the limited period (in connection with preparing the linking between different registers) disclosed the PINs of the sampled study population. However, the PINs were not available to the researchers at the Medical Management Centre because the data manager for the DISS at Umeå University sent the distribution of data with PINs to Statistics Sweden. The files received from Statistics Sweden did not contain PINs. Moreover, the corresponding diabetes studies conducted in the 1990s, to our knowledge, did not result in any complications as far as personal integrity issues or other undesirable consequences. Because all results from the analyses are presented at large group levels, no individuals can be identified using background characteristics.

The study was approved by the Regional Ethics Committee in Stockholm (2007/214/31).

## 5 FINDINGS

### 5.1 CHARACTERISTICS OF THE STUDY POPULATION

Socio-demographic characteristics of the study population are described in Table 4. Because of the matching procedure, there were few differences in the socio-demographic characteristics between the individuals with diabetes and the control individuals. However, there were more men than women in the cohorts, which reflected the higher incidence of Type 1 diabetes among men in this age group in Sweden (95). Eight years after diagnosis, there was a lower proportion of married or cohabiting individuals among men with diabetes than among the corresponding control individuals. One year after diagnosis, the level of education was significantly lower among men with diabetes than among the corresponding control individuals.

Ninety-nine per cent of the individuals with diabetes stated that they had a blood glucose meter at home, and 96% stated that they measured their blood sugar levels. The mean use of a control procedure was 17 times/week (SD 15.5), based on the most recent week's usage (Table 5).

In this study, 4.2% of the patients 1 year after diagnosis used an insulin pump. In the other three cohorts, about 14% used an insulin pump. In the early 1990s, none of the patients 1 year after diagnosis used an insulin pump, whereas 3.2% of the patients 8 years after diagnosis did (23).

**TABLE 4.** Socio-demographic characteristics of the individuals with diabetes and of the control individuals by disease duration

	Diabetes duration													
	1 year			8 years				15 years			24 years			
	2008 cohort			1999 cohort				1992 cohort			1983 cohort			
	Case	Control	p <sup>1</sup>	Case	Control	p <sup>1</sup>	Case	Control	p <sup>1</sup>	Case	Control	p <sup>1</sup>		
n=142	(%) n=255	(%)	n=217	(%) n=392	(%)	n=229	(%) n=433	(%)	n=274	(%) n=530	(%)	p <sup>1</sup>		
<i>Sex</i>														
Men	89 (63)	150 (59)	0.45	120 (55)	216 (55)	0.96	134 (58)	253 (58)	0.98	158 (58)	324 (61)	0.34		
Women	53 (37)	105 (41)		97 (45)	176 (45)		95 (42)	180 (42)		116 (42)	206 (39)			
<i>Mean age</i> <sup>2</sup>	26	26		34	34		40	40		50	50			
<i>Marital status</i>														
Married/cohabiting	57 (42)	132 (52)	0.06	148 (68)	305 (79)	0.005	167 (73)	323 (75)	0.57	205 (75)	401 (76)	0.72		
Single/divorced	80 (58)	123 (48)		69 (32)	83 (21)		61 (27)	106 (25)		69 (25)	127 (24)			
<i>Highest level of education</i>														
Primary school	13 (9.4)	11 (4.3)	0.006	20 (9.2)	26 (6.7)	0.54	39 (17)	40 (9.3)	0.02	66 (24)	102 (19)	0.21		
Secondary school	82 (59)	131 (51)		97 (45)	170 (44)		110 (48)	209 (49)		113 (42)	207 (41)			
College	24 (17)	55 (22)		52 (24)	90 (23)		35 (15)	98 (23)		44 (16)	115 (22)			
University degree	13 (9.4)	52 (20)		42 (19)	95 (24)		40 (18)	75 (17)		42 (16)	76 (14)			
Other	7 (5.0)	6 (2.4)		6 (2.8)	8 (2.1)		3 (1.3)	7 (1.6)		6 (2.2)	16 (3.0)			
<i>Employed</i>	72 (52)	146 (58)	0.31	182 (84)	340 (87)	0.26	200 (88)	371 (86)	0.56	223 (83)	455 (87)	0.13		

<sup>1</sup>Comparison between cases and controls.

<sup>2</sup>Age at the end of the year the respondents received the questionnaire.



**TABLE 5.** Treatment and monitoring of blood glucose levels

	Diabetes duration								p <sup>1</sup>
	1 year		8 years		15 years		24 years		
	2008 cohort		1999 cohort		1992 cohort		1983 cohort		
	Case		Case		Case		Case		
	n=142	%	n=217	%	n=229	%	n=274	%	
<i>Treatment</i>									
Diet	5	3.5	5	2.3	2	0.9	3	1.1	0.19
Oral hypoglycemic agents	15	10.6	24	11.1	17	7.4	17	6.2	0.19
Insulin pen (prefilled)	43	30.3	85	39.2	100	43.7	116	42.3	0.06
Insulin pen (multiple use)	76	53.5	99	45.6	108	47.2	148	54.0	0.18
Syringes	13	9.2	17	7.8	13	5.7	17	6.2	0.55
Insulin pump	6	4.2	32	14.7	32	14.0	38	13.9	0.01
<i>Monitoring</i>									
Blood glucose levels at home	133	95.7	207	95.8	223	97.8	258	95.6	0.55
Number of weekly controls (mean, SD)	18	16.4	19	16.3	16	14.2	17	15.2	
Measuring of ketones	0	0	22	10.3	25	11.3	34	12.9	<0.001

<sup>1</sup>Comparison between the different cohorts using Pearson chi-square.

The most commonly used insulin types in the 1983, 1992 and 1999 cohorts were Humalog™, Novorapid™ and Lantus™. In the 2008 cohort, Novorapid™, Lantus™ and Levemir™ were the most commonly used insulin types.

## 5.2 HEALTHCARE UTILISATION PATTERNS

### 5.2.1 Healthcare utilisation 1 and 8 years after diagnosis

#### 5.2.1.1 One year after diagnosis

In the 1992 cohorts, 49% of patients with diabetes had received inpatient care at departments of internal medicine and endocrinology at least once (Table 6). This was significantly higher than the control individuals (0.5%). In the 2008 cohort the difference was no longer significant, mainly because at this point in time, only 4.2% of the patients with diabetes had visited these departments, compared with 1.2% of the control individuals. In both cohorts, 45%-46% of the patients with diabetes made at least one visit to daycare, which was three times as many as the control individuals.

A significantly higher proportion of patients with diabetes made more visits to the hospital outpatient clinics than the control individuals, both for 1-2 visits, and 3 or more visits (1 year after diagnosis 74% vs. 18%; 8 years after diagnosis 72% vs. 19%). Even after excluding visits to diabetes clinics, the utilisation of hospital outpatient clinics was still significantly higher. Specifically, patients with diabetes made significantly more visits to ophthalmology clinics.

Patients with diabetes in both the 1992 and 2008 cohorts visited nurses more often than the control individuals: 11% and 16% of patients with diabetes compared with 5.4% and 4.3% of the control individuals.

### 5.2.1.2 *Eight years after diagnosis*

In the 1983 cohort, 11% of patients with diabetes received inpatient care at departments of internal medicine and endocrinology compared to 0.9% of the control individuals (Table 6). The corresponding figures for the 1999 cohort were 2.8% and 1.0%, respectively. Patients with diabetes also made significantly more visits to daycare.

Patients with diabetes had a significantly higher utilisation of all outpatient clinics. For example, more patients with diabetes made three or more visits than the control individuals. Also, after excluding visits to diabetes clinics, the utilisation of outpatient clinics among patients with diabetes was significantly higher.

Patients with diabetes visited nurses more often than the control individuals: 7.3% and 12% of patients with diabetes, which was significantly more than 4.3% and 5.1% of control individuals.

## 5.2.2 **Changes in utilisation over time**

To see changes in utilisation patterns among patients with diabetes over time, the results from the study in 1991/1993 were compared with the results from this study in 2007/2009.

### 5.2.2.1 *One year after diagnosis*

There was a significant reduction in the number of visits to departments of internal medicine and endocrinology: 49% in the 1992 cohort compared to 4.2% in the 2008 cohort. The latter figure indicates that the excess use had decreased and was no longer significant, but more in line with usage by the control individuals.

### 5.2.2.2 *Eight years after diagnosis*

Visits to departments of internal medicine and endocrinology had decreased to 11% of the patients in the 1983 cohort and 2.8% in the 1999 cohort, where the excess use was no longer significant (Table 6). However, there was a significant increase in the utilisation of daycare. Patients with diabetes in the 1999 cohort reported an approximate utilisation rate that was four times higher than the 1983 cohort (44% vs. 11%). Some of the increase in utilisation of daycare may be explained by the increase in visits to diabetes clinics.

## 5.2.3 **Diabetes-related utilisation**

Visits to the emergency room and diabetes nurse were similar in all cohorts, but visits to dietitians and podiatrists varied according to disease duration. In this section, the percentages refer to the patient cohorts in the following order of years after diagnosis: 1, 8, 15 and 24.

**TABLE 6.** Healthcare utilisation for patients with diabetes (Case) and control individuals (Control) followed-up in four cohorts 1 year and 8 years after diagnosis

	No. of visits	Follow-up 1 year after diagnosis								p	Follow-up 8 years after diagnosis								p
		1992 cohort (1993)				2008 cohort (2009)					1983 cohort (1991)				1999 cohort (2007)				
		Case	Control	OR	95% CI	Case	Control	OR	95% CI		Case	Control	OR	95% CI	Case	Control	OR	95% CI	
		n=237	n=443			n=142	n=256				n=317	n=586			n=217	n=394			
	%	%		%	%			%	%			%	%			(case-case)			
<i>Hospital inpatient care</i>																			
All departments	0	31	92			87	92			<0.001	82	91			88	94		0.03	
	≥1	69	8.4	25	16-38	13	8	1.8	0.90-3.5		18	9.3	2.2	1.5-3.3	12	6	2.2	12-4.0	
Internal medicine/	0	51	100			96	99			<0.001	89	99			97	99		0.001	
Endocrinology	≥1	49	0.5	211	51-868	4.2	1.2	3.7	0.92-15		11	0.9	14	5.2-35	2.8	1.0	2.8	0.77-9.9	
<i>Hospital daycare</i>																			
All departments	0	54	85			55	84			0.86	89	96			56	86		<0.001	
(incl. diabetes)	≥1	46	15	4.9	3.4-7.0	45	16	4.2	2.6-4.7		11	4.4	2.7	1.6-4.6	44	14	4.8	3.3-7.1	
<i>Hospital outpatient clinics</i>																			
All clinics	0	26	82			22	77			0.73	29	81			34	75		0.002	
	1-2	57	15	12	8.0-18	60	17	12	7.2-20		57	14	11	8.1-16	42	18	5.1	3.4-7.6	
	≥3	17	3.2	17	8.6-32	18	6.3	9.6	4.6-20		15	5.3	7.7	4.6-13	24	6.6	7.8	4.6-13	
<i>All non-hospital outpatient contacts</i>																			
Physician	0	73	77			81	82			0.09	74	77			71	73		0.44	
	≥1	27	23	1.2	0.82-1.7	19	18	1.1	0.63-1.8		26	23	1.1	0.82-1.5	29	27	1.1	0.74-1.5	
Nurse	0	86	92			84	95			0.55	88	93			87	93		0.84	
	≥1	14	8.1	1.8	1.1-3.0	16	5.1	3.6	1.8-7.4		12	7.2	1.8	1.1-2.9	13	7.1	1.9	1.1-3.4	

Hospital inpatient care and daycare during a 1-year period, outpatient visits at hospitals and outpatient contacts outside the hospital during a 3-month period.

About 10% of these patients responded that they had visited the emergency room because of their diabetes in the last year (11%, 9.2%, 7.0%, and 9.9%). Around 90% had visited a diabetes nurse (94%, 88%, 90%, and 89%). Visits to dietitians were more common by the patient with a one-year diagnosis (25%) than by other cohorts (10% to 14%). Visits to a podiatrist were more common with longer disease duration (16%, 18%, 22%, and 33%).

The National Guidelines for diabetes care in Sweden state that fundus examinations should be made yearly for patients with Type 1 diabetes and every other year for patients with Type 2 diabetes. Our results showed that between 49% and 82% had their eyes examined in the last year. Of these 47%, 71%, 71%, and 78% had fundus photographs taken.

#### **5.2.4 Gender aspects on utilisation**

Although Study I was not designed for gender analyses, data divided by sex showed several significant differences. Approximately twice as many women with diabetes visited ophthalmology clinics as men with diabetes in all cohorts except for the 1992 cohort. The observed excess use of emergency services in the 1992 and 1999 cohorts is largely explained by the fact that women with diabetes had three times higher utilisation than the control individuals.

### **5.3 EXCESS COSTS**

#### **5.3.1 Healthcare utilisation costs**

In all four cohorts, the following categories account for the largest part of total healthcare costs for patients with diabetes: hospital outpatient care (58%-65%), daycare (13%-20%), and inpatient care (11%-20%). A similar pattern was evident for the control individuals.

The excess costs for healthcare utilisation as a percentage of total healthcare costs were as follows:

- 65% 1 year after diagnosis (31 149 SEK)
- 58% 8 years after diagnosis (25 882 SEK)
- 34% 15 years after diagnosis (15 631 SEK)
- 45% 24 years after diagnosis (25 672 SEK)

Patients with diabetes had significantly higher costs for hospital inpatient care 8 years after diagnosis (excess cost=5,159 SEK,  $p=0.030$ ) compared to the control individuals. Significant differences were also found in hospital outpatient care when emergency care was both included and excluded ( $p<0.001$ ). However, the control individuals in the 1992 cohort reported higher utilisation of daycare and non-hospital outpatient care than the patients with diabetes. Thus, their costs were equal to or greater than the costs for patients with diabetes. Diabetes-related utilisation of services such as visits to diabetes nurses, dietitians, podiatrists and ophthalmologists resulted in an additional average annual cost of about 4 200 SEK per patient.

Costs were generally higher for women with diabetes compared to men with diabetes. The exceptions were emergency care 8 years after diagnosis and total hospital inpatient care 24 years after diagnosis; for this care, men incurred higher care costs. A similar pattern was found among the control individuals with the exceptions in the costs of emergency care 8 and 24 years after diagnosis, in inpatient care 15 years after diagnosis, and in daycare 24 years after diagnosis.

### **5.3.2 Costs for glucose-lowering treatment and monitoring**

Of all patients with diabetes, 94% reported they had insulin treatment. The annual average costs per patient for glucose-lowering treatment and monitoring were as follows:

- 20 108 SEK 1 year after diagnosis
- 27 111 SEK 8 years after diagnosis
- 24 680 SEK 15 years after diagnosis
- 24 278 SEK 24 years after diagnosis

In all cohorts, 43%-48% of the costs were attributable to insulin and prefilled insulin pens. Comparisons among the four cohorts showed significant differences in costs for insulin ( $p<0.001$ ), syringes and needles ( $p=0.008$ ), as well as in the costs for insulin pumps ( $p=0.013$ ) and associated materials ( $p=0.050$ ). Post-hoc tests revealed that these differences in most cases were to be found between patients 1 year after diagnosis and all other cohorts.

The costs for insulin were generally higher for men than for women. In particular, this was true for patients 8, 15 and 24 years after diagnosis. For the patients, 8 and 24 years after diagnosis the costs for prefilled insulin pens were significantly higher for men than for women ( $p=0.012$  and  $p=0.001$ , respectively). One year after diagnosis, the costs for syringes and needles were higher among women than men, and 15 and 24 years after diagnosis the costs for insulin pumps and associated materials were significantly higher for women than for men ( $p=0.005$  and  $p=0.020$ , respectively).

### **5.3.3 Total direct costs and excess costs**

The total direct costs (healthcare utilisation, and glucose-lowering medications and test materials combined) corresponded to a cost ratio of 4.0, 3.8, 2.3 and 2.6 between the patients with diabetes and corresponding control individuals for each cohort (1, 8, 15 and 24 years after diagnosis). The excess costs as a percentage of total direct costs were as follows (Table 7):

- 75% 1 year after diagnosis (51 258 SEK)
- 74% 8 years after diagnosis (52 994 SEK)
- 57% 15 years after diagnosis (40 311 SEK)
- 61% 24 years after diagnosis (49 949 SEK)

**TABLE 7.** Distribution of excess costs by disease duration (in Swedish crowns, 2009 prices<sup>1</sup>)

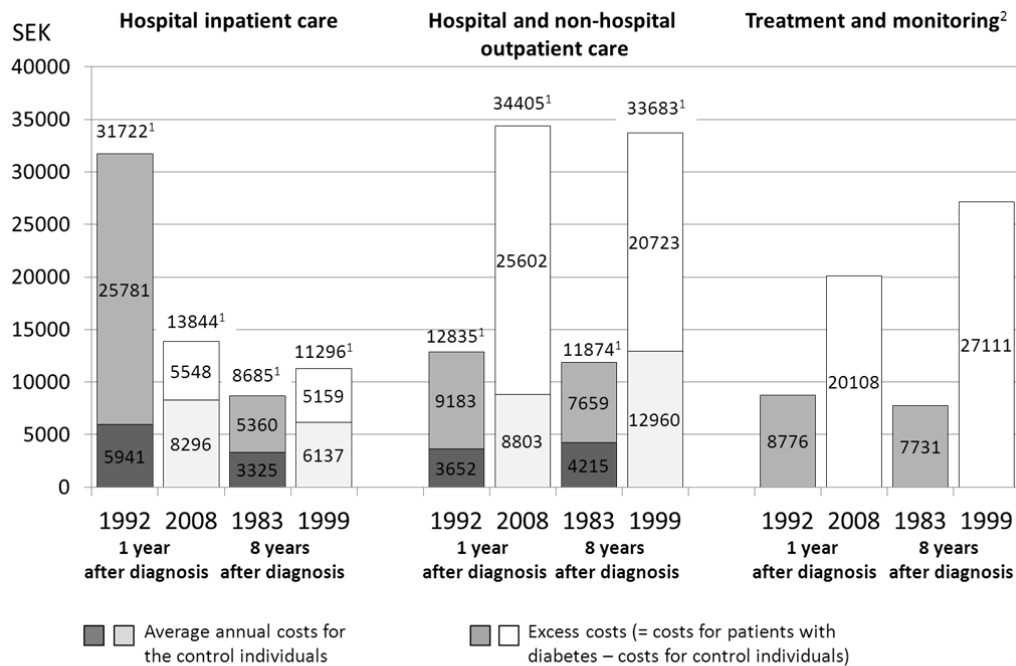
	Diabetes duration											
	1 year		1 year		8 years		8 years		15 years		24 years	
	1992 cohort Excess costs	%	2008 cohort Excess costs	%	1983 cohort Excess costs	%	1999 cohort Excess costs	%	1992 cohort Excess costs	%	1983 cohort Excess costs	%
Hospital daycare	7803	16	3164	6	1453	7	2751	5	-61	0	2849	6
Hospital inpatient care	22664	47	2384	5	3906	19	2409	5	1896	5	419	1
Hospital outpatient care (incl emergency care)	8611	18	24664	48	7186	35	20754	39	14110	35	21868	44
Non-hospital outpatient care	572	1	938	2	473	2	-31	0	-314	-1	535	1
Glucose-lowering treatment and monitoring	8776	18	20108	39	7731	37	27111	51	24680	61	24278	49
<b>Total</b>	<b>48426</b>		<b>51258</b>		<b>20749</b>		<b>52994</b>		<b>40311</b>		<b>49949</b>	

<sup>1</sup> Estimates from the previous study in the early 1990's have been inflated from 1997 to 2009 year prices using the Swedish Consumer Price Index.

### 5.3.4 Comparison with the previous study

In the previous study conducted in the early 1990s, the cost ratios for the diabetes and control groups 1 year and 8 years after diagnosis were estimated at 5.6 and 3.8, respectively, compared to 4.0 and 3.8 in the present study. In the intervening years, there has been a clear shift from hospital inpatient care to hospital and non-hospital outpatient care 1 year after diagnosis (Figure 3). A similar prominent rise in costs for hospital and non-hospital outpatient care could be seen 8 years after diagnosis, while hospital inpatient care increased, although excess costs decreased slightly. For patients in the 1 year and 8 years after diagnosis cohorts, there was also a two-to-threefold increase in the costs for glucose-lowering medications, materials and test devices.

The distribution of excess costs 1 year after diagnosis differed between the two studies. In 1993, 47% of the excess costs were attributable to hospital inpatient care whereas only 5% in 2009 were attributed to such care. In 2009, costs for hospital outpatient care, which accounted for 48% of the total costs, was the largest category of costs compared to 18% in 1993 (second highest together with treatment costs). Both studies showed that 8 years after diagnosis, costs for glucose-lowering treatment costs and monitoring were the highest (37% and 51%, respectively), followed by costs for hospital outpatient care (35% and 39%, respectively). There were no apparent gender differences in the distribution of these costs.



<sup>1</sup> Average annual costs for patients with diabetes

<sup>2</sup> Applicable only for patients with diabetes

**FIGURE 3.** Comparison of the distribution of average annual costs for hospital care, outpatient care, and treatment and monitoring of blood glucose levels between the two studies

## 5.4 HEALTH-RELATED QUALITY OF LIFE

Self-assessed health status in relation to disease duration in diabetes patients 1, 8, 15 or 24 years after diagnosis was analysed using the generic HRQoL instrument EQ-5D.

### 5.4.1 Reported problems in EQ-5D dimensions

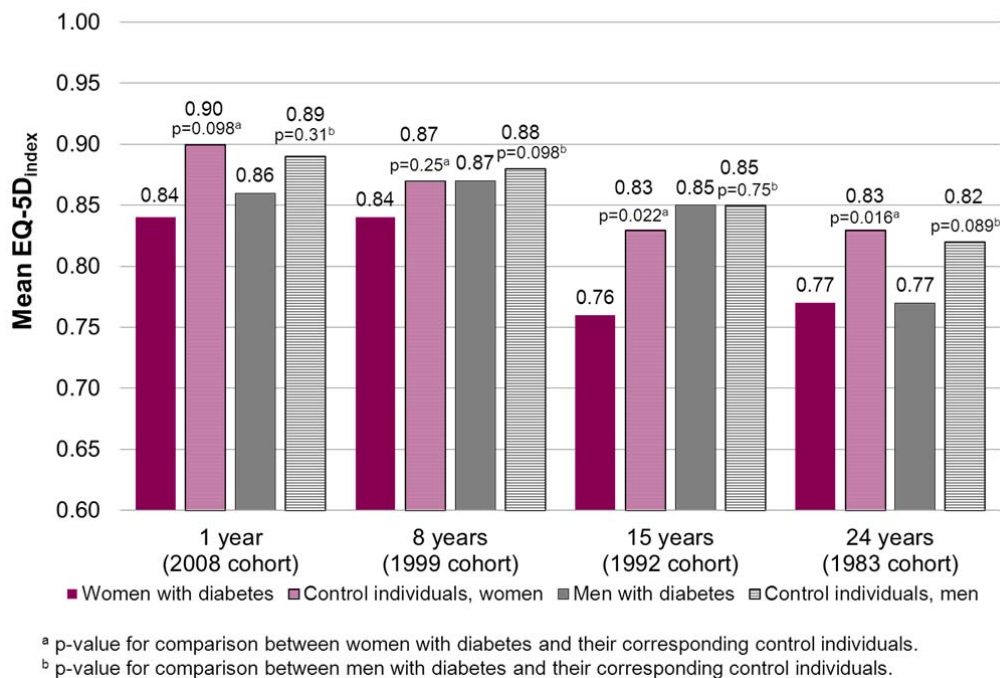
Compared with control individuals, both women and men with diabetes reported significantly more problems in the dimension usual activities 1 year after diagnosis ( $p=0.048$  and  $p=0.033$ , respectively). Eight years after diagnosis, women with diabetes reported more problems in the dimension pain/discomfort than the control individuals ( $p=0.050$ ). Fifteen years after diagnosis, women with diabetes reported more problems in the dimensions usual activities ( $p=0.029$ ) and pain/discomfort ( $p=0.013$ ) than the control individuals, and men with diabetes reported more problems in the dimension mobility than the control individuals ( $p=0.033$ ).

Twenty-four years after diagnosis, women reported more problems in the dimensions mobility ( $p=0.049$ ), self-care ( $p=0.023$ ) and usual activities ( $p=0.001$ ) than the female control individuals. In general, the combined prevalence of moderate and severe problems increased in all five dimensions by disease duration for individuals with diabetes. However, 15 and 24 years after diagnosis, significant differences were found only in the dimensions self-care ( $p=0.023$ ) and pain/discomfort ( $p=0.013$ ) among women with diabetes and for mobility ( $p=0.033$ ) and pain/discomfort ( $p=0.012$ ) among men with diabetes. Similar overall patterns were found for control

individuals who reported significantly more problems with pain/discomfort among women and with mobility and pain/discomfort among men.

#### 5.4.2 EQ-5D<sub>index</sub> and EQ VAS score

Among women, mean EQ-5D<sub>index</sub> was significantly lower for individuals with diabetes compared with control individuals 15 and 24 years after diagnosis (Figure 4). The comparison of women with diabetes in the different cohorts showed significant differences in mean EQ-5D<sub>index</sub>, which was also true for the control individuals. A similar pattern was seen for men with diabetes as well as for male control individuals. Post-hoc tests could not detect any significant differences among the cohorts for women with diabetes, while significant differences were found for men with diabetes between the 1983 cohort and all other cohorts.

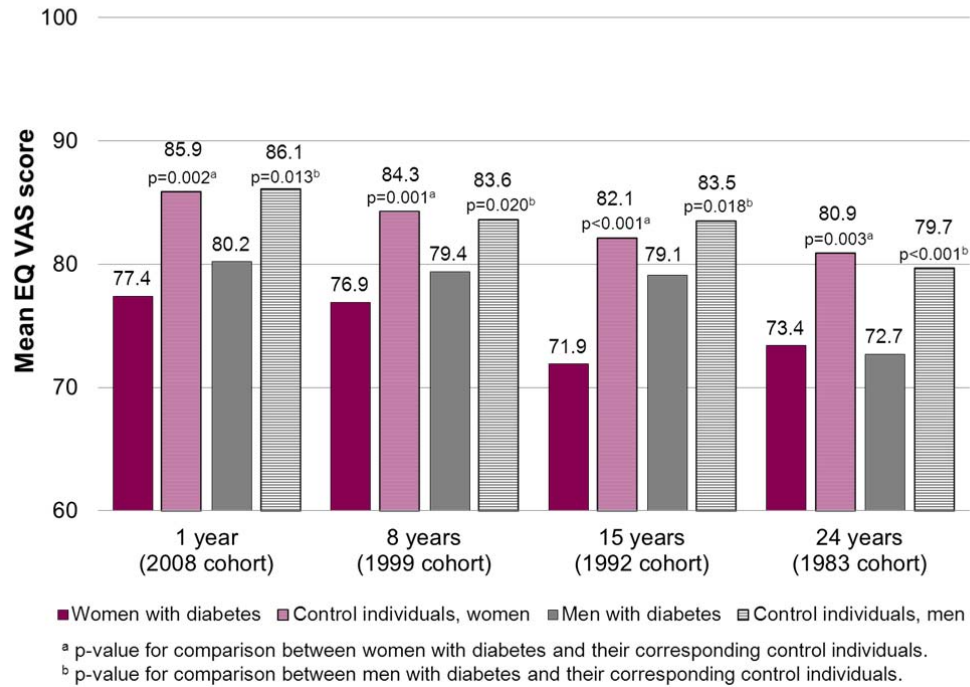


**FIGURE 4.** Mean EQ-5D<sub>index</sub> in individuals with diabetes compared to control individuals by disease duration

The comparison (ANOVA) of the cohorts for the different years of disease duration found significant differences between the different cohorts of women with diabetes (p=0.022), of female control individuals (p= 0.011), of men with diabetes (p=0.002) and of male control individuals (p=0.001), respectively. Post hoc tests could not detect where the significance for women with diabetes lay. The test, however, showed significant differences for men with diabetes between the 1983 cohort and all other cohorts (1992, p=0.002; 1999, p=0.007; 2008, p=0.027), for female control individuals between the 2008 and 1983 cohorts (p=0.025), and for male control individuals between the 1983 cohort compared with the 2008 (p=0.002) and 1999 (p=0.009) cohorts.



The mean EQ VAS scores were significantly lower for both women and men with diabetes compared with control individuals in all cohorts (Figure 5). Comparisons showed no differences between the cohorts of women with different diabetes duration. This was also true for women in the control population. However, for men with diabetes significant differences were found between the different cohorts, which was also the case for their control individuals.



**FIGURE 5.** Mean EQ VAS scores in individuals with diabetes compared to control individuals by disease duration

ANOVA and post hoc tests showed significant differences between the cohorts of men with diabetes ( $p=0.004$ ) which were found between the 1983 cohort and the 2008 ( $p=0.020$ ) and 1999 ( $p=0.028$ ) cohorts. Between the cohorts of male control individuals significant differences were found ( $p<0.001$ ) between the 1983 cohort and all other cohorts (1992,  $p=0.045$ ; 1999,  $p=0.040$ ; 2008,  $P<0.001$ ). The post hoc tests could not detect any significant differences between the cohorts for women with diabetes or for the female control individuals.

### 5.4.3 Variation on health-related quality of life

The multivariate regression analysis showed similar patterns for both the EQ-5D<sub>index</sub> and the EQ VAS score, which were used as health outcomes measures. The model showed that sex, diabetes diagnosis, education level, and not being married or cohabiting all had significant negative impact on the health outcome measures. This negative effect was shown also for disease duration of 8 years for the EQ VAS score and disease duration of 15 and 24 years for both the EQ-5D<sub>index</sub> and the EQ VAS score. Models were tested that added the independent variables separately, but these tests did not significantly impact the final model.

## 5.5 EQUITABLE CARE

Having diabetes was a significant predictor in all the final models for utilisation and SRH (Table 8). However, this condition did not predict dissatisfaction with care received. Women, who used more inpatient care, specialist care and primary care, were more often dissatisfied with the care they received. Education level was only significant in terms of predicting utilisation of primary care and SRH. In the final model, income was a significant predictor for all outcome variables except for utilisation of daycare.

Further analysis involved exploration of differences between individuals with diabetes and control individuals as far as their use of health care or their SRH were concerned. Education level was only a significant predictor of inpatient care or daycare for individuals with diabetes. Income level was significant for both individuals with diabetes and control individuals for the prediction of use of emergency services. However, for the individuals with diabetes the effect was larger. This difference in the size of Exp ( $\beta$ ) was even larger when examining the utilisation of primary care by individuals in the lower income group; such individuals with diabetes were approximately 1.5 times as likely as the control individuals to use primary care. Sex as predictor of the use of daycare was not significant for the individuals with diabetes, whereas as a predictor of the use of emergency services, sex was only significant for the individuals with diabetes. In predicting the use of specialist care for individuals with diabetes the Exp ( $\beta$ ), the effect of sex was 1.5 times greater than that for control individuals. For some independent variables, where the interaction variable was significant, there were no large differences evident in the association between the relevant independent and dependent variables. The explanation may be because of the sample size difference in the two groups.

For any variable where marital status and sex were significant, a logistic regression was run with a marital status\*sex interaction variable to examine whether the variable for marital status had a different effect in women and men. This was significant for inpatient care, emergency department, and primary care, but not for daycare. Next, for those dependent variables where the marital status\*sex interaction variable was significant, the data file was split according to marital status, and a logistic regression for sex was run for both married and unmarried groups to explore these differences. For inpatient care, sex was only significant for married respondents (married  $p < 0.001$ , Exp ( $\beta$ ) 0.407; unmarried  $p = 0.102$ , Exp ( $\beta$ ) 0.676). For emergency department, sex was not significant for either (married  $p = 0.003$ , Exp ( $\beta$ ) 0.709; unmarried  $p = 0.201$ , Exp ( $\beta$ ) 0.773), and for primary care sex was significant for both with a similar Exp ( $\beta$ ) (married  $p < 0.001$ , Exp ( $\beta$ ) 0.642; single  $p = 0.003$ , Exp ( $\beta$ ) 0.610).

**TABLE 8.** Multivariate regression exploring significant predictors for healthcare utilisation, SRH and dissatisfaction for individuals with diabetes and control individuals (final models)

Dependent variable	Inpatient care		Daycare		Specialist		Emergency		Primary care		Dissatisfaction		SRH								
	$\chi^2$	df	$\chi^2$	df	$\chi^2$	df	$\chi^2$	df	$\chi^2$	df	$\chi^2$	df	$\chi^2$	df							
	Sig.		Sig.		Sig.		Sig.		Sig.		Sig.		Sig.								
	67.378	5	<0.001	159.413	2	<0.001	529.173	8	<0.001	69.253	5	<0.001	69.824	6	<0.001	43.937	4	<0.001	201.137	8	<0.001
	<i>Exp (B)</i>	df	Sig.	<i>Exp (B)</i>	df	Sig.	<i>Exp (B)</i>	df	Sig.	<i>Exp (B)</i>	df	Sig.	<i>Exp (B)</i>	df	Sig.	<i>Exp (B)</i>	df	Sig.	<i>Exp (B)</i>	df	Sig.
Independent variables																					
Case/control	0.535	1	<0.001	0.294	1	<0.001	0.113	1	<0.001	0.615	1	0.004	0.838	1	0.098				0.458	1	<0.001
Sex	0.573	1	0.001				0.714	1	0.002				0.646	1	<0.001	0.748	1	0.012			
Age (overall)							3	<0.001											3	<0.001	
Age category 1							0.519	1	<0.001										0.312	1	<0.001
Age category 2							0.750	1	0.048										0.370	1	<0.001
Age category 3							0.800	1	0.122										0.752	1	0.067
Education level			ns			ns			ns	1.302	1	0.018							1.504	1	0.002
Income (overall)		3	<0.001				3	<0.001		3	<0.001		3	<0.001		3	<0.001		3	<0.001	
Income group 1	3.894	1	<0.001				2.283	1	<0.001	4.926	1	<0.001	2.088	1	<0.001	2.226	1	<0.001	4.362	1	<0.001
Income group 2	2.351	1	0.003				1.355	1	0.051	2.484	1	0.003	1.297	1	0.106	1.254	1	0.192	2.068	1	<0.001
Income group 3	1.906	1	0.031				1.231	1	0.163	1.783	1	0.071	1.051	1	0.76	1.091	1	0.618	1.281	1	0.208
Marital status			ns	0.821	1	0.064			ns			ns									ns

## 6 DISCUSSION

Because of the excess use of healthcare services by patients with diabetes, the excess costs were calculated in this research as 40,000 to 50,000 Swedish crowns per patient per year with no significant differences among the four cohorts. Costs for care for women (in both the diabetes groups and the control groups) were almost double the costs for men in most cohorts.

The research confirmed the negative impact of diabetes on patients' HRQoL. The difference from the control individuals increased by disease duration for women with diabetes. However, there were no significant differences in EQ-5D<sub>index</sub> between individuals with diabetes 1 year after diagnosis and control individuals, which may be explained by good management of diabetes care and the relatively quick patient adaptation to the disease.

Women used healthcare services more than men did. Individuals with lower education levels or lower income levels also used healthcare services more than individuals with higher education levels or higher income levels. The former groups also reported lower SRH. Individuals at lower income levels and women were more dissatisfied with the health care provided.

Compared to a previous study conducted in the early 1990s, excess costs increased mainly due to the greater use of insulin pumps and insulin analogues. Utilisation patterns for patients with diabetes were stable except for a significant decrease in hospital inpatient care 1 year after diagnosis (60% to 13%), and an increase in daycare 8 years after diagnosis (11% to 44%). The excess costs 1 year after diagnosis were similar whereas excess costs 8 years after diagnosis more than doubled, but while the largest proportion of costs in 2009 was for hospital outpatient care, 16 years earlier most costs were for hospital inpatient care. In line with the results from the previous study, the largest proportion of costs 8 years after diagnosis were attributable to insulin treatment and monitoring of blood glucose, followed by the costs for hospital outpatient care.

### 6.1 PATTERNS OF HEALTHCARE UTILISATION

A chronic disease like diabetes is quite naturally associated with an increased need for healthcare services. The need for healthcare services varies, depending on patients' characteristics (e.g., age, gender, type of diabetes, disease duration and health status). The excess use of healthcare services observed in the early 1990s persisted 16 years later. The utilisation patterns were relatively stable except for a major decrease in inpatient care 1 year after diagnosis and an increase in daycare 8 years after diagnosis. Part of this could be attributable to a general shift from inpatient care, as an increase in the use of daycare could also be seen among the control individuals. Daycare has also been increasingly used in the continuing education on patient self-management of diabetes.

Greater knowledge concerning the differences in patterns of healthcare utilisation can be valuable for the development of effective management strategies. Efforts have been made to move patients towards primary care in order to improve access and reduce costs.

A new distribution of responsibilities among different personnel categories and levels of care was developed early on in Swedish diabetes care (122). An important finding in this study was that patients in an early phase of Type 1 diabetes are treated at hospital outpatient clinics, suggesting that the National Guidelines for Diabetes Care have had a strong impact on the patterns of care (18). Outpatient visits at hospitals were generally more common among patients with diabetes compared with the control individuals. In addition to regular control schemes, an explanation could be that patients with diabetes may be more likely to seek care when problems arise. A similar change in utilisation patterns was also seen in a study tracking diabetes-related utilisation although these patients were older and had mainly been diagnosed with Type 2 diabetes (123).

The National Guidelines for Diabetes Care (18) recommend yearly fundus examinations for patients with Type 1 diabetes and every second year for patients with Type 2 diabetes. Although our data showed a higher likelihood of visits to ophthalmology clinics among the patients with diabetes than the control individuals, it was lower than expected. This could be attributable to the recall period, which was only 3 months for that question. However, in the complementary set of questions targeted only at the individuals with diabetes, only 72% reported having had an eye examination during the past year, which is not in line with the recommendations in the guidelines.

The level of use of primary health care had not changed from the situation 16 years earlier. Looking at utilisation patterns, nurses in primary health care have been given larger responsibilities in terms of diabetes care, and 90% of the Swedish primary care units state that they have diabetes-educated nurses and 30% of them work in diabetes teams (22). This change is visible in our study, especially among the patients with diabetes and among women. The higher utilisation of primary health care among women is congruent with previous findings that women tend to use outpatient services, especially preventive services, more than men (124-128).

## **6.2 EXCESS COSTS**

It is widely agreed that long-term complications of diabetes account for most of the direct costs for diabetes care as well as for the indirect costs (52, 63, 66, 68-71). The study by Jonsson et al. (34) revealed that management of diabetes in young and middle-aged people had created a major economic challenge for the Swedish healthcare system even before accounting for the increase in the gravity and frequency of long-term complications. This research, however, which did not reveal any increases in direct costs 15 or 24 years after diagnosis, may imply that the modern treatment of diabetes has had a positive economic effect as far as the cost of long-term complications in the original cohorts (1992 and 1983).

The excess costs for medical care were estimated at around 51,000-53,000 SEK per patient per year both in the early and later stages of the disease. However, the excess costs were lower for the 15 years after diagnosis cohort (around 40,000 SEK). The increases in hospital outpatient care and daycare, and decrease in inpatient care over the last two decades could explain the reduction in cost ratio 1 year after diagnosis from 5.6 to 4.0 and the unchanged cost ratio 8 years after diagnosis of 3.8 when comparing the two studies. There was no significant difference in excess costs for healthcare utilisation among the four cohorts suggesting that the long-term complications seem to be low even 15 and 24 years after diagnosis. Our estimates are higher than previous

estimates from Swedish studies of populations including individuals with Type 1 and Type 2 diabetes (53, 54) as well as estimates from the United Kingdom (48). The European estimates are almost half those of the estimates from the United States (49, 129).

The change in the level of care, which was revealed in Study I, is not only better for patients with diabetes but also provides an economic benefit for the hospital as well as for the society as a whole. The results indicate a seemingly low prevalence of severe long-term complications 15 and 24 years after diagnosis, which may be a result of improvements made in the management of diabetes in the last few decades which, as suggested by Bolin et al. (53), may have mitigated diabetes-related complications. Studies using data DISS have also shown improvements in Swedish diabetes care over time (130, 131).

During this 16-year period, there has been a change in the treatment of diabetes with more use of insulin analogues, especially long-lasting insulin analogues. There has also been a major increase in the use of insulin pumps and associated materials as well as short-lasting insulin. This increase has led to a change in the distribution of excess costs where medications for treatment and monitoring now account for around 41%-61% of the costs compared to 20%-37% in the previous study (34).

### **6.3 HEALTH-RELATED QUALITY OF LIFE**

The self-reported mean EQ VAS score was significantly lower for individuals with diabetes in all cohorts of disease duration compared with corresponding control individuals. The mean EQ-5D<sub>index</sub> was significantly lower for women (although not for men) 15 and 24 years after diabetes diagnosis compared with the average for the corresponding female control individuals.

The diagnosis of diabetes, especially Type 1 diabetes, is generally a distressing experience for most individuals. For newly diagnosed individuals with diabetes, there is an effect in the EQ-5D dimension usual activities as well as in the mean EQ VAS score. An assumption in this research was that HRQoL would be negatively affected when treatment is in an intensive phase and that the dimension anxiety/depression would be significantly affected. However, the results did not support this assumption. Furthermore, there was no significant difference at this stage of the disease in EQ-5D<sub>index</sub> between individuals with diabetes and the corresponding control individuals. The fact that the patients in the 2008 cohort reported their HRQoL 1 year after disease onset may explain why there was no discernible difference in the EQ-5D dimensions compared with the 1999 cohort (8 years after diagnosis) except for the higher prevalence of reported problems in the dimension usual activities. It is likely that the patients 1 year after diagnosis have accepted the disease and have somewhat adapted to the new routines in their daily life. It has been indicated previously that although HRQoL decreases at disease onset, it improves within the first year after diagnosis to levels comparable to the general population (102). Another possible explanation is patient involvement. As patients take more responsibility for monitoring their diabetes, they may feel more in control of their lives.

Of the EQ-5D dimensions, problems were most prominent in the dimension pain/discomfort. Other studies have shown the same results (81, 85, 99, 103, 105, 132, 133). As stated previously, no significant differences were found in the dimension anxiety/depression 1 year after diagnosis between individuals with diabetes and control individuals. This was also true among the cohorts 8, 15 or 24 years after diagnosis. This finding may possibly be explained by the high prevalence of problems in the dimension anxiety/depression among the general population also in younger age groups (81). The lower levels of EQ-5D<sub>index</sub> and EQ VAS score among individuals with diabetes of longer duration, which was observed for both women (after 15 years) and men (after 24 years), is consistent with Hart et al.'s (85) study that reported an annual decrease in HRQoL by diabetes patients. Although women generally tend to rate their HRQoL lower than men (81, 105), it is noteworthy that the difference between individuals with diabetes and control individuals increased after 15 years for women and after 24 years for men. This finding suggests an earlier social stratification in health for women with diabetes compared with women in the general population as well as compared with men with diabetes.

The findings that HRQoL is related not only to age but also to the long-term duration of diabetes is evident from the widening gap between individuals with diabetes and the control individuals in the prevalence of problems on most EQ-5D dimensions over time. Pain/discomfort and anxiety/depression are the two EQ-5D dimensions where diabetes duration seems to have the most influence. The findings that HRQoL was negatively affected the first year after diagnosis may be an effect of intensive counselling and treatment efforts in the early stages of diabetes, although with good intentions, as this is an abrupt change of the individual's life situation and perspectives. Investments to improve supportive effort in the early phases may have positive effect on not only HRQoL but also on the level of costs from a long-term perspective.

#### **6.4 EQUITY PERSPECTIVES**

Equity in health implies that resources are distributed and processes are designed in ways that are fair and just, while recognising that different population groups have different needs and power (87, 88). The finding that women have higher utilisation of some sections of the healthcare system more than men is supported by previous findings (134-136). This finding may suggest that women, despite their greater longevity, have generally poorer health than men. Or it may suggest that women are more likely than men to recognise their own health problems and thus to seek help (43).

There was some suggestion in the research that gender and marital status are related as far as the utilisation of healthcare services. Among married or cohabiting people, men were much less likely to be admitted for inpatient care than women, but men who lived alone were more likely to be admitted for inpatient care than women who lived alone. Perhaps the partners of married or cohabiting men cared for them at home. It is also of interest that income lost its predictive strength related to the utilisation of inpatient care while sex gained strength as a predictor.

This research supports previous research (137, 138) that claims that income levels for individuals are a strong predictor of high utilisation of all types of health care except daycare. Explanations for this finding can either be that those in the lowest income group have poorer health than those in the highest income group, or that those in the

highest income group are more inclined to use private health facilities. As this study was conducted in Sweden, where healthcare is mainly provided by tax-funded facilities (139), it seems most likely that a low income is associated with poorer health. Further evidence for this conclusion is the fact that the lowest income group was far more likely to report less than good SRH. An individual in the lowest income group was also more likely to report greater dissatisfaction with health care received. Greater utilisation of health care was associated with greater dissatisfaction, which, to some extent, supports findings by Ruggeri et al. (140).

In terms of differences between the individuals with diabetes and the control individuals, it was particularly noteworthy that the lower income groups with diabetes were more likely to use emergency services or primary care services than the control individuals. For individuals with diabetes compared to control individuals, sex was a far stronger predictor of the use of specialist care. However, sex was not a significant predictor for the use of the emergency services by the control individuals whereas it was by the individuals with diabetes. That sex is stronger as a predictor for the use of specialist diabetes care calls for further concerns about inequity in diabetes care in Sweden. These findings indicate that a woman with a chronic disease will be of more concerns and more costly for the healthcare system. Swedish diabetes care seems to have difficulties meeting the needs of such women (124).

Despite their higher utilisation of healthcare, individuals with diabetes expressed no greater dissatisfaction with health care than the control individuals. The possible explanations may be that individuals with diabetes think that their healthcare needs are being met or that they are satisfied if their diabetes is under some sort of control. Usually individuals with diabetes have a long-term relationship with health care that requires on-going and appropriate care.

## **6.5 METHODOLOGICAL CONSIDERATIONS**

In this research, it was possible to use the unique registration of cases of diabetes in Sweden to compare the different types of healthcare services used by the four cohorts (with diabetes of known duration) with control individuals from the general population. This study design also allowed nationwide comparisons of HRQoL. The longitudinal development of diabetes and its consequences to the individuals and society were addressed by separate analyses in the cohorts with disease durations of 1, 8, 15 or 24 years.

There are advantages and disadvantages with conducting a repeat study using similar design and methodology. With 16 years between the two studies, the way questions should be phrased may change. However, in order to compare results it is important that any rephrasing of questions is done in such a way that comparison is still possible. Some questions were, as mentioned previously, removed from the questionnaire as they were either outdated or they had not resulted in any useable data in the study from the 1990s. However, some questions were also added (e.g., the EQ-5D questionnaire). It may seem unnecessary to include two instruments that measure HRQoL. However, the EQ-5D instrument was added because it may provide more possibilities for international comparisons with the results of this research to other studies on diabetes patients or other chronically ill individuals, or for comparisons with population studies.



Still, SWED-QUAL was retained in the questionnaire in order to make comparisons over time.

The low response rate, especially in the 2008 cohort, may be a potential limitation of this research. This rate may possibly reflect the generally declining response rates in population and patient surveys that Statistics Sweden has also experienced (115). The lower education and income levels among the non-responders (both in the diabetes group and among the general population groups) may be related to their overall poorer health. As a result, this research may have underestimated the actual healthcare utilisation and overestimated the HRQoL. However, as these deficiencies apply equally to individuals with diabetes and to the control individuals, a non-differential misclassification bias is implied.

The first three cohorts (1983, 1992 and 1999) were asked explicitly, via the questionnaire, for their permission to cross-check with LISA. Such permission was automatic for the fourth cohort (2008) because the cover letter with their questionnaire stated that, by completing the questionnaire, the responders were permitting this cross-check. In this latter situation, it is possible that such automatic permission may have depressed the response rate. In addition, only two reminders were sent to the 2008 cohort whereas three reminders were sent to the other cohorts. This reminder situation may also have affected the response rate from the 2008 cohort.

The Swedish Surveys of Living Conditions conducted by Statistics Sweden (106) guided the construction of the questionnaire (e.g., for wording and recall periods). However, those surveys use structured interviews rather than mailed questionnaires as in this research. As the sample population consisted of young and middle-aged individuals, no difficulties were expected in their comprehension of the mailed questionnaire. No answers suggested the responders misunderstood or were confused by the questions. One question that potentially could be misunderstood is the difference between daycare and outpatient care. Some of the younger individuals in the control group may have limited experience with the healthcare system and may therefore have difficulties in distinguishing between a daycare stay and an outpatient visit at a hospital.

The inclusion of young people in study populations may be problematic for analyses of socio-economic factors, such as education levels, because many young people are students. There is also a potential for non-differential misclassification regarding marital status for the population under 20 years of age. Such misclassification would result in overestimation of the positive effect of marital or cohabitation status because many students still live in the family home. Living at home could be comforting for younger individuals with diabetes.

Because of its limited scope, this research did not include the costs of prescribed and non-prescribed medications other than insulin although there was a significantly higher use of both antihypertensive and lipid-lowering medications by the patients with diabetes compared to the control individuals. However, had these costs been included, excess costs would probably have been even higher. It was also not within the scope of this research to include indirect costs such as, for example, leave of absence and early retirement. It would be interesting to take a societal perspective in investigating how indirect costs are affected by disease duration; it has been shown that a diabetes diagnosis affects education level (141) as well as future income (142).

An additional constraint of the research was the estimation of unit costs. Although the survey gave detailed data on each individual's use of healthcare services, it was not possible to collect data on the costs of care at the individual level. Instead, the unit costs were estimated from price lists that may not reflect actual costs for different levels of care. However, the estimation of excess costs was still adequate as the same unit costs were used for patients with diabetes and for the corresponding control individuals.

The concept of excess costs (i.e., the difference in costs between individuals with diabetes and the control individuals) is the central economic concept used in the analyses of this research. These excess costs should be interpreted as additional costs attributable to diabetes that can be expected in the various stages of disease for the four cohorts. Some of these costs are directly related to diabetes, such as treatment and monitoring of diabetes, whereas others may be less obvious. For the purposes of the analyses, unadjusted data for real-life populations are likely to be more useful than adjusted data in standardised trial populations.

It is possible to calculate the economic cost of diabetes in the healthcare system using cost ratios applicable to the individuals with diabetes and to control individuals. Jonsson et al. (34), in their study, compared cost ratios with those in Selby's study (68) that analysed data from a similar age group in the United States. The cost ratios in the two studies were essentially identical although absolute costs of care in the US study were higher. Cost ratios could therefore be used to compare healthcare costs by different countries even when the structure, organisation and financing of the healthcare systems may differ. The research of this study also showed that although costs had generally increased during the 16 years after the previous study (34), the cost ratios reflected the decrease in the use of inpatient care (see Study I).

The main methodological strengths of the research reported on in this thesis are its use of data derived from the large number of survey participants, the chronological data on the patients' onset of diabetes, the various disease durations (1, 8, 15 or 24 years), the population-based comparisons, and the comparisons with the previous study. Although this study is not truly longitudinal because it does not involve repeated observations of the same individuals, the research on the four cohorts with different disease durations can still provide useful information on how the duration of diabetes affects healthcare utilisation and HRQoL (other than normal ageing). Other strengths of the research are its estimation of excess costs at different stages of the disease taking into consideration many kinds of healthcare consumption and the costs for treatment and monitoring of blood glucose levels. Therefore, the research permitted calculation of direct, diabetes-related healthcare consumption (which could underestimate the impact of diabetes) and of the estimation of real-life consumption in the studied cohorts.

## 7 CONCLUSIONS

Observational studies of real-life consequences of diabetes are relatively rare, in comparison with all clinical trials that address the effectiveness of various interventions in patients with diabetes. Observations of the healthcare utilisation in individuals with various years of diabetes duration at two different points of time, and comparisons of the patterns with the general population samples provide a general overview on how developments in diabetes management are associated with the utilisation patterns and the excess use of care by patients with diabetes. Thereby, estimation of the costs for healthcare utilisation and the treatment and monitoring of diabetes may support rational resource allocation in healthcare.

This research has revealed that individuals with diabetes currently are seemingly living rather unrestricted lives with less hospital inpatient care and a higher degree of self-management than 16 years previously. However, the studies in this thesis also indicate that healthcare utilisation, costs and HRQoL may vary by gender and socio-economic background. In addition to having diabetes, being a women, having a low education level or low income, and not being married had a negative effect on almost all outcome measures addressed in this thesis.

Continued health services research that describes and analyses utilisation patterns and different outcomes of care may be a valuable complement to more clinically oriented research. Health services research may also provide valuable information in the formulation of future healthcare policies. In contrast to randomised controlled trials, follow-up studies of real-life diabetes populations living in real-world health systems can shed light on issues of access to the healthcare system as well as on associated equity issues.

### 7.1 IMPLICATIONS

This research increases the knowledge on diabetes care and costs 1 to 24 years after diagnosis. As the treatment of diabetes has changed considerably during the last three decades, it was important to continue re-examining the medical developments as well as their economic implications. As changes in the level of health system services take place continuously, repeat studies are important for comparing changes in utilisation patterns and for comparing direct costs over time. With information on real-life healthcare utilisation, new cost estimates are possible that reflect current treatment practices. These estimates can be used in the planning and rational allocation of resources in health care. The observed changes reported on in the four studies of this thesis probably reflect successive reformation of diabetes care in Sweden and may inspire further changes.

However, the four studies suggest that despite efforts to reduce inequalities in health care, there is still a need to develop strategies for monitoring the performance of the healthcare services from a gender and socio-economic equity point of view. Therefore, in planning for reforms or changes in the healthcare system, it is important to understand the differences in how these changes may affect women, men and people of different socio-economic statuses.

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