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Inpatient Hospital Care and Its Costs Among Type 1 Diabetic Patients in Finland – a Nationwide Longitudinal Study

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Helsinki 2007

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INPATIENT HOSPITAL CARE AND ITS COSTS AMONG TYPE 1 DIABETIC PATIENTS IN FINLAND

– A NATIONWIDE LONGITUDINAL STUDY

ACADEMIC DISSERTATION

To be presented with the permission of the Faculty of Medicine, University of Helsinki, for public examination in the Auditorium I, University of Helsinki (Institute of Dentistry-building, Kytösuontie 9 A), on August 28, 2007, at 12 o'clock noon.

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ABSTRACT

Background. In Finland, the incidence of type 1 diabetes mellitus (T1DM) is the highest in the world, and it continues to increase steadily. No effective preventative interventions exist either for individuals at high risk or for the population as a whole. In addition to problems with daily lifelong insulin replacement therapy, T1DM patients with long-lasting disease suffer from various diabetes related complications. The complications can lead to severe impairments and reductions in functional capacity and quality of life and in the worst case they can be fatal.

Longitudinal studies on the costs of T1DM are extremely rare, especially in Finland. Typically, in these studies, distinctions between the various types of diabetes have not been made, and costs have not been calculated separately for the sexes.

Aims. The aim of this study was to describe inpatient hospital care and costs of inpatient care in a cohort of 5,166 T1DM patients by sex during 1973-1998 in Finland. Inpatient care and costs of care due to T1DM without complications, due to T1DM with complications and due to other causes were calculated separately.

Material and Methods. The study population consisted of all Finnish T1DM patients diagnosed before the age of 18 years between January 1st in 1965 and December 31st in 1979 and derived from the Finnish population–based T1DM register (N=5,120 in 1979 and N=4,701 in 1997). Data on hospitalisations were obtained from the Finnish Hospital Discharge Register.

Results. In the early stages of T1DM, the majority of the use of inpatient care was due to the treatment of T1DM without complications. There were enormous increases in the use of inpatient care for certain complications when T1DM lasted longer (from 9.5 years to 16.5 years). For women, the yearly number of bed-days for renal complications increased 4.8-fold, for peripheral vascular disease 4.3-fold and for ophthalmic complications 2.5-fold. For men, the corresponding increases were as follows: 5-fold, 6.9-fold and 2.5-fold. The yearly bed-days for glaucoma increased 8-fold, nephropathy 7-fold and microangiopathy 6-fold in the total population. During these 7 years, the yearly numbers of bed-days for T1DM without complications dropped dramatically.

The length of stay in inpatient care decreased notably, but hospital visits became more frequent when the length of duration of T1DM increased from 9.5 years to 16.5 years.

The costs of treatments due to complications increased when T1DM lasted longer. Costs due to inpatient care of complications in the cohort 2.5-folded as duration of T1DM increased from 9.5 years to 16.5 years, while the total costs of inpatient care in the cohort dropped by 22% due to an 80% decrease in the costs of care of T1DM without complications.

Treating complications of female patients was more expensive than treating complications of men when T1DM had lasted 9.5 years; the mean annual costs for inpatient care of a female diabetic (any cause) were 1,642 €, and the yearly costs of care of complications were 237 €. The corresponding yearly mean costs for a male patient were 1,198 € and 167 €. Treating complications of female patients was more expensive than that of male patients also when the duration of diabetes was 16.5 years, although the difference in average annual costs between sexes was somewhat smaller.

Total annual inpatient costs (any cause) in the cohort were 7,163,989 € when T1DM had lasted 9.5 years and 5,555,855 €, when T1DM had lasted 16.5 years.

Conclusions. In the early phases of T1DM, the treatment of T1DM without complications causes a considerable amount of hospital bed-days. The use of inpatient care due to complications of T1DM strongly increases with ageing of patients. The economic burden of inpatient care of T1DM is substantial.

Keywords: *T1DM, Diabetes, Hospital use, Inpatient use, Inpatient costs, Finland*

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TIIVISTELMÄ

Tausta. Tyypin 1 diabetes mellituksen (T1DM) esiintyminen on Suomessa maailman suurin kasvaen jatkuvasti. Kasvu on ollut tasaista, eikä tehokkaita ehkäisyohjelmia ole näköpiirissä korkean riskin yksilöille tai väestöille. Päivittäisen, elinikäisen insuliinikäytön lisäksi ongelmia ja kärsimystä aiheutuu potilaille taudin edetessä diabetekseen liittyvistä erilaisista komplikaatioista. Komplikaatiot voivat johtaa vakaviin toimintakyvyn puutteisiin ja elämänlaadun heikkenemiseen, ja ne voivat muodostua kohtalokkaiksi.

T1DM:n kustannuksiin liittyvät pitkittäistutkimukset ovat varsinkin Suomessa erittäin harvinaisia. Yleensä näissä tutkimuksissa ei ole erotettu diabeteksen eri tyyppejä, eikä kustannuksia ole laskettu erikseen sukupuolille.

Tavoitteet. Tämän tutkimuksen tavoitteena oli kuvata sairaalakäyttöä ja -kustannuksia 5,166:n T1DM-potilaan kohortissa sukupuolittain Suomessa vuosina 1973–1998. T1DM:n hoidon sairaalakäyttö ja -kustannukset ilman taudin komplikaatioita ja komplikaatioista sekä muista syistä kuin T1DM:stä johtuva sairaalakäyttö kustannuksineen laskettiin erikseen.

Aineisto ja menetelmät. Aineisto muodostettiin kaikista alle 18-vuotiaista suomalaisista T1DM-potilaista, jotka oli diagnosoitu välillä 1.1.1965-31.12.1979 ja jotka saatiin suomalaisesta väestöpohjaisesta T1DM-rekisteristä (N=5,120 1979, N=4,701 1997). Tiedot sairaalakäytöstä saatiin hoitoilmoitusrekisteristä.

Tulokset. T1DM:n keston alkuvaiheissa suurin osa sairaalakäytöstä johtui T1DM:n hoidosta, johon ei liittynyt komplikaatioita. T1DM:n keston pidentyessä (9.5:stä vuodesta 16.5:een) eräiden komplikaatioiden sairaalahoito kasvoi voimakkaasti. Naisilla vuosittaisten hoitopäivien määrä johtuen munuaiskomplikaatioista kasvoi 4.8-kertaiseksi, ääreisverenkierron komplikaatioiden määrä 4.3-kertaiseksi ja silmäkomplikaatioiden määrä 2.5-kertaiseksi. Miehillä vastaavat hoitopäivät em. komplikaatioille kasvoivat 5-, 6.9-, ja 2.5-kertaisiksi. Viherkaihin hoitopäivien määrä kasvoi 8-kertaiseksi, nefropatian 7-kertaiseksi ja mikroangiopatian 6-kertaiseksi koko tutkimusväestössä. Kyseisenä ajanjaksona (7 vuotta) vuosittaisten hoitopäivien määrä liittyen T1DM:ään ilman komplikaatioita putosi dramaattisesti.

T1DM:n keston pidentyessä 9.5:stä vuodesta 16.5:een vuoteen keskimääräinen hoitoaika lyheni selvästi, kun taas potilaat olivat sairaalahoidossa aikaisempaa tiheämmin.

Komplikaatioiden hoidon kustannukset kasvoivat T1DM:n keston pidentyessä. Komplikaatioiden sairaalahoidon kustannukset kasvoivat kohortissa 2.5-kertaisiksi, kun taas hoidon kokonaiskustannukset vähenivät 22%, sillä hoitokustannukset liittyen T1DM:ään ilman komplikaatioita vähenivät 80% T1DM:n keston pidentyessä 9.5:stä vuodesta 16.5:een vuoteen.

Naisten komplikaatioiden hoitaminen oli kalliimpaa kuin miesten. T1DM:n keston ollessa 9.5 vuotta, keskimääräinen naisdiabeetikon sairaalahoitokustannus vuodessa oli 1,642 € ja komplikaatioiden keskimääräinen hoito maksoi 237 €. Vastaavasti, miesten hoito vuodessa maksoi 1,198 € ja 167 €. T1DM:n keston ollessa 16.5 vuotta, naisten komplikaatioiden hoitokustannukset olivat yhä miehiä suuremmat, mutta ero miehiin keskimääräisissä vuosikustannuksissa pieneni.

Vuosittaiset kokonaissairaalahoitokustannukset kohortissa olivat 7 163 989 € (T1DM:n kesto 9.5 vuotta) ja 5 555 855 € (T1DM:n kesto 16.5 vuotta).

Johtopäätökset. T1DM:n hoito ennen komplikaatioiden puhkeamista aiheuttaa huomattavasti sairaalahoitopäiviä. Potilaiden ikääntyessä komplikaatioiden sairaalahoidon määrä kasvaa voimakkaasti. T1DM:n sairaalahoito aiheuttaa huomattavia taloudellisia kustannuksia.

Asiasanat: *T1DM, diabetes, sairaalakäyttö, sairaalakustannukset, Suomi*

Contents

ABBREVIATIONS

25000/2500B	Diabetes without complications
ADA	American Diabetes Association
AR	Attributable risk
CARVASC	Cardiovascular/cardiac disease
CEA	Cost-effectiveness analysis
CERVASC	Cerebrovascular disease
COI	Cost of illness
CUA	Cost-utility analysis
CVD	Cardiovascular disease
DERI	Diabetes Epidemiology Research International
DM	Diabetes mellitus
ENDOCRIN	Endocrine complications
FHDR	Finnish Hospital Discharge Register
FIM	Finnish mark
ICD	International classification of diseases
LOS	Length of hospital stay
NEUROL	Neurological complications
PERVASC	Peripheral vascular complications
QALY	Quality-adjusted life-years
RENAL	Renal complications
RR	Relative risk
SD	Standard deviation
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
WHO	World Health Organization

1. INTRODUCTION

Hippocratic oath:
primum, non nocere
(first, do no harm)

According to the WHO (1985) definition, diabetes mellitus (DM) is chronic, systemic disease, characterised by chronic elevation of blood glucose concentration (hyperglycaemia), which results from deficient production or action of insulin, a hormone controlling glucose, fat and amino acid metabolism.

DM and allied categories of glucose intolerance have been classified as insulin-dependent diabetes mellitus (IDDM, type 1), non-insulin-dependent diabetes mellitus (NIDDM, type 2), malnutrition-related diabetes mellitus (MRDM), impaired glucose tolerance (IGT) and gestational diabetes mellitus (GDM), in which glucose intolerance is first detected during pregnancy (WHO 1985). In this study, T1DM is used as an abbreviation for type 1 diabetes (and similarly, T2DM for type 2 diabetes).

T1DM is caused by immune-mediated destruction of islet insulin-secreting beta cells. This process is associated with both cellular and humoral immune changes in the peripheral blood that can be detected before the onset of clinical diabetes. Metabolic changes, altered glucose tolerance and reduced insulin secretion deteriorate and result in clinical diabetes (Pozzilli and Di Mario 2001). Beta cells of the islets of Langerhans in the pancreas produce insulin, and in T1DM, at the time of first acute clinical presentation, probably 85-90% of these cells have been destroyed (WHO 1985). Genetic susceptibility is necessary for the development of T1DM (Hyttinen et al 2003), and the global variance in incidence suggests that environmental factors are also important in the etiology, but little is known about these factors (Karvonen et al 2000). According to a Finnish study, for instance early exposure to cow's milk formula-feeding and rapid growth in infancy are independent risk factors of childhood T1DM (Hyppönen et al 1999), but these results have not been unequivocally re-confirmed.

T2DM is a metabolic disorder, mainly caused by resistance or deficiency of insulin (Kangas 2002). T2DM is characterised by diagnosis in the age of >30 years and does not necessarily require treatment with insulin. It accounts for up to 95% of diagnosed diabetes and has modifiable risk factors, e.g. obesity and physical inactivity (Hodgson and Cohen 1999). One-third of people with T2DM are unaware of their disease (American Diabetes Association 2003a). According to Jönsson (1998), only about 50% of T2DM has been diagnosed.

Yet, another type of diabetes, LADA (latent or late-onset autoimmune diabetes of adulthood or type 1.5 diabetes), has also been proposed. It is a slowly progressive form of autoimmune diabetes of adults characterized by the presence of beta-cell specific antibodies and does not require insulin treatment during the early phase of the disease. Clinically, patients appear to be affected by T2DM, but may have the same disease process as T1DM patients (Pozzilli and Di Mario 2001). LADA represents 5-10% of all diabetic patients (Schernthaner et al 2001).

Diabetes is a major cause of premature mortality, morbidity and reduced quality of life. It may result in long-term micro- and macrovascular complications, such as retinopathy, nephropathy, cardiac and cerebrovascular disease and peripheral vascular disease with neuropathy (Currie et al 1996), which are manifested e.g. as impaired vision, hypertension, coronary artery disease, renal disorder, stroke, neurological disturbances, lower limb ulceration and gangrene. In USA., diabetes is the leading cause of blindness, end-stage renal disease (ESRD) and lower extremity amputations (Harris 1998). The probability of developing these complications is related to the duration of diabetes and the degree of metabolic control (Currie et al 1996). Diabetic ketoacidosis (DKA) and severe hypoglycaemia are acute complications, that may be life-threatening (Rewers et al 2002). Diabetes is also associated with an increased risk of mental problems, e.g. depression (Karlson and Agardh 1997; Peyrot and Rubin 1997). The extent to which diabetes increases the risk of general medical conditions other than acute glycaemic and chronic complications of diabetes is unknown (Ray et al 1996).

Mortality rates of male T1DM patients are 5-7 times higher and of female patients 9-12 times than those of the general population in the US. Life expectancy for persons with T1DM is reduced by about 15 years; 15% of patients will die by the age of 40 years (National Diabetes Data Group 1995). In Finland, the relative mortality of patients with T1DM 20-25 years after diagnosis was 8.9-fold for women and 4.7-fold for men compared with the general population based on the same cohort than the present study (Lounamaa 1993).

Diabetes is thus a disease with major long-term implications, not only for the health and well-being of affected individuals, but also for the costs to national health services (Leese 1992) and society at large. The long-term effects of diabetes are substantial in terms of limited health care resources consumed, and loss of production, life-years and quality of life. The management of diabetes aiming at preventing and treating acute and late complications requires the use of diverse health care resources (Gerard et al 1989). Diabetes generates direct costs to the health care system, individuals and society at large (e.g. hospitalisation, drugs), indirect costs due to

loss of productivity (short-term illness, early retirement, death before retirement) and psychosocial costs (pain, loss of quality of life) (Leese 1995).

The challenges imposed by diabetes on Western societies will probably be aggravated over the next few decades, as the number of people with diabetes is expected to rise dramatically. In 1997 the number of affected individuals was 124 million worldwide, and this figure is predicted to increase to 221 million by 2010 (Amos et al 1997). By 2025, the number of adults (over 20 years of age) with diabetes is estimated to rise to 300 million (WHO 1997). In USA, the annual cost of diabetes in 2002 dollars may rise to 192 billion by 2020 (American Diabetes Association 2003a).

The situation will become particularly challenging in Finland. The incidence of T1DM in Finland is the highest in the world (Karvonen et al 1993), increasing most in the youngest age groups (Karvonen et al 1999). This means that in the future the medical and financial burden will increase on Finnish society, on the health care sector and on persons with T1DM, as the number of patients with severe complications rises and complications emerge earlier. The need for and value of health economic information, especially longitudinal, will become increasingly emphasised. It is important for decision-makers to know about health care resources used and required for patients with T1DM when allocating funds and other resources within the health care sector and within society. The growing need to rationally allocate the limited health care resources poses emotional questions of science, politics, economics and ethics that patients and physicians must address (Vinicor 1998).

T1DM is a serious nationwide disease in Finland, and it is crucial that the patient is willing to exercise self-management. If that fails, a need for institutional care is evident. T1DM starts at early age, and with good treatment the capacity to work will be maintained, but if the disease is untreated, the costs will be high. (Niskanen et al 2003).

Inpatient hospital care is the major contributor to the health care costs of diabetes (Jönsson 1983; American Diabetes Association 1993b; Kangas et al 1996; American Diabetes Association 1998). Even a modest reduction in hospitalisations of people with diabetes could result in major savings of health care costs. If people at high risk for hospitalisation could be identified along with the risk factors amenable to manipulation, this burden could be reduced (Moss et al 1999). Hospitalisation data are therefore crucial in the effort to develop strategies for preventing admissions (Fishbein 1985).

Although T1DM is considered one of the most important chronic diseases (Hart et al 1997), only a few studies have so far been conducted regarding hospital utilisation by T1DM patients with their numerous severe complications. Most of the studies are cross-sectional. The aim of this study was to assess the hospital resources used by a cohort of Finnish T1DM patients and associated costs, both cross-sectionally and longitudinally.

2. REVIEW OF THE LITERATURE

2.1. Epidemiology

The range of global variation in the incidence of T1DM is large, and the incidence in Finland has been over 350-fold compared to that of, for example, China (Karvonen et al 2000, The Diamond project group 2006).

The incidence of T1DM is increasing in Finland markedly (Tuomilehto et al 1999). In 1998, the incidence in Finland was 48.5 cases per 100,000 person-years, which was the highest annual incidence rate of childhood-onset T1DM in the world ever recorded (Podar et al 2001). T1DM has increased most in the youngest age groups, and the greatest increase (4.2% per year) occurred in children under 5 years (Karvonen et al 1999). The increase in incidence has been steady, during 1965-1992 at a rate of 2.8% per year (Tuomilehto et al 1995). Remarkable is, that after the beginning of the 1990s, the incidence of T1DM has grown even faster, going beyond 60 per 100,000 person-years in 2005 (Harjutsalo 2007).

A clear geographical variations among children have been shown in the incidence of T1DM in Finland. Living in rural areas increased the risk of T1DM (Rytkönen 2004).

The global prevalence of diabetes ranges from almost 0% (New Guinea) to 50% (Indians of Arizona) (Disdier-Flores et al 2001). In Finland, at the end of 2005, the prevalence of diabetes has been estimated to be at least 4.5% of the population, about 240,000 patients, of which T1DM accounts for 45,000 patients (prevalence 0.9%) (**Table 1**). As about half of the T2DM persons are unaware of the disease (Peltonen et al 2006), the number of diabetic persons would surpass 500,000 (Reunanen 2006). In USA the prevalence is 4.2% (American Diabetes Association 2003a); in 1993, T1DM had affected around 700,000 persons (Libman et al 1993).

Table 1. Number of persons with diabetes in Finland and prevalence (%) by age groups in 2005 (Reunanen 2006)

	Age groups			
	0-29	30-64	65+	Total
TYPE 1	**10,000**	**21,000**	**14,000**	**45,000**
TYPE 2	**1,500**	**83,000**	**109,000**	**193,500**
Type 2, diet-treated	500	29,000	38,000	67,500
Type 2, drug-treated	1,000	54,000	71,000	126,000
PREVALENCE (Total)	**0.6**	**4.1**	**14.6**	**4.5**
TOTAL NUMBER OF PERSONS WITH DIABETES	**11,500**	**104,000**	**123,000**	**238,500**

2.2. Economics of diabetes

As health care resources are scarce and limited, their efficient use is essential. Two basic approaches are available for addressing the economic aspects related to a disease: economic evaluations and cost of illness studies.

Economic evaluations

Economic evaluation considers resource costs and associated health outcomes (effectiveness) of certain interventions and compares them with alternative interventions to assess the relative efficiency of the interventions (McGuire 1996). Economic evaluation can be either partial or full. If there is no comparison with an alternative, the evaluation is partial and called description (of cost and/or outcome). An analysis is also partial if only costs (cost analysis) or outcome (efficacy or effectiveness evaluation) are compared with an alternative. In full economic evaluation, both costs and outcomes of alternatives are examined and compared. Full economic evaluation can be either cost-minimisation, cost-benefit, cost-effectiveness or cost-utility analysis (Drummond et al 1997).

Cost-minimisation analysis may be used when the effectiveness of different interventions is the same. Cost-benefit analysis (CBA) values the decision options in monetary terms. CBA assigns monetary values to health effects by using two basic methods: human capital approach and willingness-to-pay (Petitti 2000). CBA is becoming less frequently used, since it is realised that health care aims at maximising health with the interventions rather than monetary benefits, and because of the controversy over the proper valuation methods of health effects in monetary terms.

In cost-effectiveness analysis (CEA), the outcome is valued in non-monetary terms, e.g. years of lives saved or disability avoided. CEA addresses the issue of comparative cost per unit of outcome for the intervention when effectiveness of two or more interventions differs. An incremental cost-effectiveness ratio, defined as the difference in cost divided by the difference in effectiveness of two interventions, may need to be calculated to determine, which intervention is the more cost-effective (Petitti 2000). Indirect costs are often neglected in CEA studies (Ament and Evers 1993).

Cost-utility analysis (CUA) uses quality-adjusted life-years (QALYs) gained as the effectiveness measure, which reflects societal or individual preferences for outcomes (Petitti 2000). CUA allow comparisons between interventions directed at different health conditions (Williams 2000). Quality of life can be measured by using e.g. a Finnish 15 D measure (Sintonen et al 1997) or various other measures (Nord 1999).

Another method developed to measure the burden of disease is the disability-adjusted life-years (DALYs) approach, which measure intangible costs associated with a certain disease, e.g. diabetes. It combines the number of healthy years lost as a result of early mortality with those lost due to disability (Jönsson 1998).

Cost of illness studies

Cost of illness (COI) studies depict the economic burden of an illness on society (Ament and Evers 1993). These are descriptive studies, that can be prevalence-, or incidence-based. These studies calculate the monetary value of resources used to prevent, detect and treat an illness (McGuire 1996). COI studies look at real resource costs rather than financial costs, so taxes and transfer payments should not be included (Tolpin and Bentkover 1983). COI studies consider the value of resources used for medical care (direct costs) and resources forgone due to reduction of productivity at paid work or unpaid housekeeping due to morbidity and mortality (indirect costs). Direct costs include expenditures for hospitalisation, outpatient care, nursing home care, services of primary physicians and specialists, dentists, drugs, rehabilitation, special devices needed (e.g. hearing aids, prostheses), research, training, construction, administrative functions, capital costs, costs of transportation and certain household expenditures (Hodgson 1983).

Indirect costs are usually estimated by measuring the time lost from paid work or housekeeping and then valuing the time in different ways. Most frequently, the valuation is based on a human capital approach. In it, time lost from paid work is valued at wages or salaries, and time lost from housekeeping is valued by using shadow prices derived with market analogues.

The human capital (HC) approach thus regards individuals as production factors whose output is valued as equal to each individual's market earnings (Songer et al 1998). Morbidity costs are calculated as the value of mean earnings the individual would have accrued without being affected by the disease. Mortality costs are calculated as the number of deaths due to a disease and the expected value of earnings by sex and age. The method considers life expectancy for age and sex groups, the changing pattern of earnings at successive ages, the varying labour force participation rates, the value for housekeeping services and the discount rate to calculate a stream of earnings to its present value (Rice 1994). The selection of discount rate may have a significant effect upon final costs so sensitivity analysis should be conducted using different discount rates. The methods of sensitivity analyses are described in more detail in the literature (Agro et al 1997; Petitti 2000).

The other approach that has been used in COI calculations, willingness to pay (WTP), estimates the values individuals place on chances such as alteration in the probability of morbidity and/or mortality from a certain illness. WTP might be helpful in assessing the burden of psychosocial costs (Hodgson 1983), which are highly subjective, difficult to estimate, and usually omitted from COI studies (Pagano et al 1999). WTP has been used in relatively few COI studies: it generally gives considerably larger cost estimates than the HC approach and is more difficult and expensive to implement (Rice 1994; Songer et al 1998). According to Ament and Evers (1993), cost-benefit analysis with WTP techniques should be used more on a macro level to set priorities. One problem with the WTP method is that it is affected by a person's ability to pay (Sintonen et al 1997).

The term cost used in COI analyses can be defined in several ways, depending on the purpose and perspective of analyses, yielding different results (Tolpin and Bentkover 1983).

Possible perspectives include e.g. society, government, ministries, patient, employer, agency providing a programme, and third-party payer. Societal perspective is broadest and always relevant (Drummond et al 1997), but no single perspective is specifically recommended for COI studies on diabetes (Pagano et al 1999).

There are two ways to conduct a COI study: 'top-down' or 'bottom-up' approaches (**Table 2**). The 'top-down' approach is based on aggregate data on mortality, hospital admissions, general practitioner consultations, etc. The approach takes advantage of available national data, but may give a misleading picture if the incidence of a disease is changing or has changed. It relies on aggregate information, which is readily identifiable (Gray et al 1995). Entire health care expenditure is calculated, after which and the share attributable to diabetes is determined (Jönsson 1998).

In the 'bottom-up' approach, data on disease incidence and prevalence are combined with information on the disease and treatment probabilities in order to estimate the annual incidence of a range of treatments and their costs (Gray et al 1995). 'Bottom-up' method permits a more comprehensive analysis of costs and allows more easily the relationship to the background characteristics of the population, such as sex and disease duration, and the costs of care, to be analysed (Jonsson et al 2000). Furthermore, international data on incidence can be utilised, and the method is more flexible, but complex to initiate (McGuire 1996). In the 'bottom-up' method, a subpopulation is first defined with a certain disease and all costs of illness are attached to it, then the costs of the subpopulation are extrapolated to the total population level. Since data are gathered from only a small population, cost extrapolation to a larger population may deviate notably from true costs (Jönsson 1998).

Table 2. Basic methods for calculating direct costs of a disease

'Top-down' approach:

* Total expenditures for hospital care **x** $\frac{\text{Use of hospital services by specific diagnosis (dg)}}{\text{Total use of hospital services}}$

E.g. hospital costs for diabetes are multiple of the total expenditures for hospital care by the percentage of all hospital services by the diabetic population.

'Bottom-up' approach:

* Average cost of hospital care by specific dg **x** Total use for hospital services by specific dg

E.g. the costs of hospital care in diabetes are calculated by multiplying the average cost of a hospital stay per day by the total number of hospitalised days attributed to the diabetic population.

Because of the problems with extrapolation, and the lack of risk of double counting, Jönsson and Henriksson prefer the 'top-down' method for assessing the economic impact of diabetes (Henriksson and Jönsson 1998; Jönsson 1998). Pagano et al (1999), by contrast, recommend use of the 'bottom-up' method for costing of diabetes because of accuracy demands due to the high costs of the disease. That method also allows different cost items to be attributed to T1DM and T2DM separately (Henriksson and Jönsson 2000).

In COI studies, the costs are assessed annually (prevalence-based) or during a lifetime (incidence-based). Prevalence-based costs can be determined by observing recent events, e.g. number of hospital admissions and average length of stay, and cost of a disease can be estimated by identifying the population and applying appropriate sampling and statistical techniques; it is not necessary to know how cost or the distribution of patients varies with time since the onset or stage of the disease (Hodgson 1994). Prevalence-based costs measure the direct and indirect economic burden incurred to society, usually during a year. The approach measures the value of resources used or lost irrespective of the time of disease onset (Rice 1994).

COI studies based on incidence include cases of the disease developing for the first time in a certain year (Henriksson and Jönsson 1998). This method measures lifetime costs from onset until cure or death. Incidence-based costing requires knowledge of the natural history of the disease, the concomitant use of medical care and its cost each year from onset until cure or death and the probabilities of cure and survival at each stage (Hodgson 1994).

Incidence-based estimates of costs are considered by some researchers to be better suited for costing chronic diseases like diabetes (Hart et al 1997; Pagano et al 1999), while others favour the prevalence approach (Henriksson and Jönsson 1998). The incidence method is more appropriate if at a later stage one wishes to undertake an economic evaluation, such as CEA, to analyse different treatments (Rice 1994; Haddix et al 1996; Hart et al 1997); prevalence data are less appropriate for evaluating interventions, as it does not take into account the development of a disease and the influence of treatments (Ament and Evers 1993). Most COI studies have used the prevalence method, since the incidence method is more difficult to use (Hart et al 1997). The prevalence-based method is better if the results are used for cost control, as the method identifies the main components of expenditures and forgone resources and identifies possible targets for controlling expenses (Rice 1994).

According to Tolpin and Benkover (1983), COI estimates may be used in (1) the evaluation of proposed research programmes; (2) the identification of cost-effective diagnostic and treatment modalities; (3) the formulation of public policy relating to health promotion, prevention, and safety regulation; and (4) the estimation of liability associated with the incidence of specific medical events. Costs of illness are also an important input to CBA (Hodgson 1983) and CEA analysis (Hodgson 1994).

COI studies are used by policy-makers, governmental and non-governmental organizations, researchers and pharmaceutical companies. Especially governmental organizations use COI studies to aid in decision-making, in determining budgetary allocations, in prioritising research funding and in justifying funding for disease programmes (Songer et al 1998).

It is questionable though whether all of these uses or suggested uses are appropriate if the purpose is to use resources efficiently, that is, cost-effectively. Resources should be allocated to the prevention and treatment of illnesses when efficient interventions exist for these purposes, not on the basis of the economic burden posed by the illnesses. When efficient interventions do not exist, allocating more resources adds to the burden.

COI studies have received abundant criticism for a host of reasons. The human capital (HC) approach has several limitations: a merely financial valuation of labour discriminates against non-workers (e.g. children, the elderly); the value of life above economic productivity is ignored; in periods with high unemployment rates, wage rates do not give an accurate production loss estimate; wages may not be a good measure of productivity, as distortions of the labour market occur; and finally, HC does not reflect the way people value their own lives (Ament and Evers 1993). Controversial issues among economists are whether the indirect costs resulting from

reduced productivity due to a disease should be counted and, if so how to measure them. If indirect cost data are used to set priorities, more resources could be directed to people of working age or certain occupations, causing ethical problems relating to equity. Short-term absence from work may be covered by others or made up by the sick worker, so the production losses to society would be overestimated. For long-term absences, a sick person's work could be covered by someone drawn from the ranks of unemployed (Drummond 1992). A method called 'friction cost' addresses this issue, including costs associated with the amount of time and costs needed to replace or substitute a sick worker (Koopmanschap and Ineveld 1992; Songer et al 1998). Another complaint about COI studies is that the human capital approach omits psychosocial (intangible) costs, e.g. pain and suffering (Drummond 1992; Rice 1994), which affect quality of life. COI estimates are generally focused on average costs, but marginal (incremental) costs are more relevant in priority-setting regarding the efficient use of resources (in addition to incremental health effects). Also lack of standardisation makes comparisons of different studies difficult (Songer et al 1998).

One problem related to estimating the of costs of diabetes morbidity is that diabetes leads to severe complications that are considered as the primary disease, while diabetes is often considered as a secondary diagnosis, but costs are calculated based on primary diagnosis, and this leads to an underestimation of costs related to diabetes (Simell et al 1996). Analyses almost always measure the use and costs based on primary diagnosis reported in medical records, the condition mainly responsible for the use of health services. According to Hogdson and Cohen (1999), a complete assessment of the costs of a medical condition requires including additional expenditures arising from (1) chronic complications of the condition, (2) unrelated conditions for which the afflicted are at a higher risk of using health care and (3) co-morbid effects of the condition that raise the cost of care. Co-morbid costs accrue from longer hospital stays and additional costs for nursing home and home health care due to secondary diagnoses of diabetes and secondary chronic complications and unrelated diagnoses attributed to diabetes. For example, a diabetic patient with pneumonia may require longer hospital care than a non-diabetic patient (American Diabetes Association 1993a).

A technique applying attributable risk (AR) attempts to overcome the underestimation of costs resulting from the use of only primary diagnosis data. This method represents the relative contribution of diabetes to the overall risk identified. It can be considered from the general or disease population perspectives (Songer et al 1998). The AR method can be used to calculate an etiological fraction (proportion of health care services for a particular medical condition attributable to diabetes) with the following formula (American Diabetes Association 2003a),

$$E_i = \frac{P \times (R_i - 1)}{P \times (R_i - 1) + 1}$$

where E_i is the fraction of health care use for medical condition "i" attributable to diabetes, P is the diabetes prevalence rate, and R_i is the relative risk of disease i among people with diabetes compared with people without diabetes.

The AR procedures attempt to estimate costs attributed to secondary diagnoses more accurately, but may fail to account for the influence of confounding factors, overstating the role of diabetes in that attribution (Songer et al 1998). Calculating the costs of diabetes as a main diagnosis is the most straightforward and conservative approach, avoiding double counting (Henriksson and Jönsson 1998).

Calculating excess costs in diabetic populations as compared with control groups appears to be the method preferred by Jonsson et al (2000). Due to the complex relationship between diabetes and various co-morbidities and deficient scientific knowledge of these associations, it may be difficult to define whether certain episodes of care are totally or partly due to diabetes (Jonsson et al 2000).

According to Pagano et al (1999), investigation of the total cost is not important when the pathology of a disease, as with diabetes, is complicated and progressive. Identifying patient subgroups according to clinical and economic criteria (type of diabetes, age, disease duration, sex, type of complication) may produce a more precise and valuable analysis since patients at different severity stages of disease require different levels of resources.

2.3. Hospital care of patients with diabetes

In 2001, the total health care expenditure in Finland was 9.5 billion euros, per capita the amount was 1,820 €, and its share of Gross Domestic Product was 7%, one of the lowest in OECD countries (average 8%). In 2001, 76% of health care was financed from public funds, and the share of private financing was 24%. Insured persons accounted for 20%. The total expenditure consisted mainly of inpatient care (39%), outpatient care (28)%, dental care (6%), medicines (16%), medical devices (4%), investments (3.5%) and administration 2%. Public financing consisted of state (17%), local authorities (municipalities) (43%) and Social Insurance Institution ('KELA') (16%) (STAKES 2003).

In 1997, 15.5% of Finnish people used inpatient care, and the average length of stay (LOS) was 11.1 days. Women's share of all bed-days was 61%. LOS for diabetes was 13 days (13,728 patients used 258,943 bed-days in 18,777 treatment periods, 1.4 periods per patient) (Pelanteri et

al 1998). In 2001, the average LOS in specialised inpatient care was 5.5 days by primary diagnosis for endocrine, nutritional and metabolic diseases. By speciality, LOS for internal medicine treatment was 6.2 days, paediatrics 3.8 days and eye diseases 2.3 days. The total average LOS for specialised inpatient care in Finland was 7 days (from 718,000 patients, 6.2 million bed-days, 0.9 million discharges); the LOS was 5 days when psychiatric diseases ware excluded (STAKES 2002).

Diabetes has a marked effect on inpatient hospital resource utilisation and costs. A Spanish study observed that diabetes accounted for 11% of total inpatient discharges, 15% of inpatient days and 16% of costs (Carral et al 2002). In Taiwan, patients with diabetes accounted for 22% of total hospital days, the average LOS being 16.8 days (Lin et al 2001).

In 1989, Finnish patients with diabetes comprised 7% of all patients receiving inpatient care; they used 12.6% of inpatient days. About 52,800 persons with diabetes received inpatient care; 90% of them were entitled to reimbursement for antidiabetic drugs. These people used inpatient care 3.6 times more than the non-diabetic population, having 1.9 admissions per year per patient (Kangas 1995). Inpatient hospital use among diabetic and non-diabetic populations in Finland between 1987 and 1989 has been studied by Aro et al (1994), who found that diabetic patients stayed longer in hospital regardless of the diagnosis. Excess use varied strongly with sex, age and disease category, commonly being 3-5 days. Notably, diabetic children (aged 0-14 years) used about 10 times more inpatient days (5.1 days) than non-diabetic children (0.5 days), their risk for hospitalisation was 6.5 times higher and 41% of diabetic children were hospitalised primarily due to diabetes.

Only few studies exist to compare hospitalisation rates of diabetic children with that in the general population. Moreover, large variation exists in hospitalisation rates and LOS between countries and time periods. Icks et al (2001) observed that diabetic children in Germany had about three times more hospital days than the control group (male 2.6 times; female 3.2 times), females having a higher hospitalisation incidence than males, especially during puberty. Mean LOS was about 7 days.

Hirasing et al (1996) studied trends in hospital admissions among children (aged 0-19 years) with T1DM in the Netherlands and observed a dramatic decrease (>50%) in hospital days between 1980 and 1991. Although the incidence rose, LOS decreased by 2.6 (to 11.9 days) days during the same period. Since the diagnostic criteria remained the same, the authors explain the decrease with improved care, education and self-management. Early diagnosis makes ambulatory treatment more feasible, and home care could be practised more using team

management. According to Sutton et al (1998), a home stabilisation programme would reduce the average LOS at diagnosis to 3-5 days for children older than 5 years.

In a study conducted in the Helsinki area in 1997, 27% of patients with T1DM had a short-term somatic hospital (duration less than a year). They used inpatient care 2.6 times more frequently than the control group, and their average length of stay (LOS) was 6.2 days. Per hospital user, there were 2.2 treatment periods (1.4 in control group) and 13.7 hospital days (11.7 in control group). By diagnosis, diseases unrelated to diabetes caused 48% of inpatient days, followed by diabetes without complications (12%), renal complications (9.5%), hypoglycaemia and ketoacidosis (6%) and other diabetic complications (5%). Among T2DM, 43% of inpatient days were due to diseases unrelated to diabetes, followed by long-term care (26%), macrovascular complications (25%), microvascular complications (3.5%) and diabetes without complications (3%) (Kangas 2001; Kangas 2002).

Fishbein (1985) studied the precipitants for hospitalisations due to T1DM. Poor diabetes control (diet/medication) and infection accounted for 54% of single and 44% of multiple admissions (duration of diabetes on average 10 years). An outpatient diabetic education programme was found to be very successful in reducing hospital admissions due to those acute causes.

Health care systems in general vary among countries, but there are global recommendations for the care of diabetic patients. Outpatient health care of people with diabetes varies substantially among countries, although only a few studies are available (Kangas et al 1996). According to Currie et al (1996), patients with T1DM aged 10-30 years have been shown to have a 7-fold increased probability for age-specific patterns of outpatient attendance. In Finland, among insulin-treated patients with diabetes (diagnosed under the age of 30 years), 28% used health centres, 63% a hospital outpatient clinic and 7.5% private health care as their primary source of outpatient health care (Kangas 1995). In the Helsinki area in 1997, 81% of patients with T1DM had used specialised outpatient care (hospital outpatient, private), the share of private health care being 16%. Individuals in the control group used primary outpatient health care 3.5 times more than patients with T1DM (relative shares 75% vs. 21%), the corresponding share for persons with T2DM being 52%. There were on average 5.5 outpatient visits to a physician and 3 consultations with a nurse per patient due to T1DM. The average age of T1DM patients in the Helsinki study was 35.7 years (SD 14.7) (Kangas 2002).

Among non-diabetic populations in Finland, women have been observed to use health centres 1.5 times more than men (Kokko 1988). Studies of hospital use among diabetic populations by sex are scarce, especially those related to T1DM.

2.4. Costs of diabetes

It is complex to estimate the cost of diabetes in any country (Turtle 2000). Cost estimates vary considerably depending on the year, country and population in question. Almost all studies have used the prevalence method, giving cost estimates for a certain year, nationally or regionally. Studies typically calculate the costs of diabetes, failing to calculate separately the shares by the diabetes type and especially by sex. In some studies, control groups have been used avoid underestimation resulting from using only primary diagnosis (Selby et al 1997; Jonsson et al 2000; Kangas 2002). Generally, comparison of studies is very difficult due to methodological differences and inclusion of different cost components.

Accurate information on costs of diabetes is scarce. The costs of T1DM in a given country depend on the incidence of diabetes and the cost-effectiveness of its treatment. The three clinical stages of T1DM differ. The initial treatment period and the late treatment period cause cost peaks, but the follow-up period after the initial treatment produces clearly smaller costs. During the late treatment period, which is the most costly of the periods, costs begin to accumulate quickly due to the long-term complications. The lifetime financial costs of T1DM and the amount of human suffering are always substantial (Simell et al 1996). The costs of initial treatment are affected greatly by length of stay in hospital. In a Finnish study, most of the costs were incurred during the first month in a two-year follow-up (Simell et al 1993).

Pagano et al (1999) conducted an analysis of 15 COI on diabetes. The authors observed a wide methodological variety, and the lack of technical details in many studies made it difficult to understand the method used. Three of the studies, those of Stern and Levy (1994); Gray et al (1995) and Hart et al (1997) were incidence-based. Only one study, that of Gray et al (1995) used sensitivity analysis to assess how changes in the main assumptions affect the baseline results. Most of the studies (11 of them) analysed diabetes as a whole, three of the studies focused on T1DM. The bottom-up approach was used by 12 studies. The main direct costs, inpatient, outpatient and drugs, were assessed separately in most of the studies. Eight studies estimated indirect costs, which in most studies turned out to be higher than direct costs. A major obstacle in estimating productivity loss due to mortality is that diabetes as a contributory cause of death is frequently not recorded on death certificates. The economic consequences of diabetes as a whole, with its complicated and progressive pathology involving several complications, are difficult to define and vary dramatically over time.

Table 3 shows cost estimates of diabetes in different parts of the world.

Table 3. Costs of diabetes in previous studies

Study	Year	Diabetes type	Included costs	Total costs	Indirect %	Per capita/year	Country/area	Cohort size	Comment
ADA (2003)	2002	1, 2	direct, indirect	132 billion US$	30	13,243 $ medical	USA	12,100,000	undiagnosed diabetes excluded
Dawson et al (2002)	1998	1, 2	direct, indirect	4.7 - 5.2 billion US$		2,675 $ medical	Canada	1,300,000	mortality costs 1.27 billion $
Kangas (2001)	1997	1, 2	direct	0.85-0.94 billion €		4,972 €	Finland	180,000	costs of diabetics
		1, 2	direct	100 million €		5,790 €	Helsinki	13,738	costs of diabetics
		1	direct	8.6 million €		3,868 €	Helsinki	2,324	2,800 € direct excess cost
		2	direct	91.5 million €		6,182 €	Helsinki	11,414	3,520 € direct excess cost
Hodgson and Cohen (1999)	1995	1, 2	direct	47.9 billion US$			USA		cost range 34-64 bill. US$
Benzi et al (1998)		1, 2	direct	1.93 billion US$		1,137 $	Italy	1,700,000	
ADA (1998)	1997	1, 2	direct, indirect	98.2 billion US$	55	10,071 $ medical	USA	7,500,000	medical expenditure 77.7 billions
Henriksson and Jönsson (1998)	1994	1, 2	direct, indirect	5.7 billion Sek	57	8,183 Sek direct	Sweden	300,000	share of complications 77 %
Hart et al (1997)	1994	1	direct	90 billion ptas		63,000 ptas	Spain	1,400,000	
		1	direct			5.1 million ptas	Spain		lifetime health care costs
Warner et al (1996)	1992	1, 2	direct, indirect	4 billion US$	58	3,461 $ direct	Texas	471,000	
Gray et al (1995)	1992	1	direct	96 million £		1,021 £	England + Wales	94,000	
		1	mortality	113 million £		(56,135 £)	"		2,013 deaths

Rubin et al (1995)	1992	1, 2	direct	105.2 billion US$		9,493 $	USA	1,620	costs of diabetics
Stern and Levy (1994)	1993	1	direct	161,000 US$		4,645 $	Israel	1	direct costs of 35 years
ADA (1993)	1992	1, 2	direct, indirect	91.8 billion US$	51	6,278 $ direct	USA	7,200,000	
McKendry (1989)	1986	1, (2)	direct			2,944 $	Canada, Ottawa	205	duration of diabetes ~18 years
Gerard et al (1989)	1984	1, 2	direct, indirect	346-804 million US$	8-60		England + Wales		
Triomphe et al (1988)	1984	1, 2	direct			882 $	France	109	
Jönsson (1983)	1978	1, 2	direct, indirect	291 million US$	57	893 $ direct	Sweden		

In USA, Rubin et al (1995) estimated the total health care costs of diabetic patients to be 14.6% of the overall health care costs (105.2 billion dollars) in 1992. Inpatient hospital care accounted for 63% of the health care costs of diabetic patients. The per capita expenditure of inpatient care for diabetic patients was 4.8-fold that of non-diabetic patients; the corresponding ratio for all expenditures was 3.6. The approach adopted in that study was broader than usual since all health care costs were included, not just diabetes-related.

A different approach, etiological fractions, was used by the ADA in calculating expenditures attributable to diabetes in USA for year 2002. They estimated the costs for diagnosed diabetes at 132 billion dollars. Direct medical expenditures alone totalled 91.8 billion dollars, comprising 23.2 billion dollars for diabetes care, 24.6 billion dollars for chronic complications attributable to diabetes and 44.1 billion dollars for excess prevalence of general medical conditions. Indirect costs totalled around 40 billion dollars (30%), the share being smaller than in other studies. Per capita medical expenditures totalled 13,243 dollars for people with diabetes compared with 2,560 dollars for those without diabetes; when adjusted for age, sex and race, the cost ratio was 2.4 times higher for persons with diabetes. Although people with diagnosed diabetes comprise 'only' 4.2% of the American population, of the health care components analysed in the study almost 1 of every 5 dollars spent on health care in USA. is for a person with diabetes. According to the authors, the ADA study underestimates the true burden of diabetes, as the analysis accounts for only 58% of the cost components of the total health care expenditures in 2002 in USA (1.5 trillion dollars). Also, undiagnosed diabetes is omitted (American Diabetes Association 2003a). Compared with previous ADA studies in 1993 and 1998, it is worth noting that the direct costs in 2002 were at the same level as total costs earlier.

Hodgson and Cohen (1999) used the attributable risk method in 1995 for the estimation of medical care expenditures of diabetes in USA. Total expenditures attributed to diabetes were about 48 billion dollars, including 18.8 billion dollars for first-listed diabetes, 18.7 billion dollars for chronic complications, 8.5 billion dollars for unrelated conditions and 1.9 billion dollars for co-morbidities. The range of total costs was 34.3 - 63.7 billion dollars. Expenditures were somewhat higher for females. The authors defined chronic complications of diabetes in the same way as defined by ADA (American Diabetes Association 1993a).

In Sweden, the economic burden of diabetes was estimated at 5.7 billion SEK in 1994 (Henriksson and Jönsson 1998), showing a 4.4-fold increase compared with an earlier calculation made in 1978 (Jönsson 1983). The studies investigated the cost of diabetes as a main diagnosis, which is a conservative and straightforward method and avoids double counting. The

cost structure remained very similar in both studies, demonstrating the share of indirect costs to be around 57%. As for direct costs, the studies concentrated on hospitalisation, outpatient care and drugs, as most COI studies do (Henriksson and Jönsson 1998).

Another Swedish study investigated excess costs of medical care 1 and 8 years after diagnosis of diabetes in two cohorts of patients with diabetes at the age of 15-34 years and matched control groups. Ninety percent of the persons with diabetes were on insulin treatment. This is evidently the first follow-up study calculating the excess costs of care during the first decade after diagnosis of diabetes, before major long-term complications may have developed. The results indicated that one year after diagnosis the annual excess costs of care were at 1997 prices 4,743 USD (men) and 4,976 USD (women). Hospital inpatient costs, accounted for over 50% of the excess costs. Eight years after diagnosis, the excess costs were 2,010 USD for men and 2,734 USD for women. The higher costs for women were mainly due to hospital outpatient care, but also due to more intensive self-monitoring. The share of inpatient care was notably lower than in the 1-year cohort. Compared with the control group, the per capita costs were 5.6 times higher after 1 year of diagnosis; after 8 years, the figure was 3.8-fold. Inpatient LOS dropped dramatically; after 1 year, it was 7.1 days, and after 8 years 1.5 days (Jonsson et al 2000).

In a Canadian stydy (Johnson et al 2006), health care use and costs in the decade after indentification of T1DM (156 patients) and T2DM (3,469 patients) were analysed. The average 10-year costs per person with T1DM (in 2001 Canadian dollars) was 33,684 $ and those due to T2DM 38,006 $. Hospital use accounted for the largest proportion of total per capita costs yearly for both types of diabetes. In the incident year in 1992, the hospitalisation costs due to T1DM were 7 times higher than the ones in the year prior to diagnosis. Five types of resource categories were included in the (direct) costs (prescriptions, physicians, hospitalisations, day surgeries and dialysis). The authors argue, that as a chronic disease, even 10 years of follow-up might be considered a too short time period for the estimation of costs of care for diabetes. To their knowledge, that study represented the largest cohort with the longest follow-up of health care use and costs published at that time (the study was accepted for publication in august 2006).

In Finland, the only nationwide estimates thus far have been provided by Kangas (Kangas 1995; Kangas 2001; Kangas 2002). Kangas observed that including all direct costs of diabetes care is impossible. In the 1995 study by Kangas, the total direct health care costs of drug-treated diabetic patients in Finland were 1.5 billion FIM. Inpatient care constituted 81% of the sum. The newer study (Kangas 2001; Kangas 2002) used case-controlled, bottom-up and prevalence methods and estimated primarily the use and costs of health services of persons with T1DM and

T2DM in Helsinki, giving also a national estimate for total costs in 1997. The strengths of this study is that it used incremental costs, separated the types of diabetes and had an age- and sex-matched control group. The costs and use of health services were not compared by sex. As to the methods used, this study was the first of its kind in Finland; Selby et al(1997) have used similar techniques earlier in Northern California.

According to Kangas (2001; 2002), the national estimate for diabetes was 0.87 billion € (5.15 billion FIM, 11% of the total Finnish national health budget in 1997). The figure includes both main types of diabetes. Incremental costs were estimated to be at least 0.47 billion € (2.8 billion FIM) in Finland. In Helsinki, persons with diabetes (2.6%) incurred 12.6% of the costs of the total health budget, so the costs of persons with diabetes were over 5-fold compared with their prevalence. Compared with the control group, short-term inpatient care (<365 days) of patients with T1DM was 3.7 times more expensive, total outpatient care 5,0 times more expensive and specialised outpatient care 8.4 times more expensive. Of the total costs of T1DM, the shares of short-term inpatient and outpatient care were both 30%, and that of drugs around 28%. Incremental costs formed 76% of total costs of T1DM and over 16% of total incremental costs (both types of diabetes combined). By disease duration of persons with T1DM, during the first 5 years the costs were 2,893 € and SD was 417 € (17,200 FIM, SD 2,480 FIM) per person per year. The costs were lowest 10-15 years after diagnosis, 2,607 € with SD being 556 € (15,500 FIM, SD 3,307 Fim), and highest 25-30 years after diagnosis, 4,710 € with SD being 1,332 € (28,000 FIM, SD 7,916 FIM). Total average costs of health care per person per year for T1DM were 3,717 € (22,095 FIM); for T2DM, the costs were 1.5-fold, 5,634 € (33,493 FIM). Compared with control groups, these costs per person were over 4-fold for T1DM, and over 2-fold for T2DM.

One of the few incidence-based studies conducted to date is that by Hart et al (1997), which modelled the direct health care costs of the incidence of T1DM in Spain in 1994. The authors developed a discrete event model simulating the natural history of a cohort of newly diagnosed patients in a given year, and calculated the average costs that would accumulate over their lifetime (n=1791). The model used national and international epidemiological data and demographic information combined with local cost data. The average life expectancy of a patient with T1DM was 59.6 years, and the average lifetime costs were 12.7 million pesetas per individual. The authors limited their study only to complications, that they assumed to have the biggest economic impact (nephropathy, retinopathy and cardiovascular complications).

A study by Gray et al (1995) calculated the costs of T1DM in England and Wales in 1992. The direct health care and social care costs of T1DM were estimated to be 96 million pounds (1,021 £ per person) in a population of 94,000 persons affected. The costs included insulin replacement therapy, hospital use, general practitioner and outpatient consultations, renal replacement therapy and payments for informal care. About half of the total costs were directly attributed to T1DM; the rest were associated with various complications of the disease. The single largest source of expenditure was renal replacement therapy. The cost estimates were most sensitive to incidence rates of T1DM, the amount of dialysis and the average duration of dialysis. A further 113 million pounds could have been lost yearly due to premature deaths resulting in lost productivity. The authors concluded that the direct and indirect costs of T1DM are significant.

In Finland, the Diagnosis Related Group (DRG) unit cost in the year 2001 for a treatment period of T1DM (patients under 35 years of age) in specialised care was 1,925 euros and LOS was 4.5 days; per bed-day, this figure is 428 euros (Hujanen 2003). The corresponding DRG cost for T2DM (patients over 35 years of age) was 1,584 euros and LOS was 6 days; per bed-day, 262 euros (Hujanen 2003).

2.5. Diabetes and use of drugs

According to many studies, diabetic patients have high overall usage of medicines, independent of treatment needed for diabetes itself. In a Scottish study, patients with T1DM diabetes were over 2 times more likely to be dispensed a drug than non-diabetic people. The adjusted risk for male patients was 2.4 and for female patients 1.9. Nearly 8% of the UK drug budget (350 million pounds) is accounted for by diabetic patients (Evans et al 2000).

Another large study conducted in Finland (N=116,224) investigated the co-morbidity, overall use and costs of drugs using age- and sex-matched control persons (Reunanen et al 2000). The use of almost all kinds of medication was markedly higher in persons with T1DM and T2DM than in controls. Costs of medications for both types of diabetes combined were 3.5 times higher than in controls; after excluding antidiabetic drugs, the costs were twice as high. In persons with T1DM, the total yearly cost was on average 1,272 dollars per patient, which was 12 times higher than in controls. Insulin treatment accounted for 62% of total drug costs. With T1DM, the costs of drugs other than antidiabetic agents were almost 5 times higher than in control persons. Of patients with T1DM, 15% had hypertension (odds ratio, OR 7.5). Coronary heart disease (OR 6.0), hypothyroidism (OR 7.3), vitamin D metabolic disorders (OR 50.4), glaucoma (OR 16.5), epilepsy (OR 2.2), transplant complications (OR 50.3), uremia requiring dialysis (OR 71.2),

rheumatoid arthritis (OR 1.7) and heart failure (OR 5.0) were also more common with T1DM patients than with controls. Cardiovascular medications were used by 21% of T1DM patients, but only 4% of control subjects (OR 5.6), ACE inhibitors were used 14 times more (OR 14.2), calcium-channel blockers, diuretics and nitrates were used almost 7 times more and lipid-lowering agents were also used more often (OR 5.2), as was also the case with antidepressants (OR 1.6) and hypnotics and sedatives (OR 1.5).

2.6. Complications of diabetes and costs

A large amount of data is available about the incidence and prevalence of complications of diabetes, but in a few studies, costs related to diabetes, have been calculated, especially indirect and marginal costs. Moreover, researchers have failed to distinguish between T1DM and T2DM. The most important contributors to costs of diabetes are complications such as eye and limb disease, heart disease, neuropathy and nephropathy (Leese 1992). Diabetic complications form the principal clinical and economic burdens of diabetes, and evidence indicates that reduction in hyperglycaemia (measured by glycosylated haemoglobin, HbA1c) reduces diabetic complications, including microvascular and neurological disease, and will likely reduce the risk of macrovascular disease (Clark 1998). It is important to have accurate estimates of the incidence and costs of care for complications of diabetes, as such data allow policy-makers and health planners to estimate the savings that could be achieved by prevention and early intervention directed at the complications. Incidence and cost data are critical for conducting cost-effective analyses for drugs and interventions that are aimed at delaying or preventing diabetes-related complications. The high incidence and costs may support aggressive early intervention for persons with diabetes (Ramsey et al 1999).

2.6.1. Acute complications of diabetes

Diabetic ketoacidosis (DKA) and severe hypoglycaemia are acute complications of T1DM that are related to insufficient or excessive insulin treatment. Both are major life-threatening complications for patients with T1DM (Rewers et al 2002).

Ketoacidosis

Ketoacidosis is a challenge especially in adolescent girls, while severe hypoglycaemia affects disproportionally the youngest patients and boys of all ages (Rewers et al 2002). May et al (1993) studied 92 cases of ketoacidosis (age range 18-81) and noticed a female predominance in total and recurrent cases. LOS was 5.7 days in their study (SD 4.9). Javor et al (1997)

investigated DKA charges relative to medical charges of adult patients with T1DM, including inpatient, outpatient, emergency room visits and drug costs. The authors concluded that DKA episodes represent more than 1 dollar of every 4 dollars spent on direct medical care for adult patients with T1DM and 1 dollar of every 2 dollars in those persons having multiple episodes, and interventions targeted to these recurrent DKA episodes could be particularly cost-effective.

Hypoglycaemia

Of acute complications, hypoglycaemia is the most frequent, the most serious, and the most feared by patients and families, often requiring hospitalisation, which can be costly. In 1992 in France, there were 10,800 inpatient hospitalisations, 90% of these lasting several days and 1.9% resulting in patient death. Mean total medical cost of a hospital stay was 2,100 dollars and mean LOS was 6.6 days. In 1995, the annual cost for the society due to hypoglycaemia (inpatient care) was estimated at 16-22 million dollars (Allicar et al 2000).

A Swedish study in 1998 investigated costs of severe hypoglycaemia of persons aged under 19 years with T1DM (n=129). The average socio-economic burden for events of severe hypoglycaemia was 174 euros yearly per person. The authors conclude, that the results in the study suggest the potential for socio-economic savings and increased quality of life for patients and families from severe hypoglycaemia prevention programs (Nordfeldt and Jonsson 2001).

2.6.2. Main chronic complications of diabetes

Long-term complications of T1DM are caused by the inability to mimic the physiological insulin responses to meals, physical activity and other regulators of insulin release. Hyperglycaemia-associated changes affect small and large blood vessels and lead to vasculopathy, which may result in retinopathy, nephropathy, neuropathy, ischaemic heart disease and obstruction of the arteries supplying the extremities. Thus, costs due to long-term complications begin to accumulate quickly (Simell et al 1996). Also genetic factors probably play an important role for the development of diabetic complications.

Acute coma is the leading cause of death for persons with T1DM in the early years of the disease, renal disease predominates in the middle years, and after 30 years two-thirds of deaths are due to cardiovascular disease (National Diabetes Data Group 1995).

Currie et al (1996) calculated relative risks (RR) using primary diagnoses and primary procedure codes for in- and outpatient hospital use for patients with diabetes and separate complications in England between 1991 and 1994. Patients with diabetes have a 12-fold increased risk of

admission for coronary heart disease, 16-fold for neuropathy and peripheral vascular disease, 10-fold for eye disease, 13-fold for renal disease and 12-fold for cerebrovascular disease compared with a non-diabetic population. Patients with diabetes occupied 9.4% of bed-days.

Donnan et al (2000) compared hospital resource use of persons with T1DM (n=864) with a control group in Scotland and observed that the highest relative risks (RR) for hospitalisation were for endocrine (RR 283), ophthalmic (RR 47), renal (RR 6.5) and neurological (RR 3.9) complications; the high rate for endocrine complications was due to ketoacidosis and hypoglycaemia. On the other hand, patients with T1DM did not stay longer in hospital than non-diabetic patients; a similar observation about LOS was made by Kangas (2002).

In Finland, Kangas (2002) investigated costs related to complications of diabetes. For both types of diabetes, around one-third of patients had at least one complication, and these persons accounted for two thirds of the total treatment costs. Yearly cost per person with T1DM without any complication was 9,355 FIM, and with complication(s) the figure was 42,385 FIM. Incremental costs of persons with T1DM who had complications were 12 times higher than those of persons with T1DM without complications (n=779, 33% had at least one complication). For T2DM, the costs were 24 times higher. The shares of incremental costs of inpatient care of persons with T1DM by main complication groups were as follows: diabetes as main diagnosis (25%), macrovascular complications (15%), microvascular complications (30%; share of renal complications 19%) and diseases unrelated to diabetes (31%). When comparing these percentages with persons with T2DM, incremental costs for diseases unrelated to diabetes were dominant (53%), followed by macrovascular complications (34%); microvascular complications constituted only 5% of incremental costs.

Ophthalmic complications

Ophthalmic complications increase with age (Jacobs et al 1991), and diabetic retinopathy is strongly associated with duration of the disease (Pajunpää 1999). Diabetic patients also have a clearly higher risk for other eye diseases than non-diabetic persons, e.g. the relative risk for glaucoma is 10-fold and for cataract 9.6-fold for persons with diabetes aged under 65 years (Jacobs et al 1991). The relative risk for ophthalmic complications in persons under 45 years of age was estimated to be 39.8 compared with non-diabetics; for older age groups, it was 1.6-3.4 (American Diabetes Association 1993a).

Retinopathy affects virtually all persons with T1DM, and proliferative retinopathy is found in 60% of patients by 20 years after diagnosis of diabetes (Harris 1998). Complications related to retinopathy are estimated to be symptomatic in 50% of the patients with T1DM with retinopathy

(Stern and Levy 1994). Retinopathy is characterised by changes in the small blood vessels of the retina. In the non-proliferative stages of the disease, the retina has micro-aneurysms, haemorrhages and exudates, but these might not result in visual loss. In the proliferative stage, retinopathy is characterised by the growth of abnormal blood vessels which can haemorrhage into the eye or produce retinal detachment, resulting in severe loss of vision. Vision loss can be prevented by a treatment called laser photocoagulation (Drummond et al 1992). Glycaemic control and lower levels of hyperglycaemia are related to reduced risk of progression of retinopathy (Klein and Klein 1998). Klein et al (1996) observed that in patients with T1DM and T2DM a 1% increase in HbA1c concentrations at baseline was associated with an almost 60% increase in the incidence of retinopathy and an almost 100% increase in the rate of progression to proliferative retinopathy.

The costs of visual problems due to diabetes are high (Pajunpää 1999), especially indirect costs as a patient may have to retire from work early and may be dependent on others for help (Leese 1995; Simell et al 1996). In USA in 1990, the total yearly expenditure for blind diabetic patients under 65 years of age was 14,296 dollars per patient (Javitt et al 1994). From the perspective of a single-payer health system, blindness has been estimated to cost 2,000 dollars per person yearly in direct medical costs (Herman and Eastman 1998). In a Finnish study, the annual expenditures to society due to one visually impaired person were 15,675 euros, direct costs accounted for 72% of this figure. When the duration of visual impairment was estimated to be 8 years, the total costs for that period were 99,904 euros (discount rate 5%) or 117,575 euros (discount rate 0%). Costs of social sector were the biggest single item, 35% of total costs, followed by lost earnings of the patient and family (30%) and costs of social security (20%). Costs due to use of health services and rehabilitation were relatively small (10% and 5.5%), respectively. Interestingly, the average age of retirement due to diabetic retinopathy was as low as 36.8 years (Pajunpää 1999). The author included transfer payments (social security costs, e.g. pension) in the total costs, meaning that the costs per visually impaired person were 'overestimated' by 20% relative to had they been omitted.

Diabetic nephropathy

Diabetic nephropathy (DN) usually develops 10-20 years after the onset of T1DM, producing a gradual loss of renal function. It is characterised by persistent proteinuria and rising blood pressure, leading to renal failure or death due to coronary disease (Mathiesen et al 1984). In a Finnish study, nephropathy in T1DM patients increased the risk of coronary heart disease and stroke by 10-fold. In T1DM with DN, cardiovascular complications occurred at 12-13 years after

diagnosis of diabetes, while in individuals without DN, the lag time was somewhat longer, 16-17 years. The incidence of cardiovascular disease was clearly related to the duration of DM (Tuomilehto et al 1998). The earliest manifestation of nephropathy is albuminuria, which is a marker of greatly increased cardiovascular morbidity and mortality in T1DM and T2DM patients (American Diabetes Association 2003b).

Progression to renal failure occurs within 3-20 years (median 10 years) after the onset of persistent proteinuria, although the process differs significantly among patients and is related to blood pressure, poor glycaemic control and smoking (Sawicki et al 1994). Mortality by the age of 45 can be 20-40 times higher in patients with T1DM with proteinuria than in those without proteinuria (Borch-Jonhsen et al 1985, Lounamaa 1993).

Diabetes is the most common single cause of end-stage renal disease (ESRD) in USA and Europe. ESRD develops in 50% of T1DM patients with overt nephropathy within 10 years and in over 75% by 20 years. In 1997, the cost for treatment of diabetic patients with ESRD was 15.6 billion dollars in USA (American Diabetes Association 2003b).

People with diabetes have a 17-fold increased risk of ESRD compared with the general population. The risk of death from renal disease for T1DM patients is 23 times higher than with non-diabetic people (Leese 1992). Approximately 33-40% of T1DM patients develop DN (Andersen et al 1983; Chukwuma 1993). About 20-30% of patients with T1DM will have to be treated with dialysis or transplantation. DN is associated with a higher incidence of ophthalmic, nervous, peripheral vascular and cardiovascular lesions, and the prevalence of retinopathy is associated with progressive nephropathy as well. Advanced diabetic retinal disease is virtually always associated with overt diabetic retinopathy. Almost 77% of deaths from T1DM are associated with renal failure, the rest are due to cardiovascular disease. The best prognosis for survival in ESRD is with transplantation, haemodialysis or peritoneal dialysis (Narins and Narins 1988).

In a longitudinal study conducted in Israel, nephropathy accounted for 32% of total direct treatment costs over 35 years (78,000 of 247,000 pounds in 1993 prices) The costs of everyday treatment (insulin, blood glucose self-tests, visits to doctor, laboratory tests) were 25%. Nephropathy comprised almost half of all direct costs of complications of T1DM. Over a period of 35 years of illness, complications accounted for 69% of total costs. The average direct cost of treatment was 7,100 pounds per patient per year (or 3,000 pounds discounted at a rate of 6%) (Stern and Levy 1994).

In a study in Taiwan in 1997, the annual in- and outpatient costs for care of dialysis patients averaged 25,576 dollars per patient-year. This cost is approximately half of that in most Western

countries and Japan. Diabetic ESRD patients produced around 12% more costs of care per patient-year than non-diabetic ESRD patients (Yang et al 2001). In a Canadian study, around 32% of the costs of dialysis were for peritoneal dialysis and 68% for haemodialysis (Johnson et al 2006). Median cost per life-year of hospitalisation for ESRD (extrapolated from data from Diabetes Control and Complications Trial) was 46,000 dollars, based on 1993 currency (The Diabetes Control and Complications Trial Research Group 1993; Turtle 2000).

In Finland, the DRG unit cost in 2001 for a treatment period of dialysis in specialised care was 2,643 euros. The corresponding cost for renal replacement was 24,600 €, with a LOS of 22 days. This cost was the 8th highest of all DRG procedures (total 495) (Hujanen 2003).

Diabetic neuropathy

Diabetic neuropathy usually occurs after several years of diabetes, and it primarily affects the sensory nerves of the lower limbs, with loss of sensation of pain and sometimes progressive destruction of soft tissues, bone and joints. Micro-organisms often enter the deep tissues of the foot and break down soft tissues, tendons and bones. When tissue destruction is extensive, amputation may be necessary. Physical or thermal trauma may precipitate gangrene in a foot. Bacterial colonisation of the necrotic tissue results in wide spread of infection, which may threaten the leg or even the survival of the patient, thus usually demanding urgent amputation. Three major factors contribute to the damage of the diabetic foot: chronic diabetic neuropathy, atherosclerotic obstruction of the arteries supplying the lower limb and bacterial infection. The combination of chronic foot ulceration, sepsis and gangrene is the main cause of prolonged hospitalisation for diabetic patients, accounting for more than half of the non-traumatic amputations performed in some developed countries (WHO 1985). Still, problems with definition, classification and diagnosis as well as uncertainties related to pathophysiology, natural history and prognosis have made it difficult to quantify the incidence, prevalence and costs of diabetic neuropathy (The Carter Center of Emory University 1985; Kangas 2002).

According to Reiber (1992), foot problems are the most common complication of diabetes leading to hospitalisation. In a study by Jacobs et al (1991), diabetic patients under 45 years of age were 46 times more likely to be hospitalised due to neuropathy than the non-diabetic population. The ADA reported relative risk to be 27.4 for neurological complications compared with a control group (American Diabetes Association 1993a). Currie et al (1998) observed that the highest average LOS was for chronic ulcer of the skin: 25.3 days for diabetic patients vs. 19.1 days for non-diabetic patients. The probability of lower-extremity amputation has been reported to be 27 times higher among diabetic persons compared with their non-diabetic peers

(Nabarro 1988). Of patients with diabetes, 5-15% require amputation of a lower extremity during their lifetime (Bild et al 1989). At least half of the patients with T1DM have developed symptoms of neuropathy by 25 years after diagnosis (American Diabetes Association 1993a; Stern and Levy 1994). The high economic burden of neuropathy has also been addressed in other studies (Ward 1995).

The costs of foot ulcers were extraordinarily high in a study by Ramsey et al (1999). Costs of foot ulcers in patients with diabetes were much higher than equivalent costs in patients without diabetes. In Sweden, gangrene was reported to be the most expensive single complication of diabetes, accounting for as much as 25% of the costs of inpatient care (Jönsson 1983). Another extensive Swedish study by Tennvall et al (2000), calculated costs to the health care sector of deep foot infections in patients with diabetes. This study was unique since it calculated total treatment costs for in- and outpatient care from diagnosis until healing of a deep foot infection in a population of consecutively included diabetics over a 10-year period (n=220). Duration of diabetes was 19.6 years, and 77% of the patients had T2DM. Total cost of healing without amputation was 136,000 SEK per patient, cost of healing with minor amputation was 260,000 SEK and cost with major amputation was 234,500 SEK; these costs are at 1997 price level. The cost of topical treatment was 51% of total costs. Wound healing duration and repeated surgery explained 95% of costs. The mean healing time for patients without amputation was 29 weeks; the corresponding times after minor and major amputation were 52 and 38 weeks. According to the study, costs of antibacterials (4% of total costs) should not be used as an argument in the choice between early amputation and conservative treatment. The authors also maintained that the high costs associated with the diabetic foot and variations of these costs are mostly explained by the heterogeneity of foot ulcers and their treatment and outcome. Variations in study design, definitions, settings and changes in treatment practice over time also explain differing costs between studies. Many of the health economic studies are conducted from different perspectives, which are often connected to differing patterns of health care financing across different countries (e.g. Europe vs. USA).

The average lifetime cost per case of lower-extremity amputation has been calculated to be 48 152 dollars (Eckman et al 1995). In the Netherlands in 1992, the mean costs associated with diabetes-related hospitalisations for amputation were 10,531 pounds (n=1,575) compared with 8,151 pounds per hospitalisation (n=1,760) for the non-diabetic population. The mean LOS was correspondingly 41.8 and 31.8 for these populations. The authors estimated, that approximately 10% of diabetes-related health care costs were associated with lower-extremity amputations (van Houtum et al 1995). In Finland, the DRG unit cost in 2001 for a treatment period for amputation

of a limb due to endocrinologic, nutritional or metabolic cause was 6,036 euros and LOS was 10 days (Hujanen 2003).

Macrovascular diseases

Coronary heart disease occurs more frequently and is more severe in diabetics than in non-diabetics (Tuomilehto et al 2004). Atherosclerotic disease of the small arteries in diabetics is responsible for the high incidence of cerebral infarction, stroke, and diffuse cerebrovascular disease (WHO 1985, Tuomilehto et al 2004).

In a study by Jacobs et al (1991), the risk for diabetic patients for hospitalisation due to atherosclerosis was 10-fold that of a control group. Moreover, the risk of cerebrovascular accident and heart disease was 6-10 times higher in diabetic patients. In a study by Currie et al (1997a), the relative risk (RR) of stroke in diabetic men versus non-diabetic men was 3.7, and in women 4.4. Approximately 15% of acute hospital care of cerebrovascular disease was related to diabetes in a UK population. According to the ADA, the RR for cardiovascular complications of diabetic patients aged under 45 years was 18.9 for heart diseases and 17.9 for arterial disorders; for venous disorders, the RR was 2.7 (American Diabetes Association 1993a). Macrovascular disease usually occurs 25 years or later after the initial outbreak of T1DM (Stern and Levy 1994). Over 20% of deaths from T1DM are associated with cardiovascular disease (Chukwuma 1993). During the early years of T1DM, renal disease is the leading cause of death (Diabetes Epidemiology Research International Mortality Study Group 1991b); after 30 years of the disease two-thirds of the deaths are due to cardiovascular diseases (Krolewski et al 1985; Borch-Johnsen et al 1987).

Currie et al (1997b) discovered that patients with diabetes constituted 17% of coronary heart disease-related hospital admissions. Stern and Levy (1994) calculated that macrovascular disease accounts for 21% of total lifetime direct costs of a person with T1DM who has lived with the disease for 35 years (51,000 pounds in 1993 prices). In a study by Kangas (2002), macrovascular diseases accounted for 11% of total costs of T1DM in Helsinki; for comparison, in T2DM, the share was 27%.

2.7. Interventions, prevention and treatment of diabetes

Diabetes and its numerous complications also cause vast amounts of intangible costs (pain, suffering, decline in length and quality of life, which may be measured with e.g. QALYs lost). These psychosocial costs are alleviated and deferred by various treatments and prevention programmes. Chronic diseases such as diabetes incur lifetime costs, so money invested in

interventions and preventive care now may not bring benefits in terms of reduced complications for many years (e.g. 20-30 years), and this has little appeal to governments (Leese 1995). Effective local disease registers and screening for complications have been estimated to lead to annual savings of 1,200 million dollars, and the avoidance of 25,000 amputations and 10,000 cases of blindness yearly in the European Community (Piwernetz 1990; Leese 1995).

Three levels of prevention for diabetes have been presented (Alberti 1991; Tuomilehto et al 1992, Leese 1995; Turtle 2000):

- primary prevention: reducing the incidence of diabetes
- secondary prevention: controlling metabolic abnormalities after diagnosis of diabetes (e.g. diet and exercise for elderly people with T1DM, education, tight glucose control, screening)
- tertiary prevention: limiting the consequences of diabetic complications once they have emerged (e.g. laser treatment)

Regarding T2DM, interventions (lifestyle change, weight reduction, exercise) have been effective in primary prevention (Tuomilehto and Lindström 2003), although they are difficult to implement due to limited acceptance (Turtle 2000). An example of a successful lifestyle intervention is a Finnish study, which managed to reduce the incidence of T2DM in persons at high risk by 58% (Tuomilehto et al 2001, Lindström 2006). Determining the cost-effectiveness of approaches for preventing T1DM is not possible yet, because it is unclear how T1DM could be prevented.

Klonoff and Schwartz (2000) conducted an economic analysis of 17 widely practised interventions for diabetes. The interventions were classified as follows: 1) clearly cost-saving, 2) clearly cost-effective, 3) possibly cost-effective, 4) non-cost-effective or 5) unclear. The interventions included the following actions: 1) eye care, 2) pre-conception care, 3) nephropathy prevention in T1DM and T2DM, 4) improved glycaemic control, 5) self-management, 6) case management, 7) medical nutrition therapy, 8) self-monitoring of blood glucose, 9) foot care, 10) blood pressure control, 11) blood lipid control, 12) smoking cessation, 13) exercise, 14) weight loss, 15) HbA1c measurement, 16) influenza vaccination and 17) pneumococcus vaccination.

For eye care, diabetic retinopathy screening and treatment programmes prevent blindness by detecting proliferative diabetic retinopathy (PDR) and macular edema (ME), and practising laser photocoagulation therapy. According to the authors, more economic studies have been reported

on prevention of retinopathy than on any other intervention for diabetes. In the review by Klonoff and Schwartz (2000), there were 10 retinopathy screening studies, and the economic benefits were expressed as costs or savings per sight-year gained. In 9 of these studies, savings exceeded costs. Diabetic retinopathy screening and treatment programmes have been shown to be clearly cost-saving and worthwhile from both medical and economic perspective.

Monte Carlo simulation was used to determine the cost-effectiveness of screening diabetic retinopathy in studies by Crijns et al (1999) and Javit and Aiello (1996). Crijns et al (1999) observed that for juvenile-onset patients ophthalmic care can reduce the prevalence of blindness by at least 52%, and savings in disability facilities and production losses surpass direct costs. In the study by Javitt and Aiello (1996), the incremental cost-effectiveness of screening and treatment of eye disease in patients with T1DM was 1,996 dollars per QALY gained. The authors concluded that these kinds of interventions are highly cost-effective health investments for society, as diabetic eye disease causes much blindness in working-aged individuals in USA. In Finland, Pajunpää (1999) calculated that the screening and treatment costs of finding one preventable case of visual impairment were 31,115 euros. The screening costs per diabetic person screened were 25 € with the photographic method and 11.5 euros with the ophthalmoscopic method. The author argues that retinal photographic screening is worthwhile, if at least 49 visual impairments can be prevented.

Diabetic nephropathy screening and treatment programmes prevent end-stage renal disease (ESRD) by detecting microalbuminuria or clinical nephropathy and controlling blood pressure or using angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker therapy.These medications preserve renal function, independent of their antihypertensive effects, in diabetic patients who have microalbuminuria and proteinuria (Lewis et al 1993; Ravid et al 1993; Klonoff and Schwartz 2000). According to the ADA, screening of persons with T1DM should begin after a disease duration of 5 years. Use of ACE inhibitors is recommended for all patients with microalbuminuria or advanced stages of neuropathy. Protein restriction and other treatments, e.g. phosphate-lowering therapies may also benefit selected patients (American Diabetes Association 2003b).

The economic impact of the aforementioned interventions can be determined by comparing programme costs with savings associated with delaying or deferring dialysis or transplantation for ESRD (Klonoff and Schwartz 2000). Six nephropathy interventions were reviewed by Klonof and Schwartz (2000), and all of these interventions extended life or prevented ESRD. The authors concluded that nephropathy screening and treatment interventions provide additional

life-years and QALYs for persons with T1DM clearly cost-effectively; patients with T2DM also appear to obtain both economic and medical benefits.

Borch-Johnsen et al (1993) analysed by using simulation the cost-benefit of screening for and antihypertensive treatment of early renal disease indicated by microalbuminuria in patients with T1DM. Screening and treatment interventions were likely to have life-saving effects and generate marked economic savings.

ACE inhibitor therapy has been shown to be cost-effective in preventing diabetic nephropathy in various studies (Rodby et al 1996; Hendry et al 1997; Kiberd and Jindal 1998). Rodby et al (1996) observed that treatment with captopril resulted in direct cost savings of 32,550 dollars per patient with T1DM and nephropathy over a lifetime compared with placebo.

A modern intervention approach is pancreas transplantation when the recipient no longer needs insulin injections, but must receive chronic immunosuppressive therapy, which is often accompanied by severe side-effects. Approximately 85% of the pancreas transplant recipients have also received a kidney transplant (Stern and Levy 1994). Cost-effectiveness and cost-utility analyses relating to pancreas transplantation have been conducted by Douzdjian et al (1998; 1999), who analysed the different treatments by using a decision tree with a 5-year time horizon. The outcome was that simultaneous pancreas-kidney transplant (SPK) is the optimal strategy for a patient with T1DM, with a 5-year cost of 102,422 dollars per QALY. The respective costs with the other strategies were dialysis 317,746 dollars, kidney-alone transplant from a living donor 123,923 dollars and from a cadaver 156,042 dollars.

Interventions aimed at improved glycaemic control are clearly cost-effective, as such interventions in simulated populations of T1DM and have added life-years and QALYs (Klonoff and Schwartz 2000). The Diabetes Control and Complications Trial demonstrated that intensive treatment of persons with T1DM delays onset and slows progression of retinopathy, nephropathy and neuropathy by a range of 35% to over 76%. The study assumed that 70% of conventional therapy patients and 30% of intensive therapy patients would develop proliferative retinopathy by the age of 70. Intensive therapy should, however, be implemented with caution due to increased risk of hypoglycaemia (The Diabetes Control and Complications Trial Research Group 1993). The DCCT Research Group (1996) conducted a health-economy analysis to examine the lifetime benefits and costs of intensive therapy, and whether it would be preferable to conventional therapy from the perspective of the health care system. On average, intensive therapy patients gained 7.7 additional years of sight, 5.8 years free from ESRD, and 5.6 years free from lower extremity amputation compared with conventional therapy patients. The gain

from any significant microvascular or neurologic complication was 15.3 life-years. Patients treated with conventional and intensive therapy lived on average 56.5 years and 61.6 years, respectively. Thus, intensive therapy yielded an increase of 5.1 years in survival. On average, intensive therapy costs were 33,746 dollars higher than the costs of conventional therapy (99,822 vs. 66,076 dollars) per patient over a lifetime, or 28,661 dollars per year of life gained (discounted at 3% yearly). The incremental cost per QALY gained was 19,987 dollars (costs and benefits discounted at 3%). According to the authors, these ratios can be considered cost-effective and they represent good monetary value for the investment. A sensitivity analysis revealed that a decrease in costs of slightly more than 50% would even make intensive therapy cost-saving option.

According to the ADA, the yearly cost of intensive therapy was three times the cost of conventional therapy, a large portion of the costs relating to bigger use of outpatient services and resources used in self-care. Although more expensive, intensive therapy offers hope of cost-savings due to averted complications (American Diabetes Association 1995b). Potential long-term personal and economic savings of continuing a tight metabolic control are notable (Simell et al 1996).

Stern and Levy (1996) noted in Israel that the cost of intensified insulin treatment is three times higher than the cost of the standard treatment per year. For a 35-year period when intensified treatment was applied to all T1DM patients, the total costs exceeded the costs of standard care, although the costs for complications were smaller in intensified treatment. The authors suggest that the decision to adopt intensified therapy should be based on medical, ethical, political and economic principles, and the therapy should be applied to selected, motivated and prepared patient groups. Nephropathy is the most common and severest complication, and intensified therapy seemed to be most effective for these patients.

In seven of nine self-management interventions, benefits exceeded costs. For every 1 dollar spent on training of patients, there was a net savings of 0.44 to 8.76 dollars. The authors classify diabetes self-management programmes as possibly cost-effective, because these programmes have deficiencies in their methodologies and they measured only short-term savings over 1 year (Klonoff and Schwartz 2000).

For foot care, economic analyses are scarce. Klonoff and Schwartz (2000) assume, though, that interventions of foot care prove to be clearly cost-effective or even cost-saving. Ollendorf et al (1998) estimated that economic benefits of strategies to reduce amputation risk ranged from 2,900 to 4,442 dollars over 3 years per person with a history of foot ulcer. Educational interventions produced

the highest benefits in that study. A foot intervention, which consists of podiatric care, education and specially fitted shoes can reduce the amputation rate by 50% (Bild et al 1989).

As to other interventions applied, acetylsalicylic acid (i.e aspirin) therapy has been recommended for persons over 29 years of age, who have at least one risk factor for CVD and who have evidence of large-vessel disease. According to Rolka et al (2001), almost every adult in USA with diabetes has at least one risk factor for CVD, and may be considered a potential candidate for acetylsalicylic acid therapy. During 1988-1994 only 20% took acetylsalisylic acid.

Treatment of dyslipidaemia (e.g. simvastatin therapy) has provided good value for money in diabetic patients with cardiovascular disease, demonstrating a good cost-effectiveness ratio and reducing hospitalisations. For diabetic patients in Sweden, the estimates of cost per life-year gained ranged from 1,600 € (based on clinical history) to 3,200 € (based on ADA criteria). In Finland, the corresponding range was from from 2,944 to 7,280 € (Jönsson et al 1999).

Home-based management for newly diagnosed diabetic children has given good results, yielding better metabolic control and psychosocial outcomes than traditional hospital-based care (Dougherty et al 1999).

In Finland, two T1DM predictive strategies were compared. A genetically targeted strategy together with auto-antibody follow-up of persons at high risk proved to be clearly cost-saving compared with a pure immunological strategy, i.e. repeated immunological screening of the entire population (Hahl et al 1998). Hahl et al (2003) have also analysed direct costs of T1DM prevention therapy with nasal insulin, by comparing two different diabetes prevention models using Monte Carlo simulation. The authors conclude that the costs of potential prevention of T1DM with nasal insulin are low when compared with estimates of the yearly direct health care costs of T1DM, and they study suggests (assuming that nasal insulin is effective in the prevention), that a 2 to 3-year delay in the T1DM onset may make prevention using the practice-oriented model cost saving.

Cost-effectiveness studies of interventions for diabetes are important to provide a basis for efforts to reduce the cost of diabetes as well as to ensure that people with diabetes are treated efficiently and with equity (Leese 1992). The key factors that affect the economic returns from medical research are the prevalence, incidence and burden of the disease in question, the costs and effectiveness of the medical intervention, the impact of the clinical trial on clinical practice and the likely time span of benefits from knowledge obtained during the trial (Drummond et al 1992). Prevention has three major prerequisites: 1) identification of subjects at risk, 2) identification of the cause of the disease and/or its precipitators and 3) understanding of the

pathogenesis of the disease (Becker et al 2000). The disease should also be a burden to the individual and society, and a safe treatment should be available, that has soundly based potential to be effective (Schatz et al 2000).

In 2007, there are still no clinically accepted prevention strategies for T1DM (Knip 2007), and it may take years, even decades to find one (Hyöty 1997, Reunanen 2004). Examples of successful prevention of certain other diseases, though, give reason to optimism (Knip 2007, Hyöty 1997).

2.8. Proposals for cost of diabetes studies in the future

According to Songer et al (1998), the cost of diabetes studies should concentrate more on narrower perspectives, like costs specific to T1DM, T2DM, gestational diabetes, subgroups (sex, age categories) or each specific complication of diabetes. More incidence-based studies are required. In addition, methods for measuring and valuing indirect costs should be refined, and better epidemiologic data are needed for calculations of attributable risks, e.g. contribution of diabetes to other diagnoses and contribution of co-morbidities to diabetic complications.

3. AIMS OF THE STUDY

The overall aims were to describe the use of inpatient care of a cohort of childhood-onset diabetic patients (T1DM) during 1973-1997 and to estimate the costs of inpatient care. The specific aims were

1. To describe:
    - 1.1. the use of inpatient care of a nationwide cohort of childhood-onset diabetic patients (T1DM),
    - 1.2. the yearly use of inpatient care by sex during 1973-1997,
    - 1.3. the cause of inpatient care (diabetes vs. other diseases),
    - 1.4. the effect of diabetes duration on hospital use, especially in the main complication groups, when diabetes had lasted on average 9.5 years and 16.5 years, respectively
    - 1.5. the use of inpatient care in the cohort in 1998

2. To estimate the costs of inpatient care by sex due to T1DM and its main complications, and the total cost of inpatient care by calculating the costs of:
    - 2.1. inpatient care as a function of T1DM duration and compare costs at 9.5 years with those at 16.5 years after the diagnosis of T1DM
    - 2.2. inpatient care in the cohort in 1998

4. MATERIAL AND METHODS

4.1. Inpatient care of T1DM patients during 1973-1997

4.1.1. Population, study period and data sources

The study population consisted of all Finnish T1DM patients diagnosed before the age of 18 years between 1 January, 1965 and 31 December, 1979 and derived from the Finnish population-based T1DM register.

At the end of 1979, the dynamic cohort of this study consisted of 5,166 patients (2,327 females, 2,839 males) and at the end of 1997 this figure was 4,701. The number of female and male patients in different years varied, as shown in **Table 4**. By the end of 1997, there were 465 deaths (157 females, 308 males). Hospital use of the study population was followed from 1973 to 1997; thus, the follow-up time was 25 years.

Table 4. Yearly number of patients in the cohort by sex between 1973-1997

Year	Total number	Females	Males
1973	2,980	1,364	1,616
1974	3,343	1,518	1,825
1975	3,692	1,679	2,013
1976	4,024	1,830	2,194
1977	4,373	1,994	2,379
1978	4,746	2,152	2,594
1979	5,120	2,315	2,805
1980	5,114	2,311	2,803
1981	5,108	2,309	2,799
1982	5,099	2,305	2,794
1983	5,091	2,304	2,787
1984	5,073	2,300	2,773
1985	5,062	2,298	2,764
1986	5,047	2,293	2,754
1987	5,027	2,286	2,741
1988	5,005	2,279	2,726
1989	4,971	2,269	2,702
1990	4,949	2,260	2,689
1991	4,916	2,248	2,668
1992	4,885	2,239	2,646
1993	4,854	2,230	2,624
1994	4,824	2,221	2,603
1995	4,787	2,206	2,581
1996	4,743	2,188	2,555
1997	4,701	2,170	2,531

The Finnish population-based T1DM register belongs to the material of the Diabetes Epidemiology Research International (DERI) Study, which has been used in evaluating mortality in T1DM (Diabetes Epidemiology Research International Mortality Study Group 1991a, Diabetes Epidemiology Research International Mortality Study Group 1991b, Asao et al 2003). The register was established by linking the Finnish Hospital Discharge Register (FHDR) with the Social Insurance Institution Central Drug Register (SIICDR) using the unique personal identification numbers recorded in both registers. T1DM patients aged 17 years or under at the diagnosis of diabetes were derived from the Central Drug Register, which was started in 1964 and contains information on all patients receiving reimbursed medication for specified chronic disorder, including diabetes. These persons can be identified with personal identification codes containing information on date of birth, sex and control digits (Tuomilehto et al 1998). The Central Drug Registry only recorded the date of approval of the free-of-charge medication, so copies of the original certificates had been collected for the years 1965-1979 from the local offices of the Social Insurance Institution in 1987 to obtain the actual dates of diagnosis that had to be during 1965 to 1979 (Tuomilehto et al 1991). The use of hospital-days of patients in the Finnish T1DM register was based on the FHDR. Dates and causes of possible deaths of the subjects were obtained from the National Cause of Death Register administered by Statistics Finland. The register is based on official death certificates and covers completely the whole study period.

Data on hospitalisations due to T1DM were obtained from the FHDR, which covers all inpatient discharges nationwide since 1968. The FHDR includes data on dates of admissions and discharges, four discharge diagnoses, the hospital identification numbers, and codes for hospital type where the patient was treated. After the first two years FHDR has been observed to be more complete (Mähönen et al 1997). The follow-up of hospitalisations for this study was started from 1973 onwards to get more accurate and reliable data. Hospital use before the diagnosis of diabetes, use due to diagnosing diabetes (the first treatment period, a total of 2,165 discharges) and use due to pregnancies or complications of pregnancies were excluded (9,082 discharges, International Classification of Diseases - ICD codes 630-676) to achieve better comparability between patients' hospital use and treatment costs in different years.

4.1.2. Variables used to describe inpatient care

The following variables were calculated separately for the total population and both sexes:

Bed-day (hospital-day): A day spent by person in a hospital ward. The days of arrival and departure are calculated as a single day.

Discharge (treatment period): Hospitalisation period lasting at least 15 hours. This period is included in the FHDR.

Average length of stay (LOS): The number of hospital days divided by the number of treatment periods (discharges).

Discharges per user: The number of discharges divided by the number of patients,who used hospital at least once during the year concerned.

Proportion of T1DM patients using hospital annually: Number of hospital users during the year concerned divided by the number of patients in the T1DM register during the same year.

Bed-days per user: The number of bed-days during the year concerned divided by the number of patients who used hospital at least once during the same year.

Discharges and bed-days per 1,000 patients yearly: The number of discharges or the number of bed-days during the year concerned divided by the number of T1DM patients during the same year; this figure is then multiplied by 1,000. The size of the cohort varied between different years, and there were more men in the cohort. This variable was calculated to make hospital use comparable between the sexes and different years.

4.2. Use of inpatient care by T1DM patients due to diabetes or other causes during 1973-1997

The same population, study period, basic data and variables as presented in the subsection 4.1. of the study were used in subsection 5.2. in results. Hospital use due to diabetes (diabetes, 250x as main diagnosis) was separated from hospital use due to other causes (main diagnosis other than 250x). Since also the main acute and the major late complications of diabetes carry the three-digit code 250, the overall hospital use due to diabetes and its late complications can be conveniently distinguished from hospital use for other diseases. In Finland, the ICD codes on hospital discharges are assigned by the treating physician, and thus, they are considered fairly accurate. During the years 1973 through 1986, the ICD-8 version was used in Finland, and since 1987, the ICD-9 classification was used. The codes in the ICD-8 version were converted to the corresponding codes in the ICD-9 version.

The following codes of diabetes were applied (according to CD-9): 2500 (no complications), 2501 (with ketoacidosis), 2502 (diabetic coma), 2503 (diabetic nephropathy), 2504 (diabetic retinopathy and other eye complications), 2505 (diabetic neuropathy), 2506 (diabetic

microangiopathy), 2507 (other specified complications) and 2508 (unspecified complications) (Lounamaa 1997).

4.3. Inpatient care depending on duration of T1DM (duration 9.5 years vs. 16.5 years).

The same population as described in the subsection 4.1., was used in subsection 5.3. of the study. Two 'cohorts' were formed based on the duration of T1DM. The hospital use due to T1DM complications according to duration of the disease was examined here. Main diagnosis was used in calculations. Two 3-year periods of duration of diabetes, 9-11 and 16-18 years, were compared in 9 complication groups. Hospital use was calculated in 3-year periods and then divided by three, indicating the effect of duration of the disease on hospital use when T1DM has lasted on average 9.5 years compared with 16.5 years. Also, the share of hospital use due to each complication was compared to the amount of use due to all complications (all complication groups combined), hospital use due to other causes than diabetes and hospital use due to all hospitalisations (inpatient use due to any cause). T1DM-related hospital use due to complication groups and that due to diabetes without complications (ICD-8 code 25000 and ICD-9 code 2500B) were presented separately.

ICD-8 codes were converted to correspond ICD-9 codes, because the coding changed in the beginning of 1987.

ICD-10 was officially adopted in 1.1.1996 in Finland (first edition was published in 1995 and the second in 1998). The ICD-10 codes for diabetes in Hospital Discharge Register changed markedly compared to the earlier versions (ICD-8 and ICD-9) and if this study would have used ICD-10 codes, another translation of the codes would have been needed, which would have complicated the study much. In National Public Health institute the Hospital Discharge Register data was still available in ICD-9 format in 1998. That made it convenient to make the follow-up period between 1973-1998.

The complication groups and complications were based on the criteria of the American Diabetes Association (1998). Cerebrovascular complications in this study were extracted from neurological disorders to present them as an own group. In addition, diabetic coma was included in the grouping as a separate group. Hypoglycaemia was calculated separately using the ICD-9 code to assess the approximate amount of hospital use caused by it, and it was assigned to the main group "other use" (there was no specific ICD-8 code for hypoglycaemia). The detailed list

of complication groups, including corresponding diseases (ICD-8 and ICD-9), is shown in Appendix 3.

The nine complication groups were as follows:

- Cerebrovascular disease
- Cardiac disease
- Peripheral vascular disease
- Neurological complications
- Renal complications
- Endocrine complications
- Ophthalmic complications
- Other complications
- Coma

The average number of patients was 5,120 in the 9.5-year cohort and 5,010 in the 16.5-year cohort. The exact dates of death were used when calculating the number of people alive (N1) at the beginning and at the end (N2) of the two periods, and then summed and divided by 2 (N1+N2 / 2) to obtain the average number of people alive during the two study periods. These figures were needed to calculate some of the variables describing the hospital use (bed-days and discharges per 1,000 patients).

The following principles were applied when calculating treatment periods and bed-days:

- If there were two days or less between two treatment periods, they were defined as two different treatment periods if the main diagnoses of the periods were different. If the main diagnoses of the periods were the same, the periods were defined as one treatment period.
- The days of admission to hospital and discharge from hospital were treated as a single bed-day (e.g. 15.7.1996 – 17.7.1996 = two bed-days).
- Overlapping treatment periods of the same patients were evidently some kind of errors in FHDR (a person cannot be in two places at the same time, e.g. in different hospitals), so the overlapping part was omitted to avoid overestimation of bed-days.

Variables used to describe inpatient care in this subsection:

Bed-day (hospital-day): A day spent by a person in a hospital ward. The days of arrival and departure are calculated as a single day.

Discharge (treatment period): Hospitalisation period lasting at least 15 hours. These and longer periods are included in the FHDR. Short consecutive hospitalisation periods were treated as one period, if the main diagnoses were the same and the time between the periods was two days or less. Otherwise, the treatment periods were considered separate.

Discharges and bed-days per 1,000 patients yearly: The number of discharges or the number of bed-days divided by the average number of diabetic patients in the study period (e.g. 9-11) and multiplied by 1,000. The average number of patients was calculated by adding the number of patients alive at the beginning of a study period to the number of patients alive at the end of a period and then dividing by two.

Average length of stay (LOS): The number of hospital days divided by the number of treatment periods (discharges) gives a yearly average length of stay. LOS was calculated (for total population) by using real hospital days during a treatment period, not by using duration criteria as in the case with bed-days and discharges. LOS for total population was calculated based on the amount of real treatment periods to get the actual average time in hospital for each complication group (e.g. a treatment period may have started before the observation period of 9-11 years or ended after it; in that case, only the bed-days contained within the observation period were taken into account). For men and women, LOS was calculated straightforwardly by dividing bed-days by discharges ('crude LOS'), as the difference between real treatment periods and crude LOS turned out to be negligible.

Discharges per user: The number of discharges divided by the number of patients who used hospital at least once during the diabetes duration period concerned.

Bed-days per user: The number of bed-days divided by the number of patients who used hospital at least once during the diabetes duration period concerned.

The variables were calculated separately for the total population and for both sexes.

4.4. Costs of inpatient care depending on duration of T1DM (duration 9.5 years vs. 16.5 years).

In subsection 5.4., the treatment costs of inpatient care were calculated when T1DM had lasted on average 9.5 or 16.5 years. The same population and the 9 complication groups described in the subsections 4.1. and 4.3. were used. Costs of treatment due to diabetes without complications (ICD codes 25000 and 2500B), which belonged in the subsection 5.3. to a group ('Other use'), are presented separately in figures and tables. Costs of treatment due to T1DM-related hospital

use (25000/2500B + complication groups combined) are also presented. Hospitalisations of patients under 16 years of age were calculated separately (as typically in Finland, they are treated in children's wards, which have different cost per bed-day prices than other inpatient wards).

The unit costs for bed-days for different complication groups were obtained from a publication by National Research and Development Centre for Welfare and Health, STAKES (Heikkinen et al 2001). These costs are average unit production costs of the health sector in Finland (at national level), including out-of-pocket payments by patients. These costs have been recommended for use in health economic analyses in Finland when resources used in health care need to be valued. These costs form a solid and general basis for different comparison purposes.

The following unit costs per bed-day by diagnosis were used for different groups (these costs were at 1999 price levels):

- Cerebrovascular disease 348 €
- Cardiac disease 348 €
- Peripheral vascular disease 348 €
- Neurological complications 328 €
- Renal complications 348 €
- Endocrine complications 348 €
- Ophthalmic complications 632 €
- Other complications 348 €
- Coma 348 €
- Hypoglycaemia 348 €
- 25000/2500B (diabetes without complications) 348 €
- Other diagnoses than T1DM-related 429 €
- Paediatrics (T1DM in children’s ward) 606 €

The treatment costs per bed-day on the internal medicine ward was 348 €, and this price was used in most of the groups. In costing hospital use other than T1DM-related, the average cost of all hospital types in Finland (429 €) was used. In other groups, the cost of the equivalent special ward was used.

Definition of certain variables used to describe inpatient costs

Cost per patient: Average costs per patient in the cohort. The number of patients depended on the duration of T1DM and on the number of female and male patients.

The costs by duration of T1DM were first calculated in the two 3-year periods (to decrease the effect of yearly fluctuations) by multiplying the number of bed-days by the hospital cost per bed-day in question. These costs were then divided by 3 (to show costs per year), and then by the average number of patients (alive in 3 years).

Cost per hospital user: Costs in the 3-year period concerned divided by the number of patients who used hospital at least once during this diabetes duration period.

Costs per treatment period: Costs and number of discharges were calculated per 1000 persons per year, and then divided by each other.

The variables were calculated separately for the total population and for both sexes.

4.5. Inpatient care and costs in 1998

In subsections 5.5. and 5.6. the same population and complication groups were used as described in the subsections 4.1. and 4.3. Use of inpatient hospital care and the corresponding costs were calculated cross-sectionally in 1998. ICD-9 classification was used. In subsection 5.6., the costs per bed-day were valued at 1999 prices, and the bed-day prices for different complication groups were considered to be the same as those in subsection 4.4. There were no patients under 16 years of age.

5. RESULTS

5.1. Inpatient care of a cohort of T1DM patients during 1973-1997

The mean age of the patients in the cohort at the end of 1973 was 14.7 years (min 2.3; max 26.7), and the mean duration of diabetes 4.4 years (min 0.04; max 9.0). At the end of 1979, the mean age was 17.6 years (min 1.1; max 32.7), and the mean duration of diabetes 7.3 years (min 0.04; max 15.1). At the end of 1997, the mean age was 35.6 years (min 19.2; max 50.7), and the mean duration of diabetes 25.4 years (min 18.1; max 33.0).

5.1.1. Rate of hospitalisation

The proportion of patients using hospital yearly remained between 26% and 30% during the first half of the follow-up until 1987 (**Figure 1**). During the next three years the hospitalisation rate dropped to 21.6%, and remained at this lower level, being 19.8% in 1997. Thus, the proportion of users was lower during the last seven years than during the first 14 years.

Women used hospital care relatively more than men, the difference being biggest during 1977 to 1987. The proportions of both female and male hospital users decreased since the late 1980s: that of females from 33.7% (1985) to 20.8% (1997) and that of males from 26.5% (1980) to 18.9% (1997).

5.1.2. Total inpatient care

During the follow-up period *the total number of hospital bed-days* used was 370,688 (**Table 5**). The yearly number of bed-days increased until 1979, after which it fell rather linearly by 50% from 20,190 (in 1979) to 10,164 (in 1997).

The total number of hospital discharges during the follow-up period was 50,287. The annual number of discharges increased during the first six calendar years and remained relatively steady after that, ranging from 1,900 to 2,400 per year.

Figure 2 shows that women had more bed-days and discharges than men, except during the last six years. The number of women's bed-days dropped during the last half of the follow-up by as much as 57% from the peak rate in 1980 to the lowest figure in 1995. The decrease during the entire study period was 47%. The number of men's bed-days declined less steeply than that of women; the decrease was 46% from the highest rate in 1979 to the lowest figure in 1997, and 39% during the entire study period.

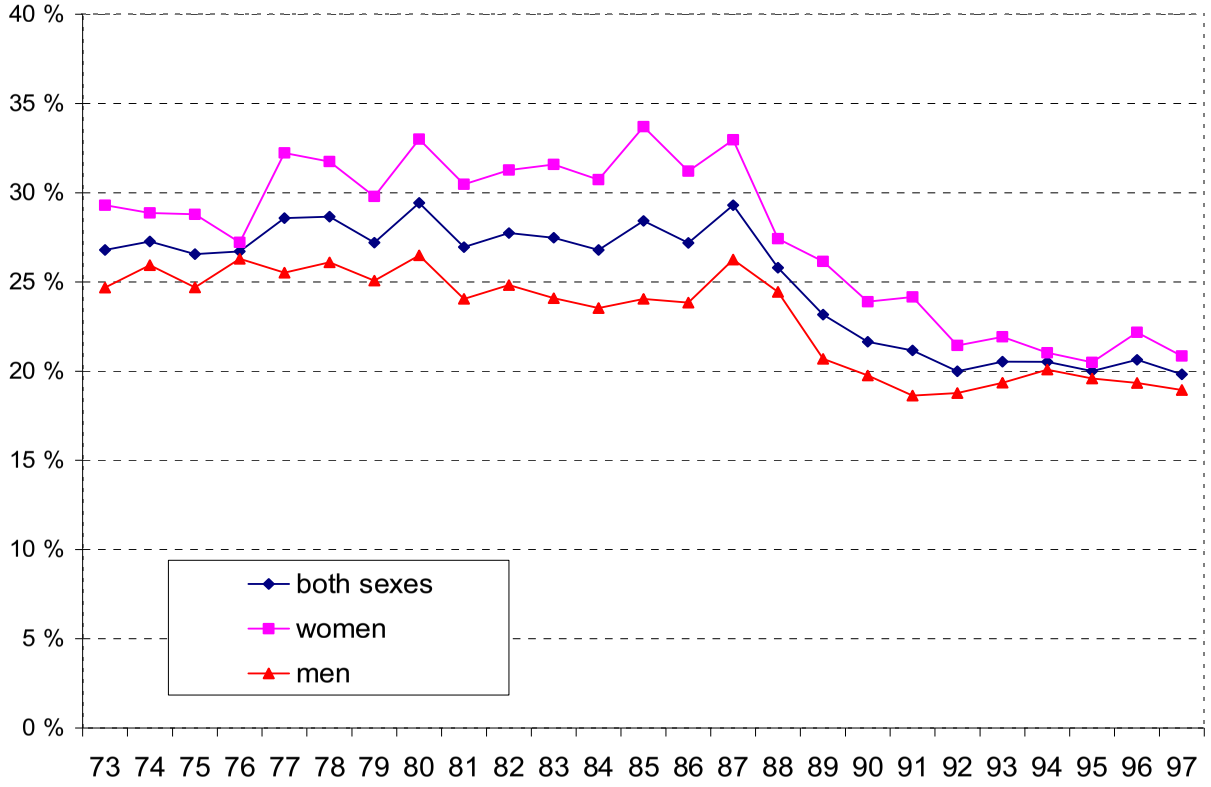

Figure 1. Proportion (%) of T1DM patients using hospital during 1973-1977 by sex

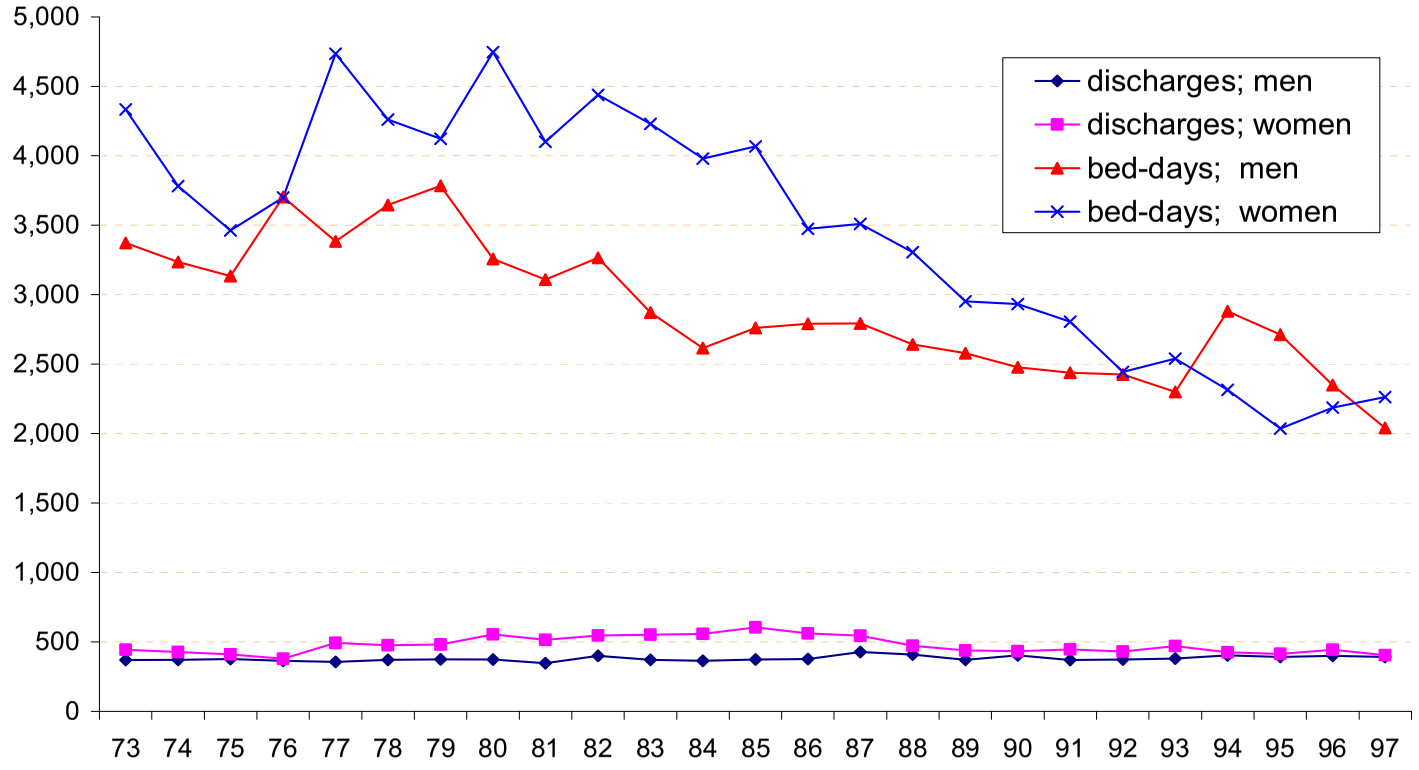

Figure 2. Total number of discharges and bed-days per 1,000 men and women during 1973-1977

Table 5. Number of total bed-days and discharges of T1DM patients diagnosed in Finland during 1965 to 1979 by the year of admission and sex between 1973-1997

Year	Bed-days total	Bed-days females	Bed-days males	Discharges total	Discharges females	Discharges males
1973	11,370	5,916	5,454	1,203	607	596
1974	11,661	5,752	5,909	1,327	650	677
1975	12,144	5,821	6,323	1,449	689	760
1976	14,900	6,771	8,139	1,495	694	801
1977	17,509	9,446	8,063	1,834	983	851
1978	18,655	9,183	9,472	1,993	1,027	966
1979	20,190	9,549	10,641	2,171	1,115	1,056
1980	20,121	10,986	9,135	2,331	1,283	1,048
1981	18,186	9,475	8,711	2,161	1,188	973
1982	19,387	10,250	9,137	2,377	1,262	1,115
1983	17,769	9,750	8,020	2,314	1,275	1,039
1984	16,459	9,167	7,292	2,300	1,286	1,014
1985	17,010	9,355	7,655	2,426	1,392	1,034
1986	15,698	7,984	7,714	2,334	1,292	1,042
1987	15,742	8,048	7,694	2,425	1,248	1,177
1988	14,801	7,559	7,242	2,198	1,079	1,119
1989	13,754	6,727	7,027	2,015	1,001	1,014
1990	13,348	6,653	6,695	2,070	981	1,089
1991	12,899	6,341	6,558	1,999	1,006	993
1992	11,964	5,493	6,471	1,966	968	998
1993	11,769	5,684	6,085	2,056	1,051	1,005
1994	12,721	5,163	7,558	2,006	947	1,059
1995	11,583	4,522	7,061	1,941	921	1,020
1996	10,884	4,822	6,062	2,009	979	1,030
1997	10,164	4,951	5,213	1,887	887	1,000
Total:	**370,688**	**185,368**	**185,331**	**50,287**	**25,811**	**24,476**

The number of discharges per 1,000 female patients increased between 1980 and 1987, but decreased after this to the level that had prevailed at the beginning of the follow-up period. The peak year was 1985. The number of discharges per 1,000 male patients remained rather constant during the 25 years. Overall, female patients used more inpatient care than male patients; they had 25.6% more discharges and 19.1% more bed-days than men during the entire follow-up.

The total *average length of stay* (LOS) decreased steadily during the follow-up from 9.5 days (1973) to 5.4 days (1997) (**Figure 3**). The drop was 44%. Male patients stayed in hospital on average for 7.6 days and female patients slightly less (7.2 days) during the follow-up. The number of yearly *hospital discharges per user* increased from 1.5 to 2.0, while the number of yearly *bed-days per user* dropped from 14.2 to 10.8 days during the 25-year study period.

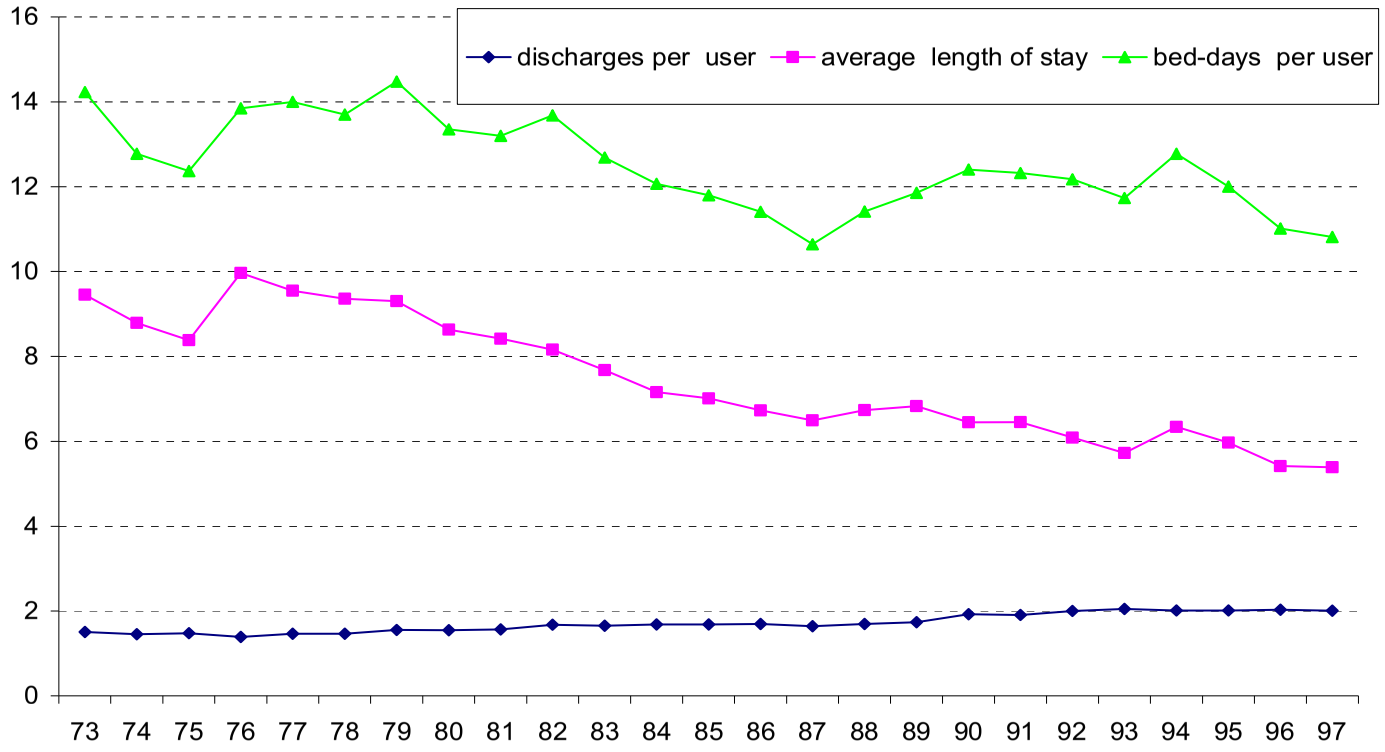

Figure 3. Total average length of stay, discharges per user and bed-days per user during 1973-1977

5.2. Use of inpatient care by T1DM patients due to diabetes or other causes during 1973-1997

5.2.1 Rate of use of inpatient care

During the first half of the follow-up period, from 1973 to 1988, the majority of inpatient care used by the patients was due to T1DM (**Figure 4**). During the last five years, from 1992 to 1997, the proportions of patients using hospital due to causes other than T1DM were higher than the proportions of persons using hospital due to T1DM. Between 1973 and 1988, approximately 20% of patients used hospital at least once a year with T1DM as the main diagnosis. After this, there was a steady fall in hospital use to 9% in 1997.

Female patients used hospital more frequently than men, especially between 1977 and 1987, when the difference was 4-7 percentage points. After this the sex difference in hospital use levelled off. From the peak year of 1977, the percentage of female patients hospitalised yearly due to diabetes dropped from 28% to 8% in 1997. The proportion of male patients using hospital yearly was around 20% during 1973-1988 after which it declined steadily to 10% in 1997.

The proportion of hospitalisations with a main diagnosis other than T1DM increased steadily from 6% in 1973 to 14% in 1997. This proportion among female patients was somewhat higher than among male patients during the entire 25-year period. Compared with hospitalisations due to T1DM, the turning point for hospitalisations due to other diseases was the year 1992 (when the duration of diabetes ranged from 13 to 27 years and the attained age from 13 to 44 years). Since then, the percentage of hospital users due to other causes overtook that due to T1DM, and thereafter, a steadily increasing majority of hospitalisations was attributed to other diseases than T1DM.

5.2.2. Use of inpatient care due to diabetes as the main diagnosis

There were a total of 247,668 bed-days and 33,189 hospital discharges during the follow-up period with *diabetes (ICD 250) as the main diagnosis*. These bed-days decreased by 67% from the peak year of 1980 (14,984 bed-days) to 4,952 bed-days in 1995. Since 1990, the yearly number of bed-days remained unchanged. The number of yearly discharges due to T1DM first increased, being highest (1,750 discharges) in 1985, 108% higher than in 1997 (843 discharges). The yearly discharge rate remained more or less unchanged between 1979 and 1987, and dropped relatively steeply between 1988 and 1992.

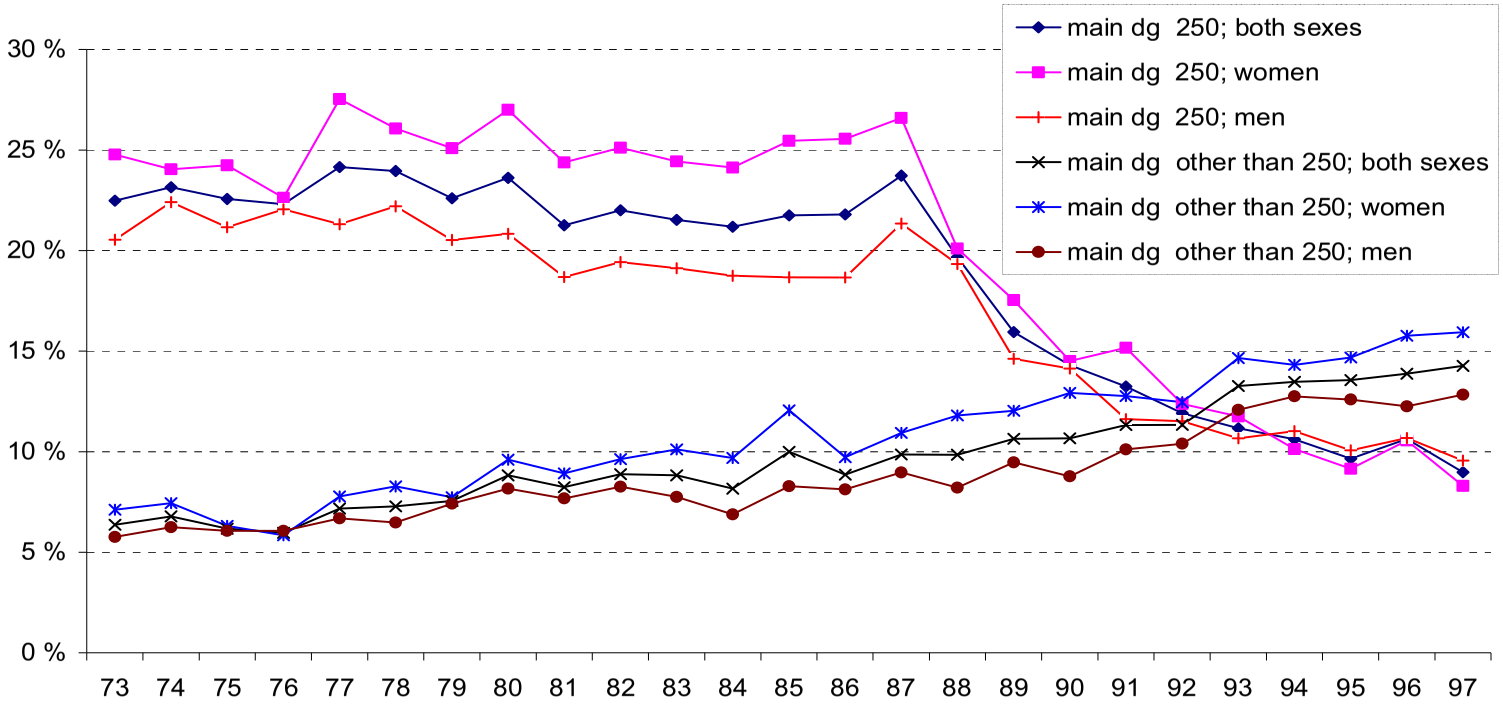

Figure 4. Proportion (%) of T1DM patients using hospital by main diagnosis (dg), (dg 250=diabetes) during 1973-1977

Figure 5 shows the number of yearly discharges and bed-days by sex per 1,000 patients during the follow-up period. Female patients had consumed more bed-days and had more discharges than male patients until 1987. After this, the sex differences levelled off. During the entire follow-up period females had consumed on average 21% more bed-days and experienced 26% more discharges than males. In female patients, hospital admissions due to T1DM were relatively frequent during the first 10 years of the follow-up period, decreasing then steadily until the mid-1990s and levelling off thereafter. In females, the drop in the number of hospital bed-days from 3,669 in 1980 to 872 in 1995 was more dramatic (76%) than that in males (49%).

The yearly number of bed-days was high during the first five years of the study, decreasing thereafter and levelling off in the early 1990s. The decrease in bed-days related to T1DM was less in male than in female patients; in males, the number of bed-days decreased by 62% from the peak year in 1978 (3,013 bed-days) to the lowest year in 1993 (1,149 bed-days). During the 25 years, the yearly number of bed-days among males decreased by 57%, while in females the drop was 73%.

In female patients, the number of yearly hospital discharges increased steadily until the peak year of 1985. The steepest decline in discharges was observed during 1988-1990. From 1985 to 1997, the drop in rate of female patients' yearly discharges was 63%. In the entire 25-year period, the number of discharges for females fell from 359 to 166 (54%) per 1,000 patients per year. The discharge rate for males remained steadier than in females during the follow-up. During the 25-year period, yearly discharges in males dropped from 296 to 190 (36%) per 1,000 patients.

The *LOS* due to T1DM remained steady during 1973-1978, then slowly decreasing until the early 1990s (**Figure 6**). After this the change in LOS levelled off among diabetic men. The drop was 4.4 days from 1978 (9.8 days) to 1995 (5.4 days). The essential decrease took place between 1973 and 1984 (3 days). In 1997, the total LOS was 6.0 days. During the entire 25-year period, the LOS was 7.4 days; for male patients, it was slightly longer than for females (7.6 days and 7.2 days, respectively). The longest average LOS in males was in 1978 (10.4 days) and in females in 1973 (9.8 days).

The number of *bed-days per user* due to T1DM first decreased from 13.9 days in 1973 to 9.5 days in 1987, after which it gradually increased up to 12.0 days in 1997. The average number during the entire period was 11.4 days per year. Although the average numbers of yearly bed-days per user during 1973-1997 were similar for both sexes (11.4 days), the number was higher for female than for male patients during 1980-1985, while male patients had more yearly bed-days per hospital user during the latest follow-up years. The overall trend in bed-days per user

was relatively stable until the beginning of the 1980s, after which there was a fall until 1987, particularly for females, followed by an increasing trend, particularly for males.

The number of *discharges per patient* due to T1DM was on average 1.6 discharges per year during the 25-year study period. There was a steady increasing trend in discharges per patient for both sexes, from 1.3 to 2.0 discharges per year. Patients thus seemed to be hospitalised due to T1DM more often as they grew older and as the duration of diabetes became longer, but they stayed in hospital for shorter periods at one time.

5.2.3. Use of inpatient care due to other causes (main diagnosis other than 250)

The use of inpatient care with a main diagnosis other than diabetes showed somewhat different patterns and trends than use when T1DM was the primary diagnosis. There were 123,642 bed-days and 16,750 discharges due to other causes during the entire 25-year follow-up period; this was approximately half of those with T1DM as the main diagnostic code. The total yearly number of discharges due to other causes showed a steady increasing trend from 509 in 1979 (when the entire cohort was complete in terms of number of patients) to 1,050 in 1997, an increase of 106%.

Figure 7 shows *the number of yearly discharges and bed-days by sex per 1,000 patients due to other causes than diabetes.* During the entire study period, female patients had 25% more discharges and 15% more bed-days than male patients. The yearly number of discharges per 1,000 male patients increased by 186% and among females by 183% during the 25 years. During 1973-1997, the yearly number of bed-days per 1,000 male patients increased by 24%, mainly during the first four years. In the late 1980s through 1995, another steep increase took place. The number of bed-days per 1,000 male patients escalated by 207% from 502 in 1974 to 1,541 in 1995 and declined then by 40% in the next two years. The number of bed-days per 1,000 female patients increased by 52% in 25 years, from 870 to 1,325 per 1,000 patients per year. In female patients, the number of bed-days increased by 162% between 1975 and 1990, declining thereafter such that the number in 1997 was the same as in 1985 (about 1,300). During 1982-1991, female patients had used one-third more bed-days than males.

The *average LOS with the main diagnostic code other than 250* dropped steadily, from 12.6 days in 1976 to 5.0 in 1997 (60%) (**Figure 8**). During the entire follow-up period, the average LOS was 7.9 days; 8.2 days among males and 7.6 days among females. During 1978-1982 and 1992-1996, the LOS of male patients was 1-3 days longer than that of females. The LOS dropped from

12.7 days in 1976 to 4.4 days in 1997 for male patients, and the corresponding drop for women was from 12.5 to 5.5 days.

The yearly number of *bed-days per user* also decreased steadily, from 16.0 in 1976 to 7.7 in 1997. The overall trend indicated a 50% decline in female and a 54% decline in male patients from the mid-1970s to 1997. During 1990-1995, the number of bed-days increased markedly, falling again thereafter.

The number of *discharges per user* increased from 1.2 to 1.6 during the 25-year study period, similarly for both sexes. Overall, the number of discharges per user was 1.4 per year, for both sexes.

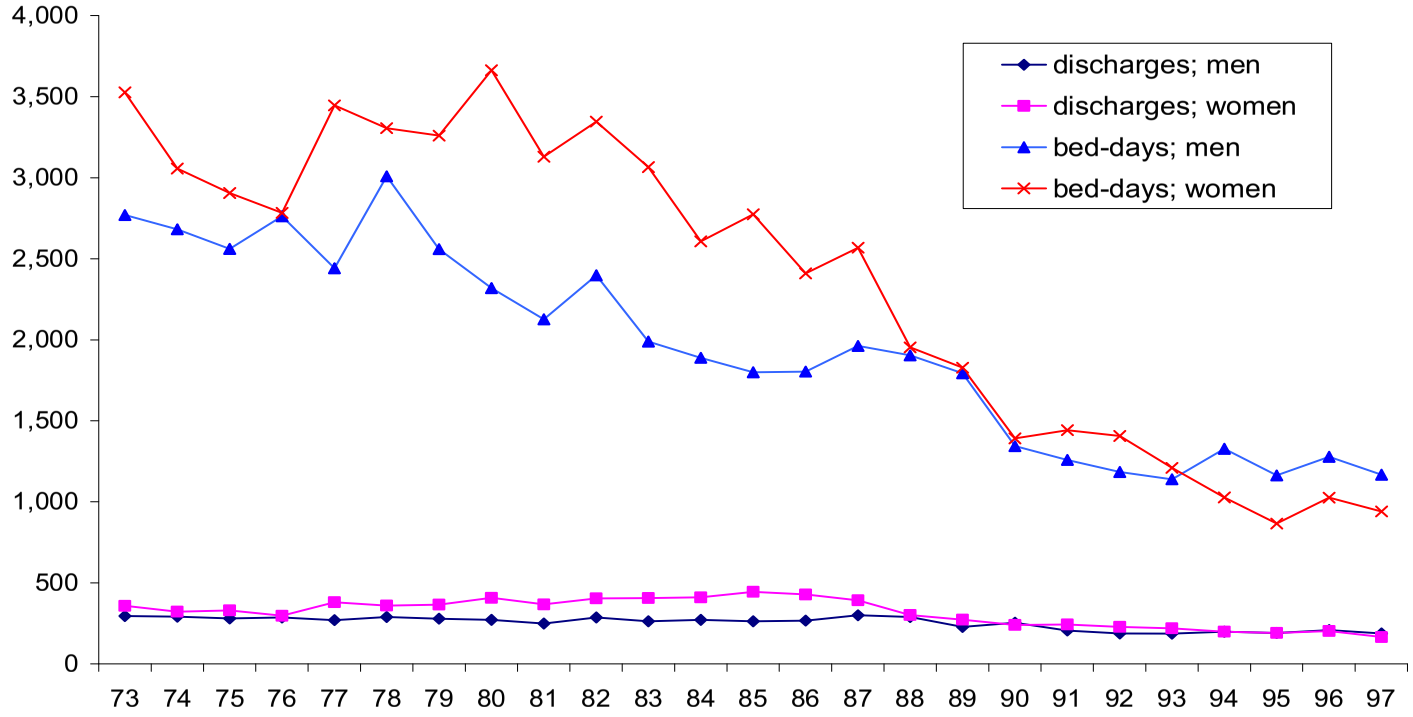

Figure 5. Discharges and bed-days per 1,000 patients per year with diabetes as the main diagnosis by sex during 1973-1977

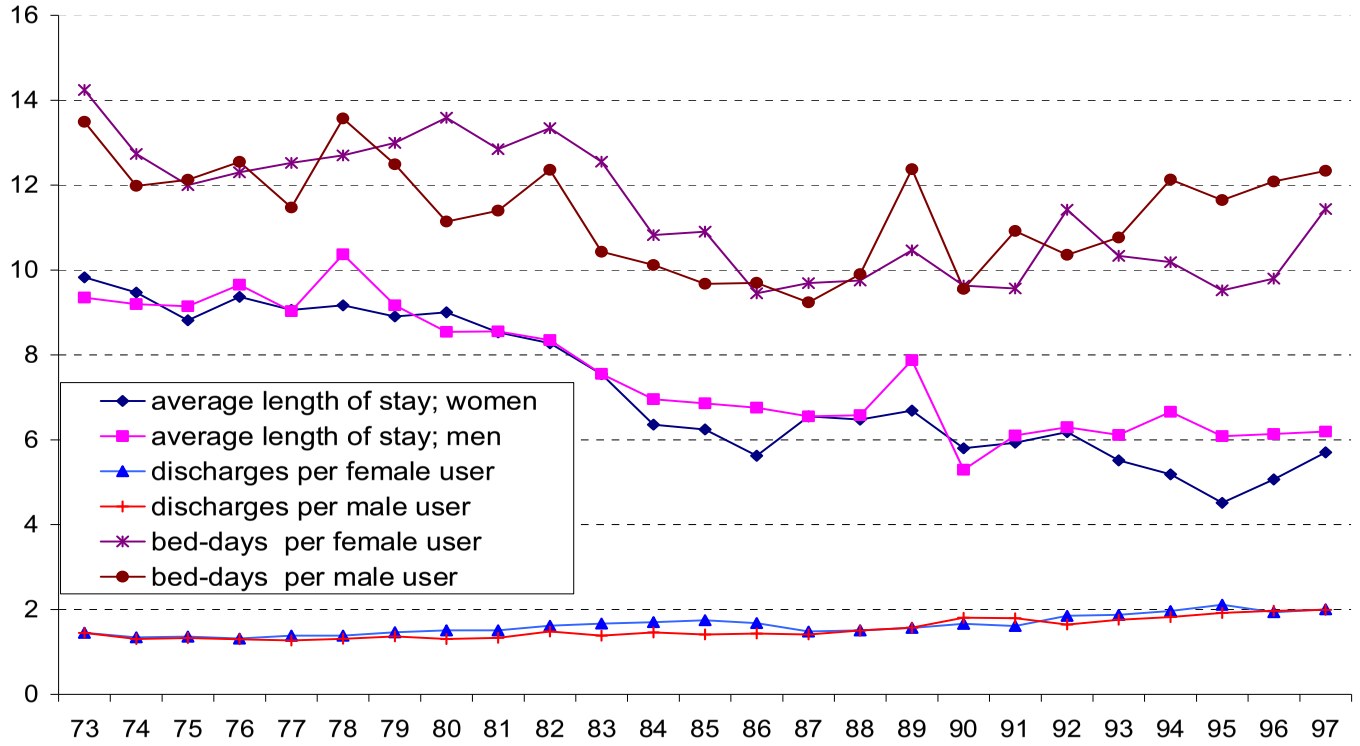

Figure 6. Average length of stay, discharges per user and bed-days per user with diabetes as the main diagnosis by sex during 1973-1977

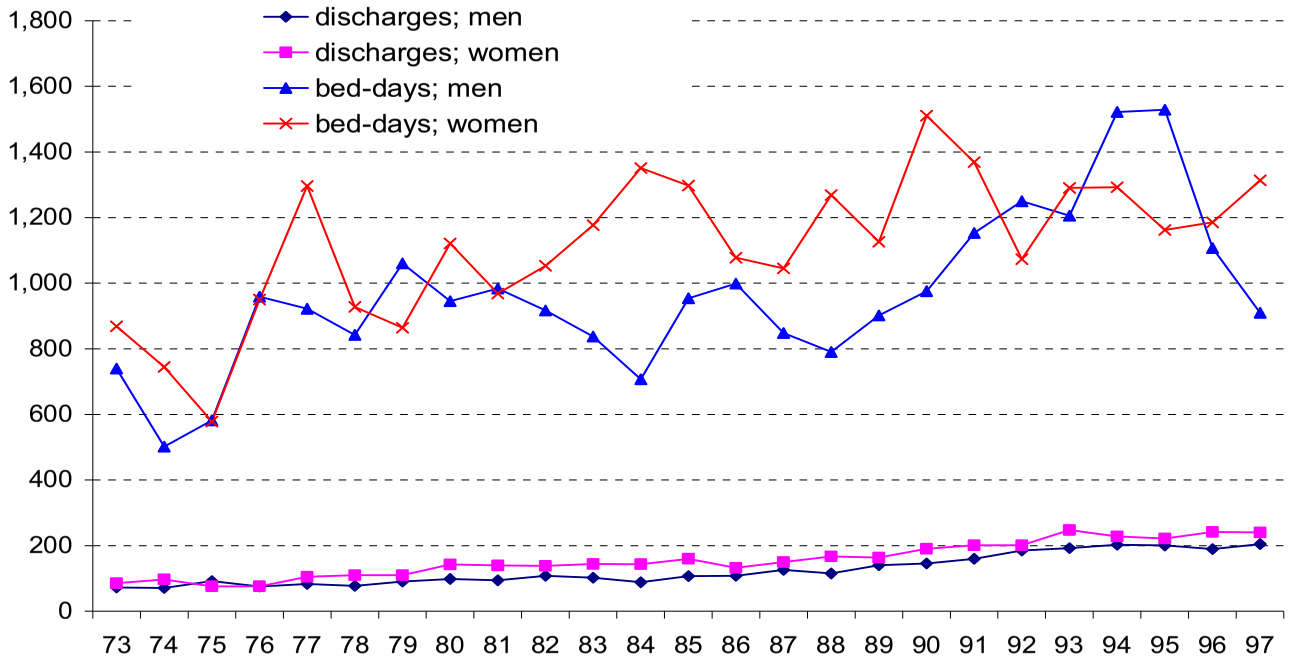

Figure 7. Discharges and bed-days per 1,000 patients per year with other disease than diabetes as the main diagnosis by sex during 1973-1977

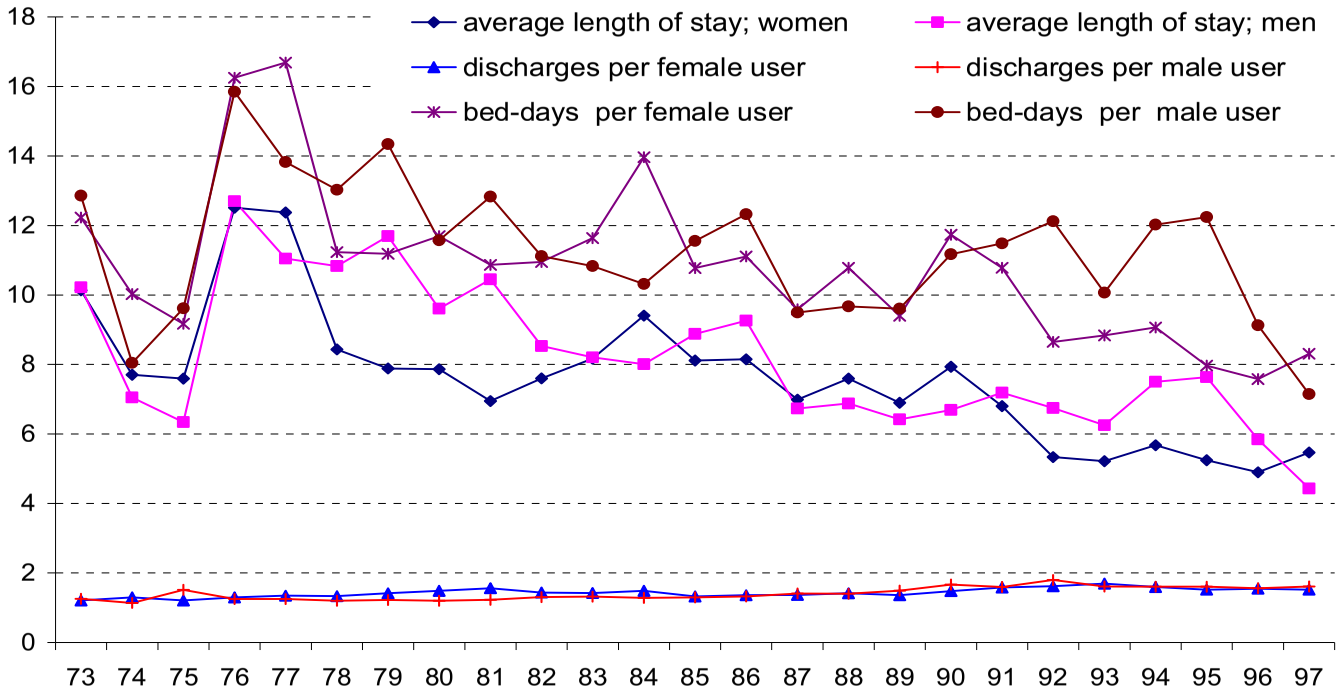

Figure 8. Average length of stay, discharges per user and bed-days per user with other disease than diabetes as the main diagnosis by sex during 1973-1977

5.3. Inpatient care of T1DM patients by duration of diabetes (9.5 years vs. 16.5 years) and sex

The mean age at diagnosis in the cohort was 10.3 years (SD 4.4; min 0.7 and max 17.9). When the average duration of diabetes was 9.5 or 16.5 years, the mean ages of patients were 20 years (min 10; max 27.5) and 27 years (min 17; max 34.5), respectively. The mean age at diagnosis for men was 0.7 years older than that for women in both cohorts with different durations of T1DM.

5.3.1 Hospital users

Table 6 shows the numbers of hospital users during the 3-year periods by sex, complication group and duration of diabetes (9.5 or 16.5 years on average). Hospital users due to T1DM without complications (ICD codes 2500B/25000) are also shown.

The total number of hospital users and the number of users due to other causes than complications declined, but the number of users due to complications almost doubled when the duration of diabetes increased. The number of users due to peripheral vascular complications increased almost 5-fold, that due to renal complications 3.5-fold and that due to ophthalmic complications 2.8-fold. The figure for neurological complications doubled. Although there were about 20% more men than women in both cohorts defined by the duration of diabetes, more women than men used hospital, and the sex difference was especially marked in use due to renal and ophthalmic complications.

5.3.2. Discharges

Total population

In **Figures 9** and **10,** the yearly shares of the discharges of each complication group from the total amount of discharges of all complications are depicted in the two cohorts with a different duration of T1DM. In the first cohort, with a T1MD duration of 9.5 years, other, ophthalmic and renal complications and coma were the most common complication groups and their shares of the total number of all discharges due to any cause were 5.2%, 3.8%, 1.9% and 1.7%, respectively. The nine complication groups presented in **Figure 9** formed 14.1% of the total number of all discharges during the follow-up period in the first cohort.

In the second cohort, with a T1DM duration of 16.5 years (**Figure 10**), ophthalmic, other, renal and peripheral vascular diseases formed the biggest shares of the numbers of discharges due to all complications. The growth of the share of discharges due to renal and ophthalmic

complications and the decrease of discharges due to other complications and coma are striking. Here, the nine complication groups formed 41.3% of the total number of all discharges, indicating a remarkable increase compared with the share in the first cohort. The shares of the discharges due to ophthalmic, other, renal and peripheral vascular diseases of the total number of all discharges rose to 13.8%, 11.4%, 10.1% and 2.7%, respectively.

Figure 11 shows the numbers of discharges per 1,000 patients per year by duration of diabetes. Ophthalmic diseases became the biggest complication group when the duration of diabetes increased. Peripheral vascular (+479%), renal (+457%), cardiovascular (+327%), ophthalmic (+281%), other (+129%) and neurological complications (+117%) showed the greatest increases in the yearly numbers of discharges per 1,000 patients when the duration of diabetes increased. Interestingly, the number of discharges due to diabetic coma showed a decline (-37%). Measured by discharges per 1,000 patients per year, the total number of discharges for these nine complication groups altogether had a 3-fold increase (+208%, from 57 to 175 discharges per 1,000 patients per year). In comparison, inpatient hospital use due to causes other than these complications decreased by over 28% (346 to 249 per 1,000 patients per year), and the total number of discharges due to any causes increased by 5% (403 to 423 per 1,000 patients per year), when the duration of diabetes increased.

Figure 12 shows the relative shares of the discharges per 1,000 patients per year of each complication group compared with 'itself' (shares of each complication group of the total discharges of that complication group in the two periods). As the duration of T1DM increased, the biggest relative increases were due to renal, peripheral vascular, cardiovascular and ophthalmic complications. The number of patients due to endocrine complications was negligible.

Figure 13 shows the mean numbers of yearly discharges per user in each complication group and for other use and total use in the two duration cohorts. Renal, cardiovascular and other complications showed the biggest rise (each +0.8 discharges per user) when the duration of T1DM increased. The mean figure for all nine complication groups changed from 1.5 to 2.5 discharges per hospital user. For total hospitalisations, the change was from 2.3 to 2.7 discharges per hospital user.

Table 6. Number of hospital users during the periods of three years by group of complication, sex and duration of diabetes.

	Nr. of females, T1DM 9-11 yrs.	Nr. of males T1DM 9-11 yrs.	Nr. of females, T1DM 16-18 yrs.	Nr. of males T1DM 16-18 yrs.	Total nr. of patients, T1DM 9-11 yrs.	Total nr. of patients, T1DM 16-18 yrs.
CERVASC	3	2	7	3	5	10
CARVASC	2	7	8	15	9	23
PERVASC	11	12	60	53	23	113
NEUROL	11	18	32	25	29	57
RENAL	47	33	173	107	80	280
ENDOCRIN	0	0	0	1	0	1
OPHTHALMIC	104	77	271	230	181	501
OTHER complicat.	112	122	166	164	234	330
COMA	45	38	18	32	83	50
Complications total	**295**	**274**	**555**	**495**	**569**	**1,050**
Hypoglycaemia	1	3	15	16	4	31
2500B/25000	1,106	1,042	469	457	2,148	926
OTHER use	1,249	1,268	968	901	2,517	1,869
TOTAL use	**1,349**	**1,378**	**1,213**	**1,171**	**2,727**	**2,384**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);

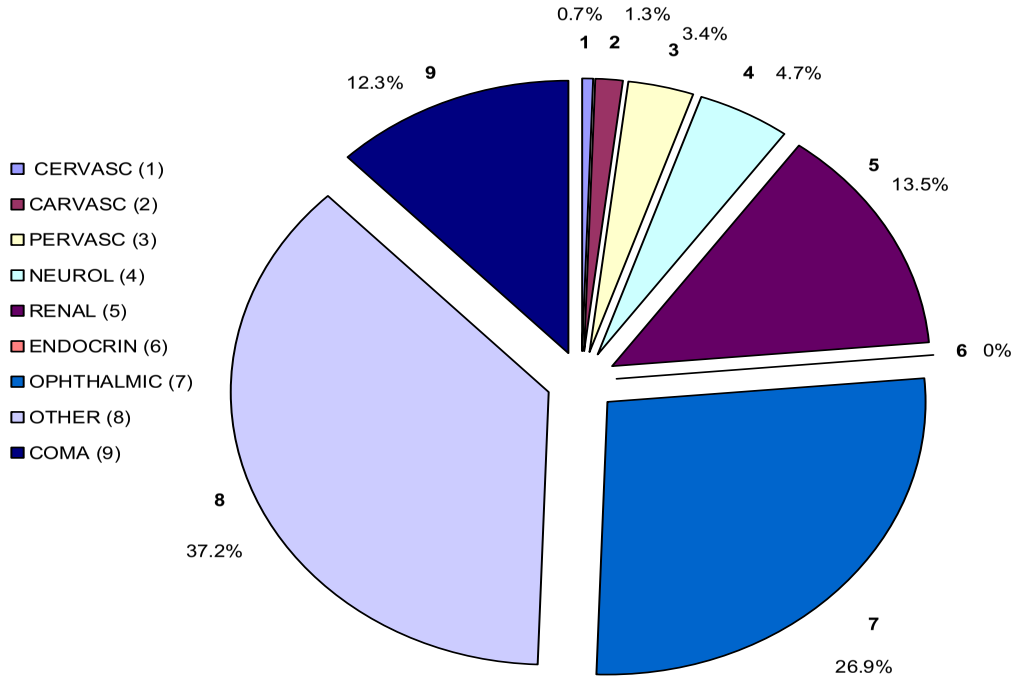

Figure 9. Percentages of yearly discharges due to complications by complication group, duration of T1DM 9.5 years

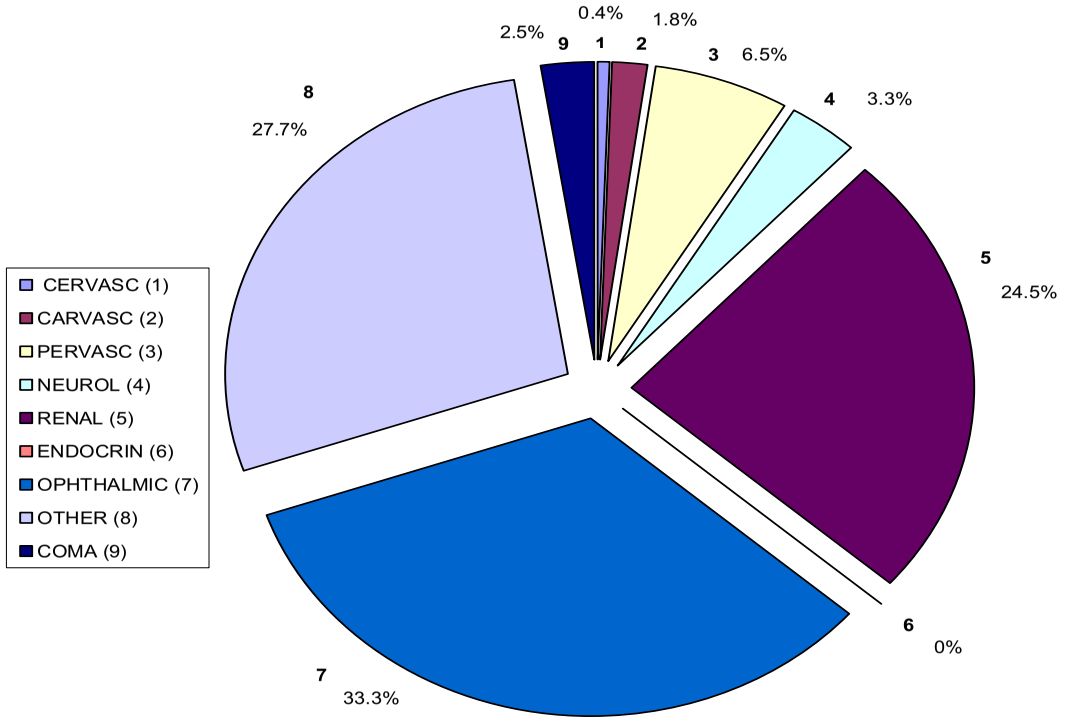

Figure 10. Percentages of yearly discharges due to complications by complication group, duration of T1DM 16.5 years

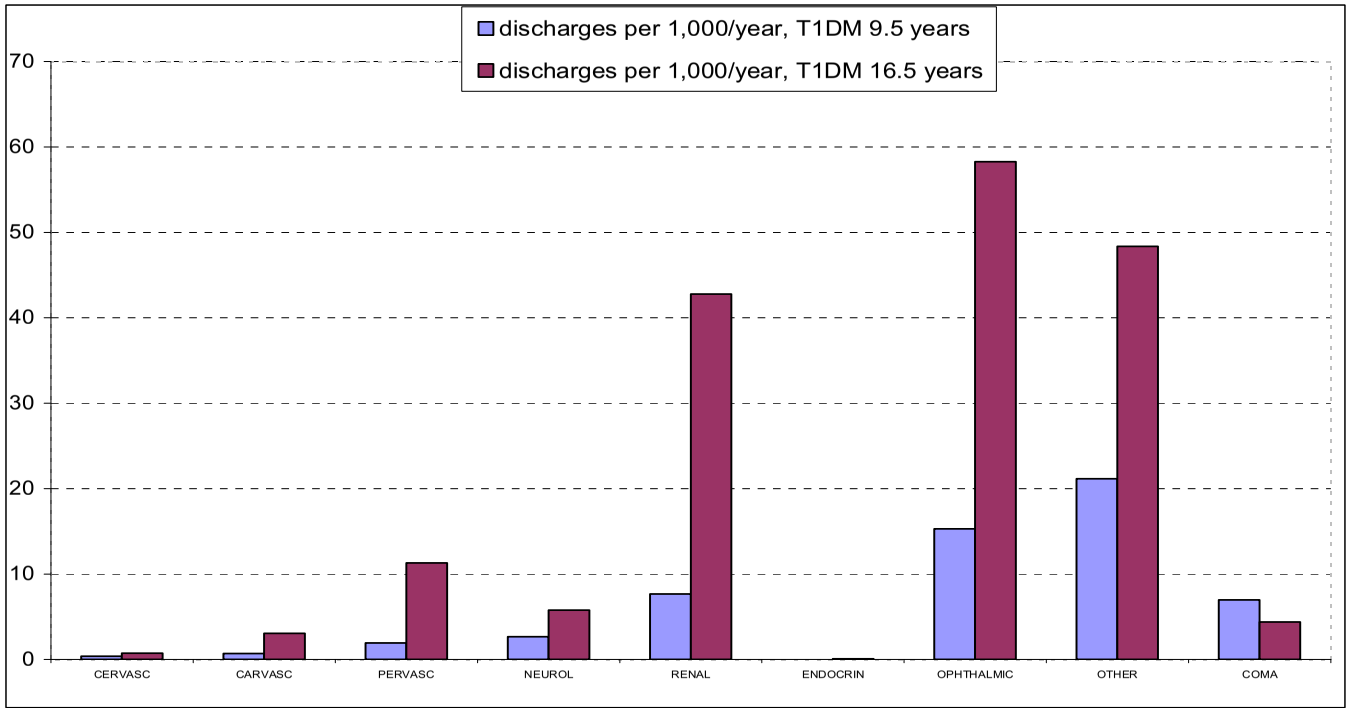

Figure 11. Mean number of yearly discharges per 1,000 patients by complication group and duration of T1DM

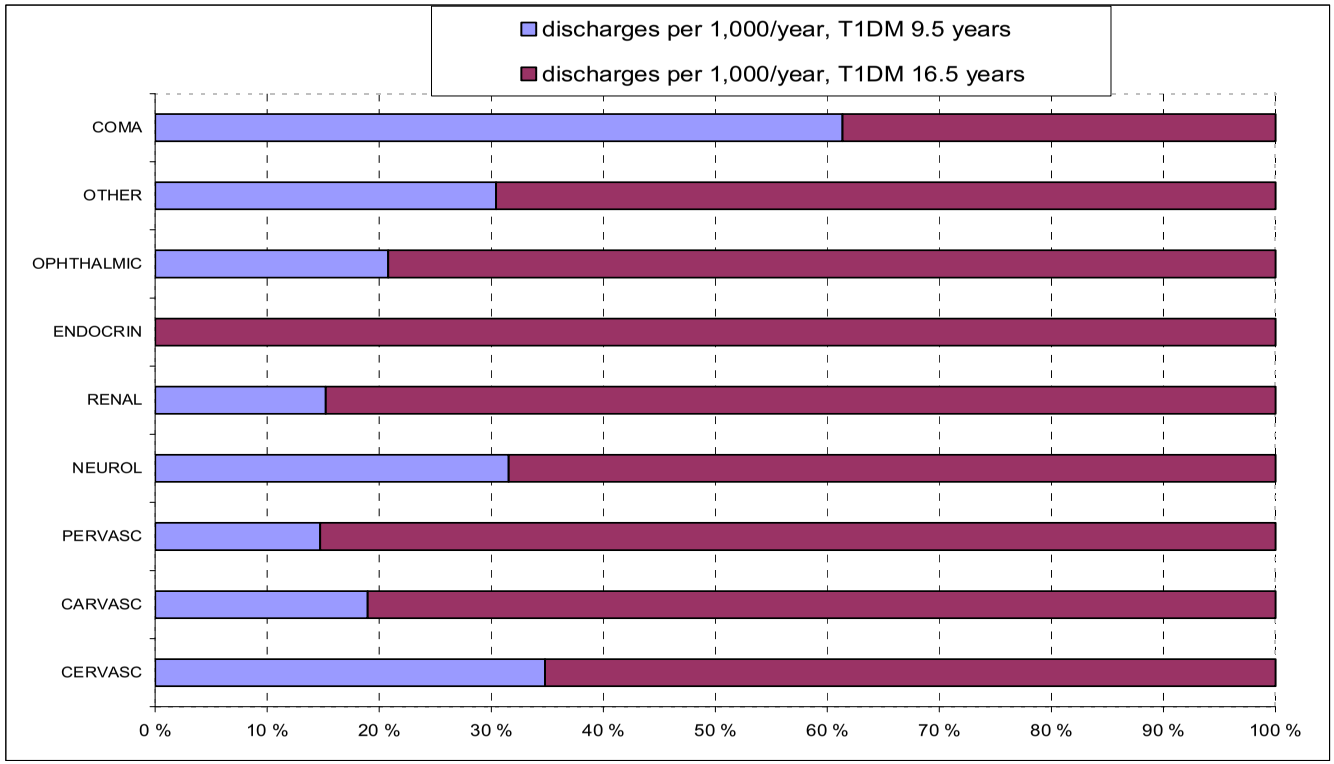

Figure 12. Proportional shares of yearly discharges of each complication group when the two observation periods are combined

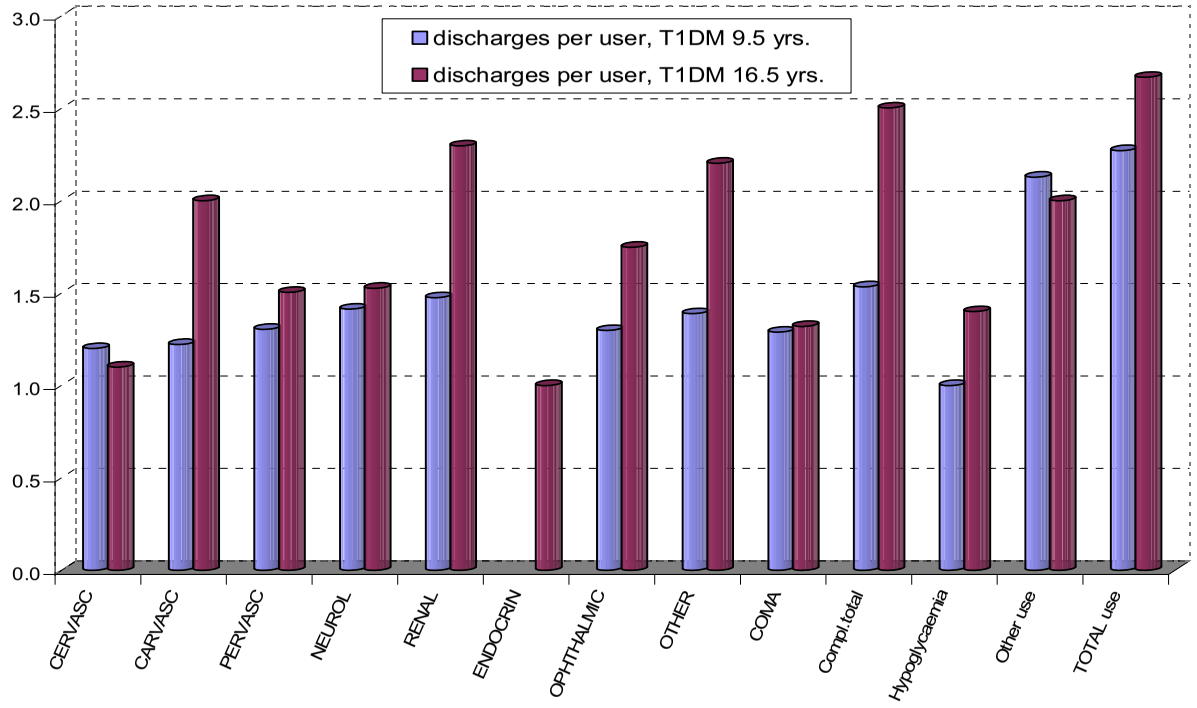

Figure 13. Mean numbers of yearly discharges per hospital user in each complication group and for other use and total use by duration of T1DM

Discharges by sex

In **Figure 14,** the shares of the yearly discharges of each complication group from the discharges of all complications are shown by sex in the two cohorts with a different duration of diabetes.

Among women, other complications, ophthalmic and renal complications and coma were the most common complication groups when the T1DM duration was 9.5 years. When the duration of diabetes increased, the share of the discharges due to coma showed the biggest drop in percentage units (-10.8%), while ophthalmic (+2.7%), renal (+13.9%) and other (-9.4%) complications remained the biggest groups. The growth of the shares of the discharges from total hospitalisations for any cause was biggest for renal (2.0% to 11.5%) and ophthalmic (4.3% to 13.7%) complications when the duration of diabetes increased.

Among men, other complications, ophthalmic and renal complications and coma were also the most common complication groups when the T1DM duration was 9.5 years. When the duration was 16.5 years, ophthalmic (+10.6%), other (-9.8%), renal (+7.5%) and peripheral vascular (+3.5%) complications were the biggest complication groups. Discharges due to coma dropped (-8.6%). The growth of the shares of the discharges from total hospitalisations for any cause for men was biggest for ophthalmic (3.2% to 13.8%) and renal (1.8% to 8.5%) complications when the duration of diabetes increased.

The biggest *differences between sexes* (**Appendix 2, Figure 1**) were the higher share of discharges due to ophthalmic complications among women in the 9.5-year cohort and the bigger share of discharges due to renal complications among women in the 16.5-year cohort. The biggest changes in the shares of discharges due to complications were the increases in the shares of women's renal complications and men's ophthalmic complications. In both cohorts, men's share of discharges due to other complications was somewhat higher than women's.

Figure 1 in **Appendix 2** shows the mean numbers of discharges per 1,000 patients per year by sex and duration of diabetes. Discharges of all complications increased clearly except, those due to coma, endocrine complications and cerebrovascular complications in men.

The most obvious *difference between sexes* was that women had clearly more discharges per 1,000 persons per year than men; in the 9.5-year cohort 45% more and in the 16.5-year cohort 40% more than men for all hospitalisations, and correspondingly, the shares were 39% and 36% more for complications. The biggest differences between sexes were that women had almost twice more yearly discharges due to ophthalmic complications than men in the first cohort and 39% more in the second one, and 53% more due to renal complications in the 9.5-year cohort and 89% more in the 16.5-year cohort.

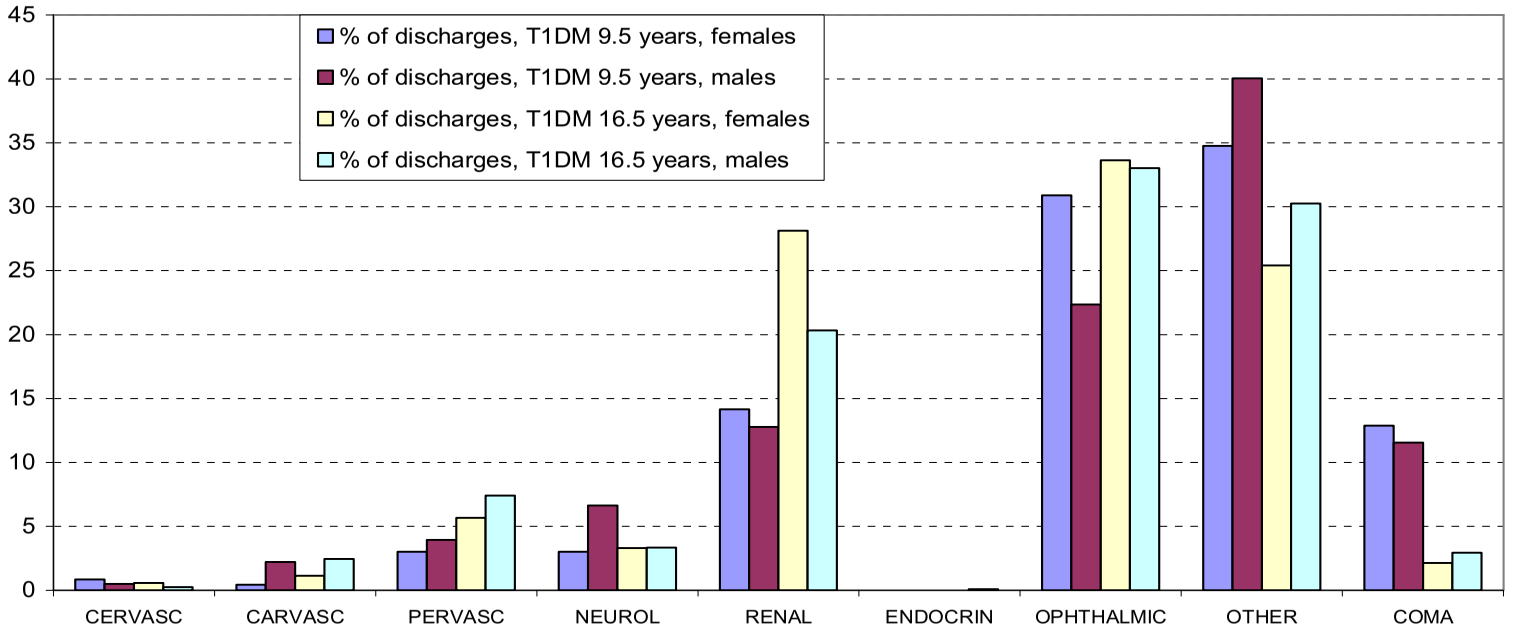

Figure 14. Percentages of yearly discharges due to complications out of all discharges due to complications by complication group and duration of T1DM and sex

The proportional changes in discharges between the cohorts are presented in **Appendix 2**, **Figure 2,** which shows marked increases in yearly discharges due to renal (+505%), peripheral vascular (+473%), neurological (+234%) and ophthalmic (+231%) complications among women. Yearly discharges due to cardiovascular complications had the biggest increase (+712%), but the number of users was small.

The mean number of yearly *discharges per 1,000 female* patients for the nine complication groups altogether had a 3-fold increase (+204%, from 67 to 205 discharges per 1,000 women per year). In comparison, the mean number of yearly discharges per 1,000 female patients due to causes other than these complications decreased by over 29% (419 to 296 per 1,000 women per year), and the mean number of yearly discharges due to any cause increased by 3% (486 to 501 per 1,000 women per year) when the duration of diabetes increased.

Proportional changes in yearly numbers of *discharges per 1,000 men* between the two duration cohorts are also shown in **Appendix 2**, **Figure 2**. Considerable increases can be seen in yearly discharges due to peripheral vascular (+484%), renal (+394%), ophthalmic (+358%) and cardiovascular (+242%) complications. The mean number of discharges for all complication groups increased over 3-fold (+210%, from 48 to 150 discharges per 1,000 men per year). Yearly discharges due to causes other than complications decreased by over 27% (287 to 209 per 1,000 men per year), and the mean number of discharges due to any cause increased by 7% (336 to 359 per 1,000 men per year) when the duration of diabetes increased.

Figure 3 in **Appendix 2** shows the mean numbers of yearly *discharges per hospital user by sex* during the 3-year follow-up periods in the two duration cohorts. Among women, the biggest increases occured in the hospital use due to cardiovascular (+1.0 discharge per user), renal (+0.9), all (+0.9) and other (+0.7) complications. Among men, the use due to other (+1.0 discharge per user), all (+1.0), renal and cardiovascular (+0.7 each) complications showed the biggest rises. The number of discharges per user was highest for renal (2.3 for both sexes), other and cardiovascular complications when the duration of diabetes increased.

5.3.3. Bed-days

Total population

The shares of yearly bed-days of each complication group (of bed-days of all complications) are described in the two duration cohorts in **Figures 15** and **16**. In the 9.5-year cohort, the shares of bed-days of other complications, ophthalmic complications, renal complications and coma were the highest, and their shares of the total amount of bed-days (any hospital use during the 3-year

period) were 6.0%, 3.6%, 2.2% and 1.5%, respectively. The nine complication groups formed 14.7% of the total amount of bed-days due to any cause during this period.

In the 16.5-year cohort (**Figure 16**), other, renal, ophthalmic and peripheral vascular diseases constituted the biggest shares of the amount of bed-days of all complications. Peripheral vascular, cardiovascular and especially renal complications showed the biggest increases in shares, while the shares of other complications and coma dropped clearly. The shares of other**,** renal**,** ophthalmic and peripheral vascular complications of the total amount of bed-days were 15%, 12.1%, 11.3% and 3%, respectively. The share of the first four complication groups combined (cerebro-, cardio-, peripheral vascular-, and neurologic complications) increased from 1.3% to 5.5%, as calculated from the total amount of bed-days.

Calculated as a total yearly number of bed-days used due to complications during the first and second follow-up periods of three years, the hospital use due to complications increased (6,742 to 18,158), while the number of bed-days used due to any cause decreased (45,986 to 40,669). The share of the bed-days of the nine complication groups of the total amount of bed-days rose from 14.7% to 44.6%, while the share of bed-days used due to treatment of other diseases than complications dropped considerably (from 85.3% to 55.4%).

The mean numbers of yearly *bed-days per 1,000 patients* per year by the complication group and the duration of diabetes are presented in **Figure 17**. According to this measure, other complications remained the biggest complication group when the duration of diabetes increased, while renal diseases replaced ophthalmic diseases as the second biggest group.

Measured by yearly bed-days per 1,000 patients, the hospital use due to cardiovascular (+1,406%), peripheral vascular (+474%), renal (+387%), ophthalmic (+185%), cerebrovascular (+131%), other (+126%) and neurological (+52%) complications increased when the duration of diabetes increased. Endocrine complications were practically non-existent (only 1 patient, 3 bed-days/3 years). Yearly bed-days due to diabetic coma decreased by 54%. Bed-days due to renal complications had the biggest absolute change (+261 bed-days per 1,000 patients per year).

In the amount of bed-days per 1,000 patients per year, there was a 2.8-fold increase (175%) for the nine complication groups (439 to 1,208 per 1,000 patients per year) when the duration of diabetes increased, but a drop (41%) for other diseases than complications of diabetes and even a decline (10%) in the total yearly number of bed-days (from 2,994 to 2,706 per 1,000 patients per year).

Figure 18 shows the relative shares of the yearly bed-days per 1,000 patients of each complication group compared with 'itself' (shares of each complication group of the total bed-days of that complication group in the two periods). The biggest relative increases were due to

cardiovascular, peripheral vascular, renal and ophthalmic complications as duration of T1DM increased.

Figure 19 shows mean yearly *bed-days per hospital user* during the two periods of three years. Notable is that those using hospital bed-days due to cardiovascular complications (increase from 3.0 to 17.3), other complications (11.8 to 18.5) and renal complications (12.9 to 17.6) used more bed-days per year when the duration of diabetes increased. Bed-days per user due to neurological diseases and coma and other diseases than complications decreased. The mean bed-days per user for all complications combined increased from 11.8 to 17.3 days.

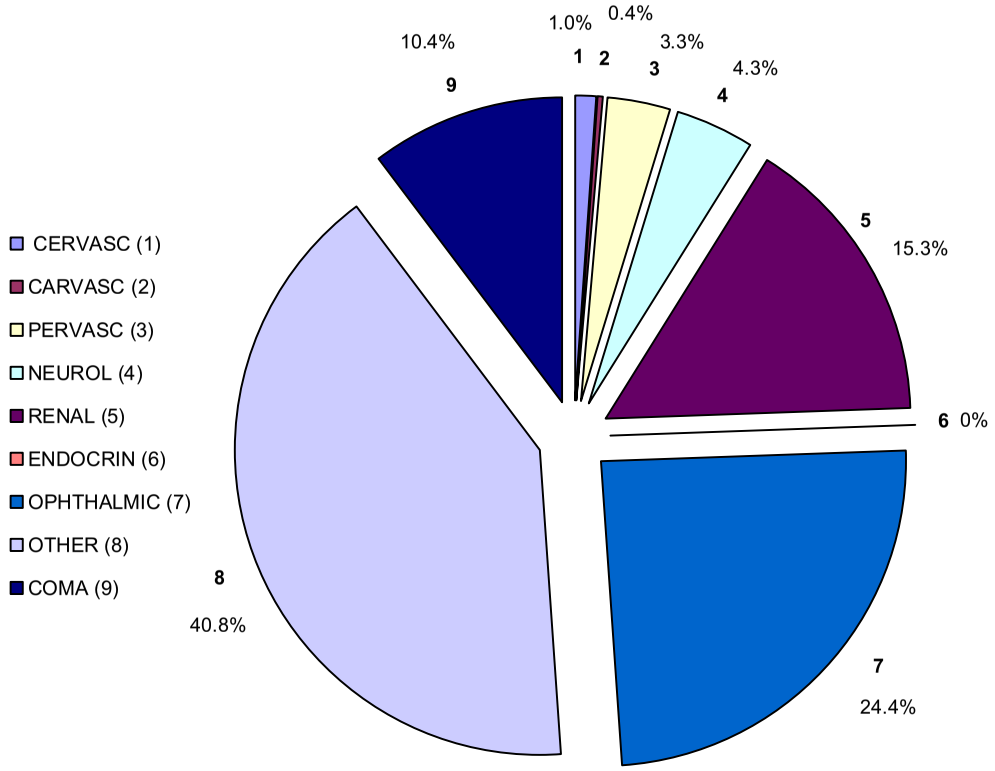

Figure 15. Percentages of yearly bed-days due to complications by complication group, duration of T1DM 9.5 years

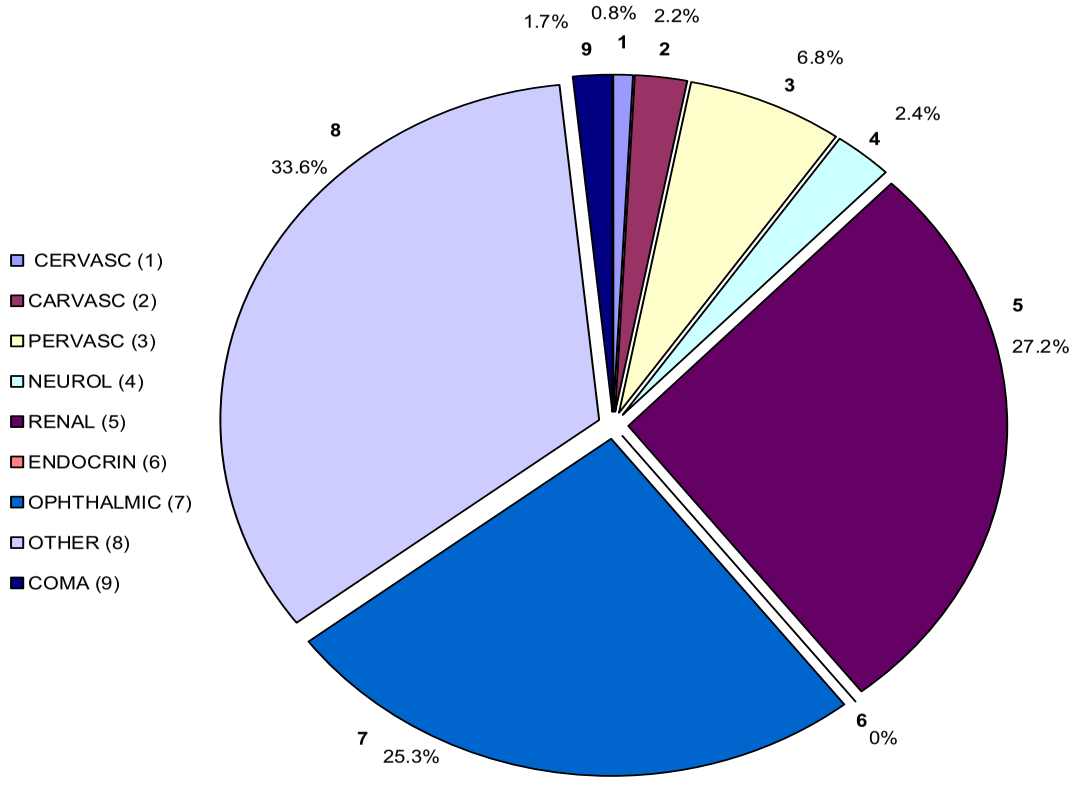

Figure 16. Percentages of yearly bed-days due to complications by complication group, duration of T1DM 16.5 years

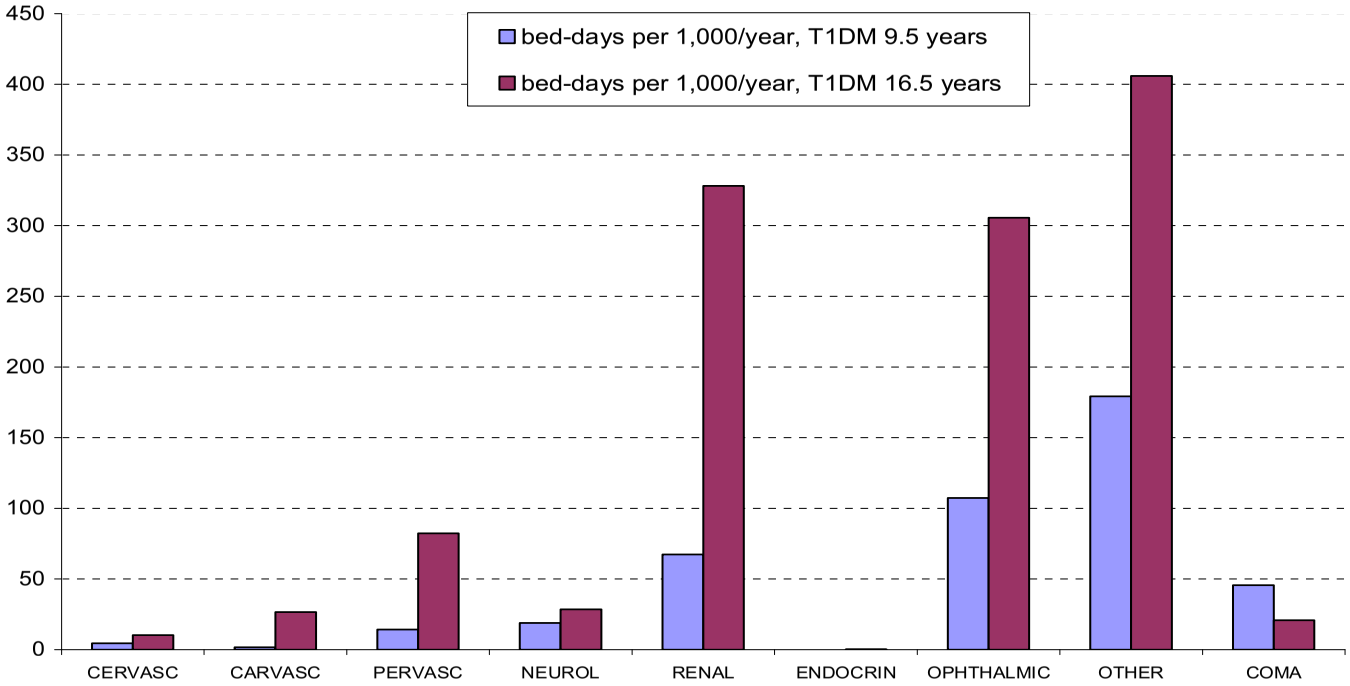

Figure 17. Mean number of yearly bed-days per 1,000 patients by complication group and duration of T1DM

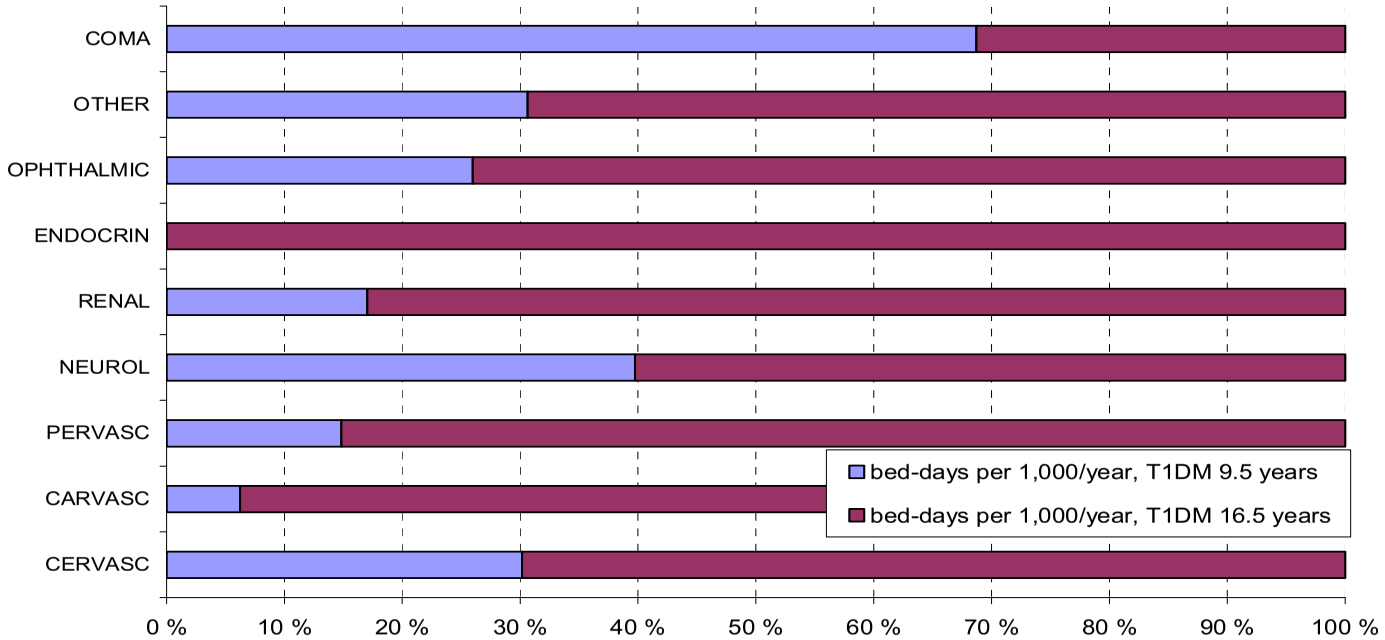

Figure 18. Proportional shares of yearly bed-days per 1,000 patients of each complication group when the two observation periods are combined

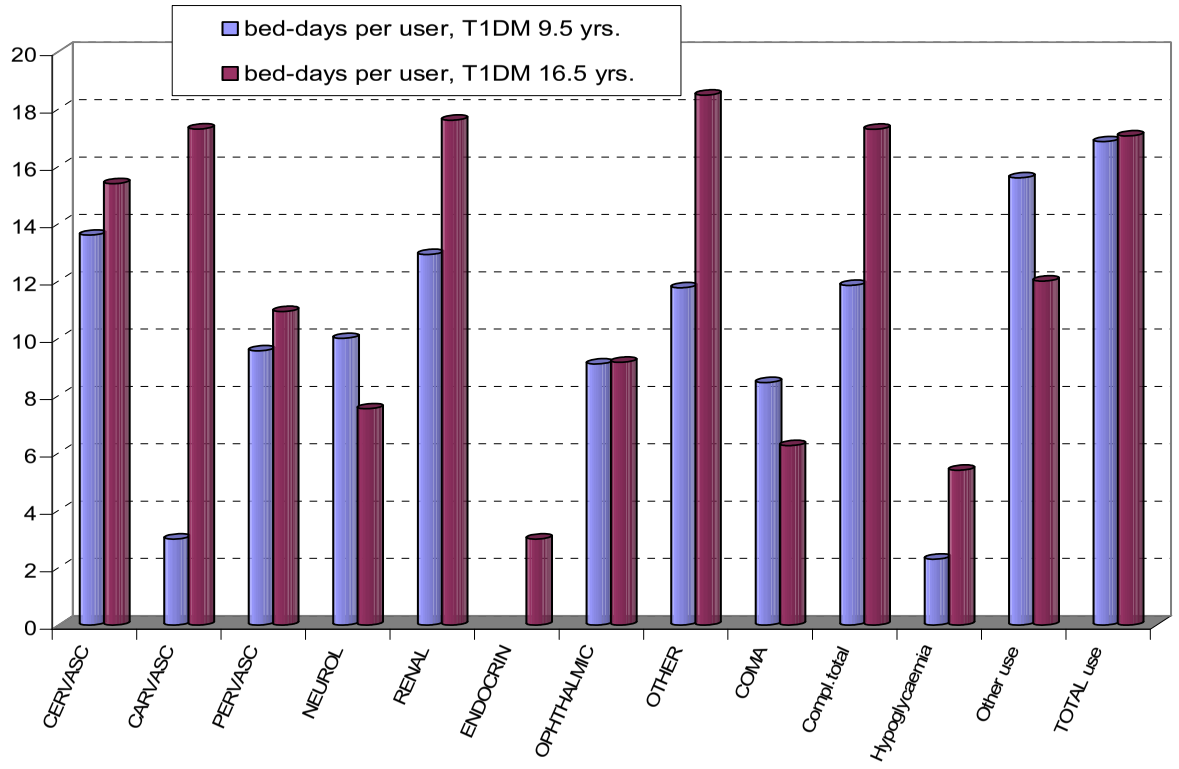

Figure 19. Mean numbers of yearly bed-days per hospital user in each complication group and for other use and total use by duration of T1DM

Bed-days by sex

Figure 4 in **Appendix 2** depicts the shares of yearly bed-days of each complication group (from the total amount of bed-days due to complications) by sex in the two duration cohorts. *Among women*, other and ophthalmic complications caused the highest number of bed-days in the 9.5-year cohort, followed by renal complications and coma. When the duration of diabetes increased, the share of bed-days due to coma showed the biggest drop in percentage units (-9.5%), while other (-5.4%), renal (+12.6%) and ophthalmic (-2.7%) complications became clearly the biggest groups, followed by peripheral vascular complications (+1.7%).

The growth of shares in bed-days of the total amount of bed-days for any cause was biggest for renal (2.4% to 13.1%), other (5.3% to 14.1%) and ophthalmic (4.2% to 11.9%) complications when the duration of diabetes increased. The combined share of bed-days for the nine complication groups of total hospitalisations increased considerably (14.3% to 44.4%) with the increase of the duration of diabetes.

Among men, measured by bed-days, other complications clearly formed the most common complication group in the 9.5-year cohort, followed by ophthalmic and renal complications and coma. In the 16.5-year cohort, other complications remained still the biggest group (change -9.3%), followed by renal (change +10.9%), ophthalmic (change +4.3%) and peripheral vascular complications (change +5.5%). Bed-days due to coma dropped (–7.9%).

The growth of shares in bed-days of the total amount of bed-days for any cause among men was biggest for other complications (6.8% to 16%), renal (2.1% to 11.1%) and ophthalmic (2.9% to 10.7%) complications when the duration of diabetes increased. The change in the shares of bed-days of all complication groups combined was notable (15.1% to 44.9%).

The biggest *differences between sexes* were the bigger share of bed-days due to ophthalmic complications among women (difference 9.7 percentage units) and that due to other complications among men (difference 8 percentage units) in the 9.5-year cohort, that due to renal complications among women (difference 4.7 percentage units) and that due to peripheral complications among men (difference 4.6 percentage units) in the 16.5-year cohort. The biggest changes in the shares of bed-days of complications were the increases in the shares of women's and men's renal complications.

Figure 5 in **Appendix 2** shows the mean number of *bed-days per 1,000 patients* per year by sex and duration of diabetes. *Among women* bed-days of all complications, except those due to coma, increased clearly. The proportional changes between the duration cohorts are shown in **Figure 2** of **Appendix 2.** Considerable increases occurred in yearly bed-days per 1,000 females due to

renal (+379%), peripheral vascular (+340%), neurological (+222%) and ophthalmic (+151%) complications. Bed-days due to cardiovascular and cerebrovascular complications had big increases, but here the numbers of female users were small. Yearly numbers of bed-days for coma dropped markedly (-64%).

The total number of yearly bed-days per 1,000 female patients for these nine complication groups altogether had a 2.7-fold increase (+173%, 506 to 1,383 bed-days per 1,000 women per year). In comparison, the yearly bed-days per 1,000 female patients due to causes other than complications decreased by over 43% (3,038 to 1,731 per 1,000 women per year) and the total number of yearly bed-days due to any causes decreased by 12% (3,543 to 3,114 per 1,000 women per year) when the duration of diabetes increased.

Proportional changes in yearly numbers of *bed-days per 1,000 men* between the duration cohorts are also shown in **Figure 2** in **Appendix 2**. Considerable increases can be seen in yearly bed-days due to peripheral vascular (+589%), renal (+397%), ophthalmic (+239%) and cardiovascular (+689%, n=7 to 15 patients) complications. The yearly number of bed-days due to coma dropped (-43%). The total yearly number of bed-days used per 1,000 men due to all complication groups increased 2.8-fold (+177%, from 384 to 1,063 bed-days per 1,000 men per year). Yearly bed-days due to causes other than complications decreased by over 40% (2,158 to 1,303 per 1,000 men per year) and the yearly total number of bed-days due to any causes decreased by 7% (2,542 to 2,366 per 1,000 men per year) when the duration of diabetes increased.

A distinct *difference between sexes* was that women clearly used more bed-days per 1,000 patients per year than men; in the 9.5-year cohort 39% more and in the 16.5-year cohort 32% more than men for all hospitalisations, and correspondingly, 32% and 30% more for complications.

The biggest differences between sexes were that women had almost 100% more yearly bed-days (per 1,000 patients) due to ophthalmic complications than men in the 9.5-year cohort and 47% more in the 16.5-year cohort, and 60% more yearly bed-days due to renal complications in the 9.5-year cohort and 55% more in the 16.5-year cohort. Men had 52% more yearly bed-days due to peripheral complications when diabetes lasted longer. The number of women's bed-days due to coma dropped more than men's.

Figure 6 in **Appendix 2** shows the mean numbers of yearly *bed-days per hospital user* by sex during the 3-year follow-up periods in the duration cohorts. *Among women*, the biggest increases occurred in the amount of bed-days due to other (+6.4 bed-days per user), all (+5.1) and renal

(+3.6) complications. The mean numbers of bed-days per user of cardiovascular (+24.8) and cerebrovascular (+6.4) complications had notable increases, but the numbers of hospital users due to these complications were smaller than those due to other complication groups. Bed-days due to other causes than complications dropped (16.9 to 12.2 bed-days per user).

Among men, the mean number of cardiovascular bed-days per hospital user (+9.2), other (+7.1), renal (+6.6), all (+5.8) and peripheral vascular (+5.2) complications showed marked increases. When the duration of diabetes was longer, men clearly had more bed-days per user due to peripheral vascular (15.1 vs. 7.3) and renal (20.1 vs. 16.1) complications than women.

5.3.4. Length of stay

Total population

Figure 20 depicts the average LOS in inpatient care according to the duration of diabetes. Generally, LOS was longest for the treatment of cerebrovascular complications, and here it also increased with the longer duration of diabetes. The biggest increase in LOS was for the treatment of cardiovascular complications (2.5 to 8.7 days). LOS for the treatment of neurological and opthalmic complications and coma had a drop of about 2 days. All complication groups combined had a drop in LOS from 7.9 to 7 days, and LOS for total inpatient care (for any cause) dropped from 7.6 to 6.9 days.

Length of stay by sex

Figure 7 in **Appendix 2** shows LOS by sex and duration of diabetes. Generally, among both sexes, LOS for many complications seemed to decrease as diabetes lasted longer, and men seemed to have stayed slightly longer in hospital during their treatment periods than women. LOS due to ophthalmic complications and coma had a clear drop among both sexes, as did LOS due to renal complications among women, when the duration of diabetes increased. LOS due to peripheral vascular complications clearly dropped among women, but increased among men, when diabetes lasted longer. However, LOS due to cardiovascular complications increased in both sexes when the duration of T1DM increased. LOS due to cerebrovascular complications increased in women, but decreased in men. However, the number of patients in these groups was small, which affect the reliability of these results. LOS due to other causes than complications dropped more than LOS due to complications.

Table 7 shows the mean LOS calculated by two different methods. In calculating 'LOS by time', bed-days in the treatment period, that started before or continued after the observation period were omitted. 'LOS by discharge' takes into account all bed-days within a particular treatment period. As shown, 'LOS by discharge' may yield a somewhat longer LOS than 'LOS by time'.

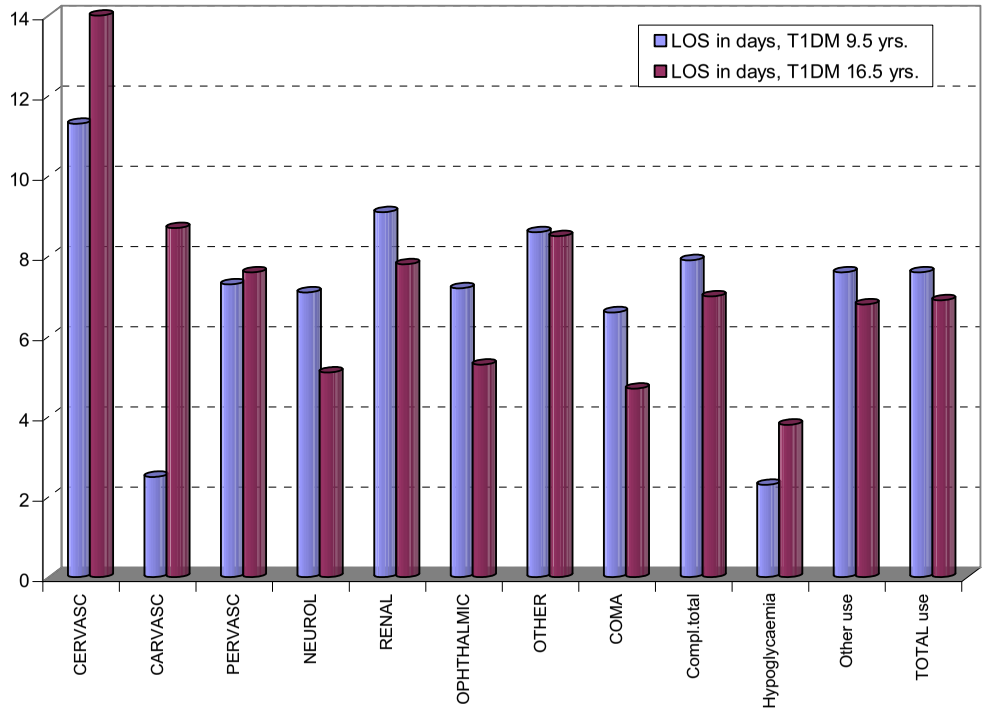

Figure 20. Mean length of stay (LOS) in hospital in each complication group and for other use and total use by duration of T1DM

Table 7. Mean lengths of stays (LOS) in hospital and their standard deviations (SD) by complication group, duration of T1DM and sex

	T1DM 9.5 years											
	Females				Males				Total			
	LOS by time	SD	LOS by discharge	SD	LOS by time	SD	LOS by discharge	SD	LOS by time	SD	LOS by discharge	SD
CERVASC	9	8.7	9	8.7	16	19.8	16	19.8	11.3	11.7	11.3	11.7
CARVASC	1	0	1	0	2.8	1.3	2.8	1.3	2.5	1.4	2.5	1.4
PERVASC	7.2	7.6	7.2	7.6	7.4	5.9	7.4	5.9	7.3	6.6	7.3	6.6
NEUROL	5.5	5.6	5.5	5.6	7.9	7.8	7.9	7.8	7.1	7.1	7.1	7.1
RENAL	8.9	10.5	9.6	11.9	8.6	8.9	8.6	8.9	8.8	9.8	9.1	10.7
ENDOCRIN												
OPHTHALMIC	7.1	5.3	7.3	5.5	6.9	5	7.1	5.1	7	5.2	7.2	5.4
OTHER complic.	8	7.3	8	7.3	8.9	12.2	9.2	12.7	8.5	10	8.6	10.4
COMA	6.4	4.6	6.4	4.6	6.8	5.1	6.9	5.2	6.6	4.8	6.6	4.9
Complications total	**7.5**	**7**	**7.7**	**7.4**	**7.9**	**9.3**	**8.1**	**9.6**	**7.7**	**8.1**	**7.9**	**8.5**
Hypoglycaemia	5		5		1.3	0.6	1.3	0.6	2.3	1.9	2.3	1.9
Other use	7.3	9	7.6	12.6	7.5	12.3	7.6	12.7	7.4	10.6	7.6	12.6
Total use	**7.3**	**8.7**	**7.6**	**12.1**	**7.6**	**11.9**	**7.7**	**12.3**	**7.4**	**10.3**	**7.6**	**12.1**

	T1DM 16.5 years											
	Females				Males				Total			
	LOS by time	SD	LOS by discharge	SD	LOS by time	SD	LOS by discharge	SD	LOS by time	SD	LOS by discharge	SD
CERVASC	16.1	17.3	16.1	17.3	8.3	4	8.3	4	14	15.1	14	15.1
CARVASC	12.9	16.2	12.9	16.2	6.4	6.5	6.4	6.5	8.7	11.2	8.7	11.2
PERVASC	5.5	5	5.5	5	8.8	10.3	9.3	11.8	7.3	8.4	7.6	9.4
NEUROL	5.3	7.2	5.6	7.4	4.5	5.3	4.6	5.3	4.9	6.3	5.1	6.5
RENAL	7.1	10.1	7.2	10.2	8.6	10.2	8.9	10.6	7.7	10.2	7.8	10.4
ENDOCRIN					3	0	3	0	3	0	3	0
OPHTHALMIC	5.4	4.5	5.4	4.5	5.1	4.3	5.1	4.3	5.2	4.4	5.3	4.4
OTHER complic.	8.4	13	8.6	13.7	8.4	11.5	8.4	11.5	8.4	12.2	8.5	12.6
COMA	4.5	3.4	4.5	3.4	4.9	5.2	4.9	5.2	4.7	4.4	4.7	4.4
Complications total	**6.8**	**9.4**	**6.9**	**9.7**	**7.1**	**9**	**7.2**	**9.3**	**6.9**	**9.2**	**7**	**9.5**
Hypoglycaemia	6.2	11.9	6.2	11.9	2.1	2	2.1	2	3.8	7.9	3.8	7.9
Other use	5.8	26.3	6.6	56.2	6.2	20.5	7	36	6	24	6.8	48
Total use	**6.2**	**21.1**	**6.7**	**43.6**	**6.6**	**16.7**	**7.1**	**28**	**6.4**	**19.2**	**6.9**	**37.3**

LOS by time= the bed-days belonging to the observation period

LOS by discharge= all the bed-days belonging to the actual treatment period, which a patient stayed in a hospital

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);

5.3.5. Most common diagnoses

Table 1 in Appendix 1 shows the individual diagnoses (ICD-8/ICD-9), that caused the most bed-days during the two 3-year observation periods. Regarding total inpatient care, diabetes without complications (25000/2500B) was a dominating diagnosis when diabetes had lasted 9-11 years, representing 61% of all bed-days and 71% of bed-days due to other causes than complications. The number of bed-days due to the treatment of diabetes without complications was 4.2-fold that due to the treatment of complications when diabetes had lasted 9-11 years. Its share dropped by 72%, when the duration of diabetes increased, representing 19% of all bed-days and 34% of bed-days due to other causes than complications. It is notable that the number of bed-days due to treating complications was now 2.4-fold that due to treating other diseases than complications.

The number of bed-days for treating diabetic nephropathy (25004/2503B) showed a 7-fold rise when the duration of diabetes increased.

The numbers of bed-days for treating all other defined complications (25008/2507B), ophthalmic complications and retinopathy (25002-3/2504B/3620B) increased over 3-fold, while the number of bed-days for treating non-defined complications (25009/2508B) decreased 63% when the duration of diabetes increased.

The treatment of mental diseases and disorders (e.g. various personality disorders. schizophrenia. depression) seemed to cause a lot of bed-days and long treatment periods, although most of the inpatient periods were caused by only few patients. The longest treatment periods were for treating schizophrenia (71 days in the younger cohort and 330 days in the older one). Bed-days due to certain other mental disorders also increased as diabetes lasted longer.

Measured by bed-days and discharges, ketoacidosis (2501B), diabetic microangiopathy (2506B), diabetic neuropathy (25005/2505B) and coma (25007/2502B) were among the most common diagnoses in the cohort with a longer duration of diabetes.

The changes in the numbers of bed-days during the two 3-year periods relating to certain diagnoses in opthalmic complications turned out to be interesting. The number of bed-days due to treatment of glaucoma (375.xx/365.x) was 8-fold and that due to treatment of diabetic retinopathy (25002/3620B) 2.7-fold in the older cohort compared with the younger one. The number of bed-days due to treating cataracts (25001/3664A/374.xx/366.x) increased by 36% as diabetes lasted longer.

5.3.6. T1DM-related hospital use

T1DM-related hospital use (ICD-8 code 25000 and ICD-9 code 2500B, and complications) is presented below in this subsection separately, as is total hospital use.

Table 8 shows the numbers of total and T1DM-related bed-days by sex in the two 3-year observation periods in the cohort. As shown, the number of bed-days used for treatment of T1DM without complications had a considerable drop, while that for treatment of complications increased notably.

Table 8. Numbers of total and T1DM-related bed-days by sex in two observation periods of three years.

	Number of bed-days					
	T1DM 9-11 years			T1DM 16-18 years		
	Females	Males	Total	Females	Males	Total
ICD codes 25000/2500B	15,499	12,545	28,044	4,156	3,555	7,711
Complications	3,507	3,235	6,742	9,443	8,715	18,158
= T1DM use	19,006	15,780	34,786	13,599	12,270	25,869
Total use	24,571	21,415	45,986	21,265	19,404	40,669

Table 9 shows the yearly number of bed-days by sex and duration of T1DM among patients without complications (ICD codes 25000/2500B) and those with complications per 1,000 patients per year. The table clearly shows women's dominance in the use of bed-days, especially bed-days due to T1DM without complications (50.1% more bed-days than men when T1DM had lasted 9.5 years and 40.4% more after a duration of 16.5 years). Women had 30%-50% more bed-days than men in all of the categories shown in the table. The sex difference in T1DM-related hospital use levelled off somewhat as diabetes lasted 16.5 years (46.3% to 33.1%).

Table 9 shows that there were notable changes in 7 years (duration of T1DM 9.5 years vs. 16.5years) in the use of bed-days. The yearly number of bed-days of T1DM without complications dropped by 72% in 7 years (the amount was 3.5 times bigger in the 9.5-year cohort), while bed-days due to complications of T1DM 'acted' in the opposite way, their number increased 2.8-fold in 7 years. The number of bed-days of T1DM-related hospital use dropped by

24% (females -27%. males -20%) in 7 years; its share was almost one-third bigger in the 9.5-year cohort. The number of total bed-days for any cause per 1,000 patients per year decreased by 9.6% (females –12%. males –7%) in 7 years.

Table 9. Numbers of total and T1DM-related yearly bed-days by sex per 1000 patients by duration of T1DM

	Number of bed-days per 1,000/year			
	T1DM 9.5 years			
	Females	Males	Total	Difference (%) between sexes
ICD codes 25000/2500B	2,235	1,489	1,826	50.1
Complications	506	384	439	31.7
= T1DM use	2,741	1,873	2,265	46.3
Total use	3,543	2,542	2,994	39.4
	T1DM 16.5 years			
	Females	Males	Total	Difference (%) between sexes
ICD codes 25000/2500B	609	433	513	40.4
Complications	1,383	1,063	1,208	30.2
= T1DM use	1,992	1,496	1,721	33.1
Total use	3,114	2,366	2,706	31.6

There were considerable changes in the structure of hospital use with longer disease duration. When diabetes had lasted on average 9.5 years, 61% of the total yearly bed-days per 1,000 patients was due to T1DM without complications, compared with 19% when diabetes had lasted 16.5 years. The corresponding shares due to complications were 14.7% and 44.6%; and 75.6% and 63.6% for T1DM-related hospital use when the disease lasted longer. Between sexes, the differences in the structures were rather small; when T1DM had lasted 9.5 years, women seemed to use slightly more bed-days for the treatment of T1DM without complications than male patients. The difference levelled off with longer disease duration.

Around 20% of T1DM-related bed-days was due to complications when diabetes had lasted on average 9.5 years, but the share rose to over 70% when diabetes had lasted 16.5 years.

Table 10 shows the numbers of discharges due to T1DM without complications, due to T1DM with complications, due to total T1DM-related hospital use and due to total hospital use (for any cause) per 1,000 patients per year by sex and duration of diabetes, and the differences between the sexes. Women's dominance was even clearer in the yearly numbers of discharges than in

those of bed-days, especially in the numbers of discharges when the duration of diabetes was 9.5 years; women used hospital over 55% more frequently than men due to T1DM without complications, and their T1DM-related hospital use was almost 52% more frequent.

Table 10. Numbers of total and T1DM-related yearly discharges by sex per 1000 patients by duration of T1DM

	Number of discharges per 1,000/year			
	T1DM 9.5 years			
	Females	Males	Total	Difference (%) between sexes
ICD codes				
25000/2500B	312	201	251	55.2
Complications	67	48	57	39.6
= T1DM use	379	250	308	51.6
Total use	486	335	403	45.1
	T1DM 16.5 years			
	Females	Males	Total	Difference (%) between sexes
ICD codes				
25000/2500B	123	85	102	44.7
Complications	205	150	175	36.7
= T1DM use	328	235	227	39.6
Total use	501	359	423	39.6

There were notable changes in 7 years (duration of diabetes 9.5 years vs. 16.5 years) in the frequency of discharges. The yearly number of discharges per 1,000 patients due to T1DM without complications dropped by 59% in 7 years (their amount being 2.5 times bigger in the younger cohort), while the number of discharges per 1,000 patients due to complications of T1DM increased 3-fold in 7 years. The number of discharges per 1,000 patients in T1DM-related hospital use dropped by 10% (females -14%, males -6%) in 7 years. However, the yearly number of all discharges per 1,000 patients for any cause increased little in 7 years.

Table 11 presents the LOS due to T1DM without complications. T1DM with complications, total T1DM-related hospital use and total hospital use (due to any cause) per year by sex and duration of diabetes. LOS decreased clearly with diabetes duration, especially in the treatment of

T1DM without complications (-2.3 days). In their treatment periods, male patients stayed a bit longer in hospital than female ones.

Table 11. Total and T1DM-related yearly mean LOS in hospital by sex by duration of T1DM

	Mean length of stay in hospital					
	T1DM 9.5 years			T1DM 16.5 years		
	Females	Males	Total	Females	Males	Total
ICD codes						
25000/2500B	7.2	7.4	7.3	4.9	5.1	5.0
Complications	7.5	7.9	7.7	6.8	7.1	6.9
= T1DM use	7.2	7.5	7.4	6.1	6.4	6.2
Total use	7.3	7.6	7.4	6.2	6.6	6.4

5.4. Yearly costs of inpatient care of T1DM by duration of diabetes (9.5 years vs. 16.5 years) and sex

5.4.1. Structure of costs of inpatient care

Total population

Table 2 in **Appendix 1** presents the distribution of hospital costs by complications and total hospital use. **Figures 21** and **22** show graphically how the distribution of total hospital cost due to complications, diabetes without complications (ICD codes 2500B/25000) and the rest of other use changed rather radically as the duration of T1DM increased. 'Other use' consists of use due to diabetes without complications, hypoglycaemia and the rest of other use. 'T1DM use' consists of use due to all complication groups combined (total complications) and due to diabetes without complications (ICD codes 2500B/25000).

The tables and figures mentioned above show that of the total costs of hospital use when T1DM duration was 9.5 years the costs due to complications formed around 14%, the costs due to diabetes without complications almost 61% and the costs of the rest of other use 25%. The costs of T1DM-related use formed three quarters of the total costs. Compared with the costs due to all complications, the total costs were 7-fold, the costs due to other reasons 6-fold and the costs due to diabetes without complications 4.3-fold when T1DM had lasted 9.5 years. Of all

complications, the costs due to other complications, and ophthalmic and renal complications were the highest; their combined share of total costs was around 12%, and over 84% of the costs of all complications.

When T1DM had lasted 16.5 years, the share of all complications of the total costs rose to over 45%, that due to diabetes without complications dropped to around 16% and that due to the rest of other use increased to almost 39%. Compared with the costs due to all complications, the total costs were 2.2-fold, the costs due to other reasons 1.2-fold and the costs due to diabetes without complications around one-third when T1DM had lasted 16.5 years. The most expensive complication groups were ophthalmic, other complications and renal complications; and their combined share was over 40% of total costs, and over 88% of the costs of all complications.

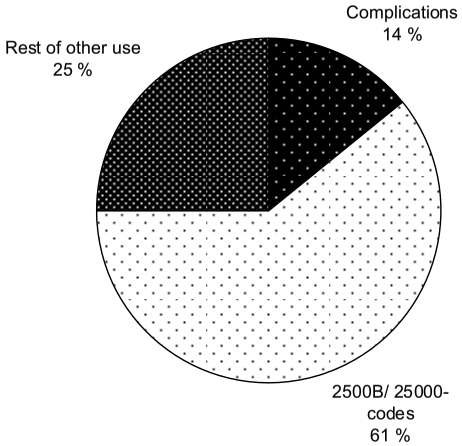

Figure 21. Share (%) of total annual inpatient costs per patient by the type of inpatient care, duration of T1DM 9.5 years

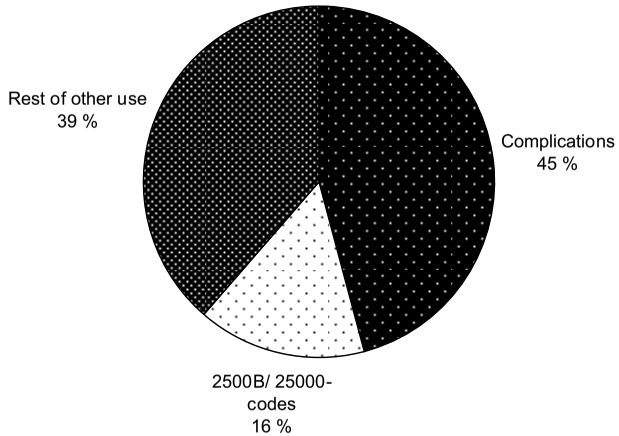

Figure 22. Share (%) of total annual inpatient costs per patient by the type of inpatient care, duration of T1DM 16.5 years

Cost structure by sex

Table 12 shows the distribution of hospital costs by sex and duration of T1DM. Women seemed to have a higher proportion of complication treatment costs due to ophthalmic complications, while those due to other complications were relatively higher in men, when T1DM had lasted 9.5 years. The latter difference somewhat levelled of, as the increased duration of T1DM .

5.4.2. Costs of inpatient care per patient

Total population

Yearly average costs per patient by duration of T1DM are presented in **Table 3 in Appendix 1** and in **Figure 23**. When the duration of T1DM was 9.5 years, the total hospital costs per patient were around 1,399 €, those of T1DM-related costs were 1,050 € and those of all complications were over 198 €. Of all complications, treatment costs of other and ophthalmic complications were clearly the most prominent.

When the duration of T1DM was 16.5 years, total yearly hospital costs per patient decreased by 20.7% (to 1,109 €), while those of all complications 2.5-folded (507 €). T1DM-related treatment costs and other hospital costs dropped notably due to a remarkable decrease (-79.5%) in costs for treating diabetes without complications (2500B). Costs of all complication groups, except those of coma, increased markedly. Costs due to peripheral vascular complications 5.7-folded, those of renal complications 4.6-folded and those of ophthalmic complications 2.8-folded as the duration of T1DM increased by an average of 7 years. Costs of treating a patient with cerebrovascular or cardiovascular complications showed big changes in percentages when T1DM had lasted 9.5 years on average, but the numbers of hospital users were small (n=5 and 9).

Table 12. Shares (%) of the annual costs of complication groups of total inpatient costs and shares(%) of the annual costs of complication groups of the costs of all complications by the duration of T1DM and sex.

	Shares (%) of total costs				Shares (%) of complication costs			
	T1DM 9.5 yrs. Females	**T1DM 9.5 yrs. Males**	**T1DM 16.5 yrs. Females**	**T1DM 16.5 yrs. Males**	**T1DM 9.5 yrs. Females**	**T1DM 9.5 yrs. Males**	**T1DM 16.5 yrs. Females**	**T1DM 16.5 yrs. Males**
CERVASC	0.1	0.1	0.5	0.1	0.8	0.8	1.1	0.2
CARVASC	0.0	0.1	0.8	0.8	0.0	0.6	1.8	1.8
PERVASC	0.3	0.4	1.7	3.5	2.1	3.0	3.8	7.7
NEUROL	0.2	0.7	0.9	0.8	1.5	5.0	2.0	1.7
RENAL	1.9	1.6	11.1	9.5	13.2	11.3	24.2	20.7
ENDOCRIN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OPHTHALMIC	5.7	3.9	18.3	16.5	39.4	28.1	39.9	36.1
OTHER complicat.	4.8	6.0	11.9	13.7	33.1	43.0	26.0	30.0
COMA	1.4	1.1	0.5	0.8	9.8	8.2	1.2	1.7
Complications total	**14.4**	**14.0**	**45.8**	**45.7**	**100.0**	**100.0**	**100.0**	**100.0**
Hypoglycaemia	0.0	0.0	0.4	0.2	0.0	0.0	1.0	0.5
2500B/25000	62.5	58.9	16.2	15.2	434.0	422.5	35.5	33.2
Rest of other use	23.0	27.1	38.0	39.2	159.9	194.3	83.1	85.8
OTHER use	85.6	86.0	54.2	54.3	593.9	616.8	118.6	119.0
T1DM use	77.0	72.9	62.0	60.8	534.0	522.5	135.5	133.2
TOTAL use	**100.0**	**100.0**	**100.0**	**100.0**	693.9	716.8	218.6	219.0

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

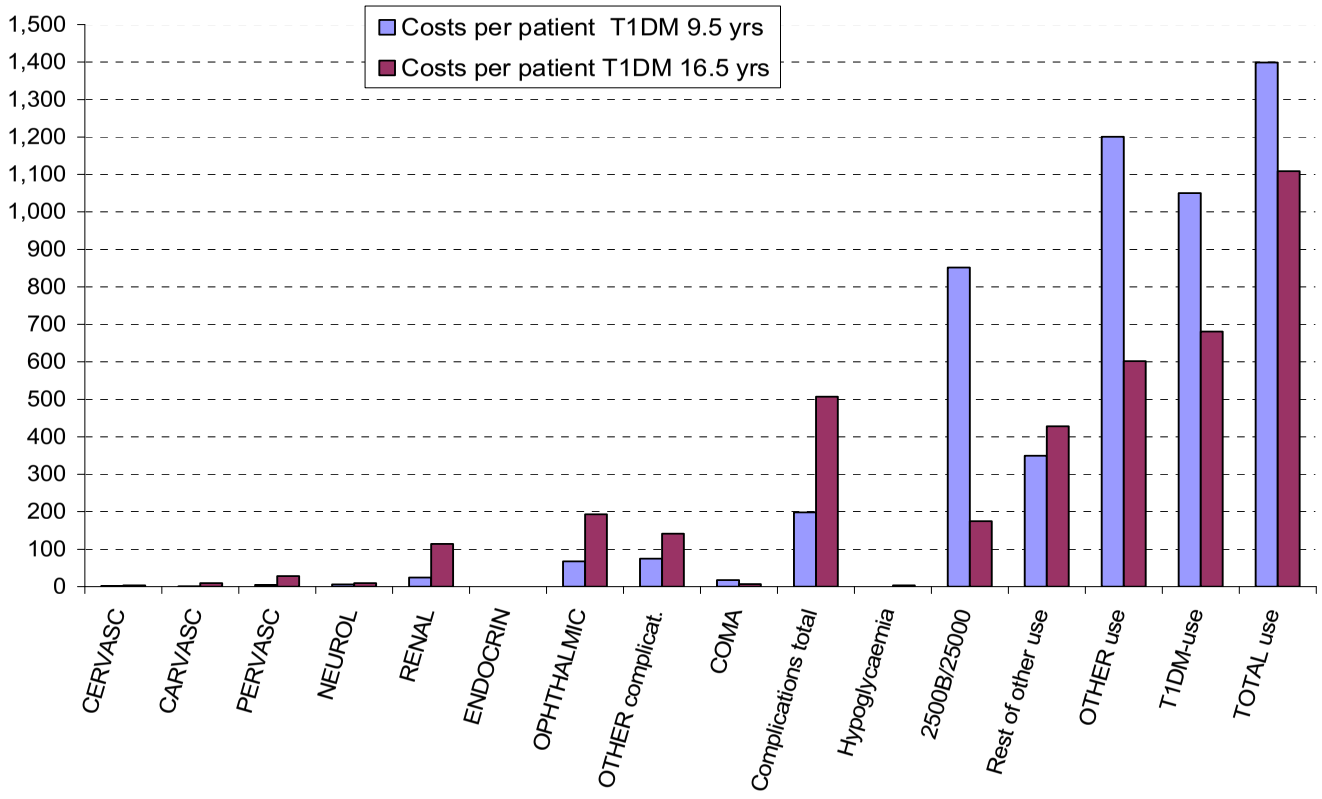

Figure 23. Average annual costs (€) per patient in the cohort by complication group and duration of T1DM

Cost by sex

Yearly costs of hospital care per female patient are presented in **Table 13**. When T1DM had lasted 9.5 years, total costs per female patient were over 1,642 €. T1DM-related costs were 1,264 € and costs of all complications were slightly over 236 €. Of all complications, treatment costs of ophthalmic and other complications were clearly the highest.

When the duration of T1DM was 16.5 years, total hospital costs per female patient decreased by 22.1%, while those of all complications almost 2.5-folded (to 586 €). Costs of all complication groups (except those of coma), increased considerably. Costs due to renal complications 4.5-folded, those due to peripheral vascular complications 4.4-folded, those due to neurological complications 3.2-folded and those due to ophthalmic complications 2.5-folded as the duration of T1DM increased. Treatment costs due to ophthalmic complications clearly remained the highest (234 €), followed by costs due to other and renal complications.

Annual hospital costs per male patient are presented in **Table 13.** When T1DM had lasted 9.5 years, total hospital costs per male patient were over 1,198 €. T1DM-related costs were slightly over 873 €, and costs of all complications exceeded 167 €. Of all complications, treatment costs of other complications were clearly the highest, followed by those of ophthalmic complications.

When the duration of T1DM increased to 16.5 years, total annual hospital costs per male patient decreased by 19.4%, while those of all complications over 2.6-folded (to 441 €). Costs of many complication groups increased substantially. Costs due to peripheral vascular complications 6.8-folded, those due to renal complications 4.8-folded and those due to ophthalmic complications 3.2-folded as duration of T1DM increased. Now treatment costs of ophthalmic complications became the highest (159 €), followed by those of other complications.

Table 13, and **Figures 8** and **9** in **Appendix 2** present the sex differences in average annual hospital costs per patient by duration of T1DM. Women dominated in almost every cost category. When T1DM had lasted 9.5 years, total hospital costs in women were 37% higher, those due to T1DM were almost 45% higher and those due to all complications were over 41% higher than the respective figures for men. Treatment costs of ophthalmic and renal complications and coma per person were 65%- 98% higher in women. Costs due to neurological complications were over two times higher in men.

As the duration of T1DM increased to 16.5 years, the cost differences somewhat narrowed but nevertheless persisted in most cost categories. The sex difference in costs per patient diminished around 10 percentage points in T1DM-related hospital costs and in costs of all complications combined. Women had distinctly higher costs in renal, ophthalmic and neurological

complications than men (around 50% higher). Treatment costs due to peripheral vascular complications were over 50% higher in men.

5.4.3. Total costs of inpatient care in the cohort

Total annual costs of inpatient care in the whole cohort are presented in **Table 14** by duration of T1DM and by sex. Total costs of inpatient care dropped from 7.2 million to 5.6 million euros, and those of care related to T1DM dropped from 5.4 million to 3.4 million euros when the duration of T1DM was longer. Conversely, treatment costs of all complications combined increased from around 1 million to slightly over 2.5 million euros. Treatment costs of ophthalmic, other and renal complications rose approximately to 1 million, 0.7 million and 0.6 million euros, respectively, when the duration of diabetes increased; treatment costs due to ophthalmic complications alone were now almost as high as those of all complications combined when T1DM had lasted 9.5 years.

Yearly total treatment costs due to inpatient care, care of all complications, other hospital use and care of many complications were higher in women than in men, although there were approximately 20% more men in both cohorts.

Table 13. Average annual costs (€) per patient in the cohort by complication group and duration of T1DM and differences, between sexes.

	Costs per female patient T1DM 9.5 yrs	Costs per male patient T1DM 9.5 yrs	Difference in costs (%) between sexes T1DM 9.5 yrs	Costs per female patient T1DM 16.5 yrs	Costs per male patient T1DM 16.5 yrs	Difference in costs (%) between sexes T1DM 16.5 yrs
CERVASC	1.8	1.3	36.6	6.6	1.1	519.8
CARVASC	0.1	1.0	929.2	10.5	8.1	28.9
PERVASC	5.1	4.9	2.4	22.3	33.9	51.7
NEUROL	3.6	8.3	127.8	11.7	7.4	57.6
RENAL	31.3	18.9	65.5	141.6	91.4	54.9
ENDOCRIN	0.0	0.0		0.0	0.1	
OPHTHALMIC	93.2	47.0	98.3	233.9	159.4	46.7
OTHER complicat.	78.4	71.9	9.1	152.4	132.1	15.3
COMA	23.2	13.8	68.3	6.9	7.5	8.3
Complications total	**236.8**	**167.2**	41.6	**585.9**	**441.1**	32.8
Hypoglycaemia	0.0	0.0		5.7	2.3	142.4
2500B/25000	1,027.6	706.4	45.5	208.1	146.5	42.0
Rest of other use	378.6	324.9	16.5	486.6	378.5	28.6
OTHER use	1,406.2	1,031.3	36.3	694.7	525.0	32.3
T1DM use	1,264.3	873.6	44.7	794.0	587.6	35.1
TOTAL use	**1,642.9**	**1,198.5**	37.1	**1,280.6**	**966.1**	32.5

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

Table 14. Total annual costs (€) in the cohort by complication group and duration of T1DM for total population and by sex

	Bed-day costs of 5,120 persons T1DM 9.5 years	Bed-day costs of 5,010 persons T1DM 16.5 years	Change in costs (%) 9.5/16.5 years	Bed-day costs of 2,312 females T1DM 9.5 years	Bed-day costs of 2,808 males T1DM 9.5 years	Bed-day costs of 2,276 females T1DM 16.5 years	Bed-day costs of 2,734 males T1DM 16.5 years
CERVASC	7,891	17,872	126.5	4,178	3,714	14,970	2,901
CARVASC	3,133	46,188	1,374.1	232	2,901	23,906	22,282
PERVASC	25,617	143,437	459.9	11,721	13,896	50,830	92,608
NEUROL	31,703	47,009	48.3	8,418	23,286	26,675	20,334
RENAL	125,657	572,241	355.4	72,470	53,186	322,270	249,971
ENDOCRIN	0	348		0	0	0	348
OPHTHALMIC	347,391	967,973	178.6	215,433	131,958	532,259	435,714
OTHER complicat.	383,216	708,019	84.8	181,340	201,876	346,756	361,263
COMA	92,275	36,324	60.6	53,595	38,680	15,783	20,541
Complications total	**1,016,883**	**2,539,410**	149.7	**547,387**	**469,496**	**1,333,449**	**1,205,961**
Hypoglycaemia	0	19,264		0	0	12,882	6,383
2500B/25000	4,359,386	874,076	79.9	2,375,769	1,983,617	473,589	400,487
Rest of other use	1,787,720	2,142,369	19.8	875,334	912,386	1,107,509	1,034,860
OTHER use	6,147,106	3,016,445	50.9	3,251,103	2,896,003	1,581,098	1,435,348
T1DM use	5,376,269	3,413,486	36.5	2,923,156	2,453,113	1,807,037	1,606,449
TOTAL use	**7,163,989**	**5,555,855**	22.4	**3,798,490**	**3,365,499**	**2,914,547**	**2,641,309**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

5.4.4. Costs of inpatient care per hospital user

Total population

Annual treatment costs per hospital user by duration of T1DM are presented in **Table 15,** and **Figure 10** in **Appendix 2**. When the duration of T1DM was 9.5 years, total hospital costs per hospital user were little over 7,881 € and those of all complications 5,361 €. Of all complications, treatment costs per hospital user for ophthalmic complications were highest (5,758 €), followed by those for other, cerebrovascular and renal complications.

Table 15. Annual costs (€) per inpatient hospital user by complication group and duration of T1DM, and changes in costs with increased duration of diabetes

	Cost per hospital user T1DM 9.5 yrs	Cost per hospital user T1DM 16.5 yrs	Change in costs (%) 9.5/16.5 yrs.
CERVASC	4,735	5,361	13.2
CARVASC	1,044	6,024	476.8
PERVASC	3,341	3,808	14.0
NEUROL	3,280	2,474	24.6
RENAL	4,712	6,131	30.1
ENDOCRIN		1,044	
OPHTHALMIC	5,758	5,796	0.7
OTHER complicat.	4,913	6,437	31.0
COMA	3,335	2,179	34.7
Complications total	**5,361**	**7,255**	35.3
Hypoglycaemia		1,864	
2500B/25000	6,089	2,832	53.5
OTHER use	7,327	4,842	33.9
TOTAL use	**7,881**	**6,991**	11.3

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes); other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);

When duration of T1DM increased to 16.5 years, total costs of inpatient care per hospital user decreased slightly, while those of all complications increased by one-third (to 7,255 €). The costs of treating a patient with diabetes without complications (2500B) dropped by over 50%. Treatment costs due to other, renal, cardiovascular and ophthalmic complications produced the highest costs per hospital user (around 6,000 €) when the duration of T1DM increaced by 7 years.

The numbers of cerebrovascular and cardiovascular patients were, however, very small.

By sex

Annual treatment costs per hospital user by duration of T1DM and by sex are presented in **Table 16,** and in **Appendix 2** in **Figure 11**. When T1DM had lasted 9.5 years, total hospital costs per female hospital user were 8,447 € and those of all complications 5,567 €. Of all complications, treatment costs of ophthalmic complications per female hospital user were clearly the highest (6,214 €), followed by costs of other and renal complications.

When the duration of T1DM increased to 16.5 years, total costs of inpatient care per female user decreased by almost 15%, while those of all complications increased by almost one-third (to 7,208 €). Treatment costs due to cardiovascular (almost 9,000 €), cerebrovascular, other, ophthalmic and renal complications produced the highest costs per female hospital user.

When T1DM had lasted 9.5 years, total hospital costs per male hospital user were 7,327 € and those of all complications 5,140 €. Of all complications, treatment costs per male hospital user for cerebrovascular, ophthalmic, other and renal complications were the highest.

When the duration of T1DM increased to 16.5 years, total hospital costs per male user decreased slightly, while those of all complications increased by over 42% (to 709 €). Treatment costs due to renal complications increased by 45% (to 7,009 €), and these costs were now the highest of all complications, followed by those of other, ophthalmic and peripheral vascular complications (which increased by over 50%), as the duration of T1DM increased. Treatment costs per male user due to coma dropped by over one-third.

The sex differences in yearly treatment costs per hospital user by duration of T1DM are presented in **Table 17,** and in **Appendix 2** in **Figure 11**. When T1DM had lasted 9.5 years, total hospital costs in women were somewhat higher (+15.3%) and those due to all complications per person were a little higher (+8.3%) than the respective costs in men. Treatment costs of ophthalmic complications were over 20% higher in women, while those due to neurological complications were 69% higher in men.

As the duration of T1DM increased to 16.5 years, the sex difference in treatment costs per hospital user narrowed in total hospital costs, and in all complications combined the difference was negligible. Women had over double the treatment costs of men for cardiovascular and renal complications, while treatment costs due to peripheral vascular complications per user were now two times higher in men, as the duration of T1DM increased.

Table 16. Annual costs (€) per inpatient hospital user by complication group, by duration of T1DM and sex, and changes (%) in costs, with increased duration of diabetes

	Cost per female hospital user, T1DM 9.5 yrs	Cost per female hospital user, T1DM 16.5 yrs	Change in costs (%) 9.5/16.5 yrs. females	Cost per male hospital user, T1DM 9.5 yrs	Cost per male hospital user, T1DM 16.5 yrs	Change in costs (%) 9.5/16.5 yrs. males
CERVASC	4,178	6,416	53.6	5,570	2,901	47.9
CARVASC	348	8,965	2,475.0	1,243	4,456	258.4
PERVASC	3,197	2,541	20.5	3,474	5,242	50.9
NEUROL	2,296	2,501	8.9	3,881	2,440	37.1
RENAL	4,626	5,588	20.8	4,835	7,009	45.0
ENDOCRIN					1,044	
OPHTHALMIC	6,214	5,892	5.2	5,141	5,683	10.5
OTHER complicat.	4,857	6,267	29.0	4,964	6,608	33.1
COMA	3,573	2,630	26.4	3,054	1,926	36.9
Complications total	**5,567**	**7,208**	29.5	**5,140**	**7,309**	42.2
Hypoglycaemia	0	2,576		0	1,197	
2500B/25000	6,444	3,029	53.0	5,711	2,629	54.0
OTHER use	7,809	4,900	37.2	6,852	4,779	30.2
TOTAL use	**8,447**	**7,208**	14.7	**7,327**	**6,767**	7.6

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);

Table 17. Annual costs (€) per inpatient hospital user by complication group, duration of T1DM and sex, and differences between sexes

	Cost per female hospital user, T1DM 9.5 yrs	Cost per male hospital user, T1DM 9.5 yrs	Difference (%) in cost between sexes T1DM 9.5 yrs	Cost per female hospital user, T1DM 16.5 yrs	Cost per male hospital user, T1DM 16.5 yrs	Difference (%) in cost between sexes T1DM 16.5 yrs
CERVASC	4,178	5,570	33.3	6,416	2,901	121.1
CARVASC	348	1,243	257.1	8,965	4,456	101.2
PERVASC	3,197	3,474	8.7	2,541	5,242	106.3
NEUROL	2,296	3,881	69.0	2,501	2,440	2.5
RENAL	4,626	4,835	4.5	5,588	7,009	25.4
ENDOCRIN					1,044	
OPHTHALMIC	6,214	5,141	20.9	5,892	5,683	3.7
OTHER complicat.	4,857	4,964	2.2	6,267	6,608	5.5
COMA	3,573	3,054	17.0	2,630	1,926	36.6
Complications total	**5,567**	**5,140**	8.3	**7,208**	**7,309**	1.4
Hypoglycaemia	0	0		2,576	1,197	115.3
2500B/25000	6,444	5,711	12.8	3,029	2,629	15.2
OTHER use	7,809	6,852	14.0	4,900	4,779	2.5
TOTAL use	**8,447**	**7,327**	15.3	**7,208**	**6,767**	6.5

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);

5.4.5. Costs per treatment period

Total population

Annual costs per treatment period by duration of T1DM are presented in **Table 18,** and in **Appendix 2** in **Figure 12**. When the duration of T1DM was 9.5 years, total inpatient costs per treatment period were slightly in excess of 3,472 €, those of T1DM-related costs were somewhat less and those of all complications were almost 3,500 €. Costs per treatment period of ophthalmic complications were highest (4,435 €), followed by those of cerebrovascular and other complications.

Table 18. Annual cost (€) per treatment period by complication group and duration of T1DM and changes (%) in costs, with increased duration of diabetes

	Costs per treatment period, T1DM 9.5 yrs.	Costs per treatment period, T1DM 16.5 yrs	Change in costs (%) 9.5/16.5 yrs
CERVASC	3,946	4,874	23.5
CARVASC	855	3,012	252.5
PERVASC	2,562	2,531	1.2
NEUROL	2,320	1,621	30.1
RENAL	3,195	2,670	16.4
ENDOCRIN		1,044	
OPHTHALMIC	4,435	3,315	25.3
OTHER complicat.	3,537	2,922	17.4
COMA	2,587	1,651	36.2
Complications total	**3,494**	**2,900**	17.0
Hypoglycaemia	0	1,313	
2500B/25000	3,392	1,710	49.6
Rest of other use	3,659	2,919	20.2
OTHER use	3,466	2,423	30.1
T1DM use	3,409	2,460	27.9
TOTAL use	**3,472**	**2,622**	24.5

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes); other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B/25000

As the duration of T1DM was 16.5 years, total inpatient costs per treatment period decreased by almost 25% (to 2,622 €) and those of all complications by 17%. Costs per treatment period of T1DM-related use and those of other hospital use dropped notably. There was also a marked decrease (-49.6%) in costs due to treating diabetes without complications (2500B). Costs per

treatment period of all complication groups decreased, except those of cerebrovascular and cardiovascular complications. Costs per treatment period of cerebrovascular complications were the highest, followed by those of ophthalmic, cardiovascular and other complications.

Again, it should be born in mind that the numbers of cerebrovascular and cardiovascular patients were small.

By sex

Costs per treatment period by duration of T1DM and sex are presented in **Table 19,** and in **Appendix 2** in **Figure 13**. The changes in costs per treatment period by the duration of T1DM were very similar in both sexes in total use, T1DM-related use, other use and use due to complications combined. In women, the costs per treatment period of coma and renal, ophthalmic and peripheral vascular complications had a clear drop, as the duration of T1DM increased. In men, the costs per treatment period of neurological complications, coma and ophthalmic complications dropped most when the duration of diabetes increased.

The sex differences in the costs per treatment period by duration of T1DM are presented in **Appendix 1** in **Table 4,** and in **Appendix 2** in **Figure 13**. As for total costs and costs due to all complications, the differences were very small. When T1DM had lasted 9.5 years, costs per treatment period due to neurological complications in men were over 43% higher than in women, those due to peripheral vascular complications were over 58% higher and those due to renal complications were nearly 22% higher when T1DM had lasted on average 16.5 years.

Table 19. Annual costs (€) per treatment period by complication group, duration of T1DM and sex, and changes (%) in costs, with increased duration of diabetes

	Costs per female treatment period, T1DM 9.5 yrs.	Costs per female treatment period, T1DM 16.5 yrs	Change in costs (%) 9.5/16.5 yrs. females	Costs per male treatment period, T1DM 9.5 yrs.	Costs per male treatment period, T1DM 16.5 yrs	Change in costs (%) 9.5/16.5 yrs. males
CERVASC	3,133	5,614	79.2	5,570	2,901	47.9
CARVASC	348	4,482	1,187.8	967	2,228	130.4
PERVASC	2,511	1,930	23.1	2,605	3,053	17.2
NEUROL	1,803	1,740	3.5	2,587	1,488	42.5
RENAL	3,293	2,460	25.3	3,068	3,000	2.2
ENDOCRIN					1,044	
OPHTHALMIC	4,487	3,397	24.3	4,350	3,220	26.0
OTHER complicat.	3,357	2,930	12.7	3,716	2,913	21.6
COMA	2,679	1,578	41.1	2,469	1,712	30.7
Complications total	**3,523**	**2,864**	18.7	**3,461**	**2,941**	15.0
Hypoglycaemia	0	2,147		0	736	
2500B/25000	3,294	1,692	48.6	3,515	1,723	51.0
Rest of other use	3,555	2,806	21.1	3,771	3,062	18.8
OTHER use	3,360	2,344	30.3	3,592	2,517	29.9
T1DM use	3,336	2,421	27.4	3,494	2,500	28.4
TOTAL use	**3,383**	**2,556**	24.4	**3,573**	**2,694**	24.6

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

5.5. Inpatient care of T1DM in 1998 by sex

In 1998, T1DM had lasted on average 25 years (18-33 years; SD 4.3), and the average age of the study population was 35.3 years (19-51 years; SD 6.1). The average age at diagnosis was 10.2 years (males 10.4 years; females 9.9 years).

5.5.1. Numbers of hospital users

The numbers of hospital users in 1998 are presented in **Table 5 in Appendix 1**. The total number of hospital users due to any cause was 566, accounting for 12% of the whole cohort (N=4701). Around 9% (412 persons) of the cohort used hospital treatment due to complications. There were 17% more men than women in the cohort in 1998. There were over 14% more males than females using inpatient care due to complications.

Of the complications, renal, ophthalmic and other complications showed a clear dominance, forming 93% of hospital users due to all complications and two-thirds of hospital users due to any cause. The proportion of hospital users due to any complication was 73% of all hospital users in 1998. Only a few patients used inpatient care due to cerebrovascular complications or hypoglycaemia, and no patient needed treatment due to endocrine complications.

5.5.2. Discharges

The proportions of discharges due to complications by diagnostic group and sex are depicted in **Table 20**. The majority of discharges were due to treatment of complications. The share of discharges due to all complications was over 70%, and the share of T1DM-related discharges (complications + diabetes without complications ICD 2500B) was over three-quarters of all hospital discharges.

By this measure of hospital use, renal complications was the biggest group of complications, forming over 44% (women 51.4%, men 39%) of discharges due to complications and almost one-third (women 35.4%, men 28.9%) of all discharges. Discharges due to other, ophthalmic and peripheral vascular complications were the next most common groups.

Table 6 in **Appendix 1** shows the numbers of hospital discharges per 1,000 patients by sex in 1998. Men had around 11% more discharges due to all complications combined and 3% more total hospital discharges than women. By complication groups, men had more discharges related to peripheral vascular complications (98% more), coma (95% more) and other complications (around 22% more) than women. Women had around 18% more renal discharges than men.

Table 20. Shares (%) of inpatient discharges due to complications and all discharges in 1998 by sex

	Shares (%) of discharges due to complications			Shares (%) of all discharges		
	Total (fem + male)	**Females**	**Males**	**Total (fem + male)**	**Females**	**Males**
CERVASC	0.3	0.3	0.4	0.2	0.2	0.3
CARVASC	3.0	3.3	2.7	2.1	2.3	2.0
PERVASC	10.5	7.3	13.0	7.6	5.0	9.6
NEUROL	2.3	0.5	3.7	1.7	0.3	2.7
RENAL	44.4	51.4	39.0	31.9	35.4	28.9
ENDOCRIN	0.0	0.0	0.0	0.0	0.0	0.0
OPHTHALMIC	12.9	13.1	12.8	9.3	9.0	9.5
OTHER complications	22.3	21.2	23.3	16.1	14.6	17.3
COMA	4.3	3.0	5.2	3.1	2.1	3.9
Complications total	**100.0**	**100.0**	**100.0**	**71.8**	**68.9**	**74.2**
Hypoglycaemia				0.1	0.0	0.1
2500B				5.0	5.6	4.6
Rest of other use				23.1	25.5	21.2
Other use				28.2	31.1	25.8
T1DM use				76.9	74.5	79.0
TOTAL use				**100.0**	**100.0**	**100.0**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code);
other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B; total use = complications total + other use

Discharges per hospital user in 1998 are depicted in **Table 7** in **Appendix 1**. Peripheral vascular complications (3.0 visits; females 1.8, males 4.2) and renal complications (2.7 visits) caused the most frequent hospital use per user. Overall, men used hospital somewhat more frequently than women.

5.5.3. Bed-days

Table 21, and **Figure 14** in **Appendix 2** show the distributions of bed-days due to complications and all bed-days by diagnostic group and sex in 1998. The bed-days of all complications combined formed around 72% of total hospital bed-days. The share of bed-days due to renal complications was overwhelming; its share of bed-days of all complications was 52.7% (women 60%, men 46.7%) and of all bed-days 38% (women 42. 6%, men 34. 2%). 'Other complications' was clearly the second biggest group, followed by peripheric vascular and ophthalmic complications.

Table 21. Shares (%) of bed-days due to complications and all bed-days in 1998 by sex

	Shares (%) of bed-days due to complications			Shares (%) of all bed-days		
	Total (fem + male)	**females**	**males**	**Total (fem + male)**	**females**	**males**
CERVASC	2.7	5.3	0.5	1.9	3.7	0.4
CARVASC	3.6	4.7	2.8	2.6	3.3	2.0
PERVASC	9.3	7.1	11.1	6.7	5.0	8.1
NEUROL	1.5	0.1	2.6	1.1	0.1	1.9
RENAL	52.7	60.0	46.7	38.0	42.6	34.2
ENDOCRIN	0.0	0.0	0.0	0.0	0.0	0.0
OPHTHALMIC	6.7	5.8	7.4	4.8	4.1	5.4
OTHER complications	21.2	15.7	25.7	15.3	11.1	18.8
COMA	2.4	1.5	3.2	1.7	1.0	2.3
Complications total	**100.0**	**100.0**	**100.0**	**72.1**	**70.9**	**73.1**
Hypoglycaemia				0.0	0.0	0.0
2500B				4.4	4.2	4.7
Rest of other use				23.5	24.9	22.2
Other use				27.9	29.1	26.9
T1DM use				76.5	75.1	77.8
TOTAL use				**100.0**	**100.0**	**100.0**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code);
other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B; total use = complications total + other use

Table 8 in **Appendix 1** and **Figure 15** in **Appendix 2** show the bed-days per 1,000 patients in 1998. Men had slightly more bed-days than women measured by either bed-days due to complications, bed-days related to T1DM or all bed-days. By groups of complications, women had 24% more bed-days due to renal and 62% more bed-days due to cardiovascular complications than men (the number of all cardiovascular complication patients was, however, rather small, n=22). Men had 70% more bed-days due to other complications, 62% more bed-days due to peripheric vascular complications, 33% more bed-days due to ophthalmic complications and 123% more bed-days due to coma than women.

Table 22, and **Figure 16** in **Appendix 2** show the bed-days per hospital user in 1998. In general, men had a little more bed-days than women. Of the complication groups, renal and peripheric vascular complications had led to a distinctly biggest amount of bed-days per user, the peak figure being 21.6 days for peripheric vascular complications in men (note, however, the presence of an outlier, which increased the mean of male patients). Men clearly also had more bed-days per user related to other and to neurological complications (the latter group contained only two female patients). The number of bed-days per user was high for patients with cerebrovascular complications, but this group contained only one female and two male patients.

Table 22. Number of bed-days per hospital user in 1998 by complication group and sex

	Bed-days per hospital user, total	**Bed-days per hospital user, females**	**Bed-days per hospital user, males**
CERVASC	50.3	136.0	7.5
CARVASC	9.4	10.0	8.7
PERVASC	16.5	11.4	21.6
NEUROL	6.4	1.0	7.4
RENAL	20.1	21.2	19.2
ENDOCRIN	0.0	0.0	0.0
OPHTHALMIC	4.4	3.6	5.2
OTHER complications	8.1	6.2	9.7
COMA	3.8	3.2	4.1
Complications total	**13.8**	**13.6**	**14.0**
Hypoglycaemia	1.0	0.0	1.0
2500B	6.6	6.3	6.9
Other use	9.0	8.9	9.2
TOTAL use	**14.0**	**13.5**	**14.4**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code);
other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related);
total use = complications total + other use

5.5.4. Length of stay

Table 23 presents the LOS (and SD) in 1998. LOS of all treatment periods was rather similar to that for the treatment of complications. These figures were slightly higher for women than for men. Patients with cardiovascular (7.7 days) and renal (7.4 days) complications appeared to have the longest LOS, but the variances (SD) of these figures were also larger than those of the other complication groups, especially in women. The shortest LOS was for patients with ophthalmic complications and coma (2.9-3.7 days).

Table 23. Length of stay (LOS) and standard deviations in hospital in 1998 by complication group and sex

	LOS total	SD total	LOS females	SD females	LOS males	SD males
CERVASC	50.3	74.2	136.0		7.5	2.1
CARVASC	7.7	9.2	9.2	11.3	6.2	6.8
PERVASC	5.5	7.7	6.3	5.0	5.1	8.7
NEUROL	4.0	6.1	1.0		4.3	6.4
RENAL	7.4	12.3	7.6	15.0	7.2	8.9
ENDOCRIN	0.0		0.0		0.0	
OPHTHALMIC	3.2	3.1	2.9	3.1	3.5	3.1
OTHER complications	5.9	5.7	4.8	4.0	6.7	6.5
COMA	3.5	4.0	3.2	3.1	3.7	4.4
Complications total	**6.2**	10.3	**6.5**	13.1	**6.0**	7.5
Hypoglycaemia	1.0		0.0		1.0	
2500B	5.5	6.1	4.7	3.7	6.2	7.7
Rest of other use	6.3		6.1		6.5	
Other use	6.2	8.7	5.9	8.9	6.4	8.6
T1DM use	6.2		6.4		6.0	
TOTAL use	**6.2**	9.9	**6.3**	12.0	**6.1**	7.8

SD= standard deviation
cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B; total use = complications total + other use

5.5.5. Single diagnoses causing the most inpatient care

Table 9 in **Appendix 1** lists the bed-days, discharges and LOS of the diagnoses/diseases, that caused the most inpatient use in 1998, sorted by the number of bed-days. The table shows that in terms of total hospital use, 'nephropathy' (belonging to renal complications) caused three times

more bed-days than number two on the list ('other defined complication'), 13 times more than number five ('ketoacidosis') and 37 times more than number 15 ('atherosclerosis'). By the end of 1998, around every sixth person in the cohort had used hospital due to nephropathy.

5.6. Inpatient costs of T1DM in 1998 by sex

5.6.1. Structure of costs of inpatient care

Table 24 shows the structure of hospital costs by complications and sex, and **Figures 17** and **18** in **Appendix 2** show the same graphically. The costs of treatment due to complications accounted for around 70% of total costs, and other hospital use around 30% (consisting of treatment periods for hypoglycaemia, diabetes without complications 2500B and the rest of other use). All costs related to the treatment of T1DM (complications total + ICD code 2500B) accounted for 73.6% of total costs. A clear majority of costs was due to renal complications; the share was half of the complication treatment costs (women 57.3%, men 44.1%) and over one-third of total hospital costs (women 39%, men 31.2%). The next most costly were other complications, ophthalmic complications and peripheral vascular complications. The rest of the complication groups accounted for a rather small share of costs.

Table 24. Shares (%) of the costs of inpatient care due to complications and shares (%) of costs of total inpatient care in 1998 by sex

	Share (%) of costs of hospital use due to complications			Share (%) of costs of total hospital use		
	Total (fem+male)	Females	Males	Total (fem+male)	Females	Males
CERVASC	2.5	5.0	0.5	1.7	3.4	0.3
CARVASC	3.4	4.4	2.6	2.4	3.0	1.9
PERVASC	8.8	6.7	10.4	6.1	4.6	7.4
NEUROL	1.3	0.1	2.3	0.9	0.0	1.6
RENAL	50.0	*57.3*	44.1	34.8	*39.0*	31.2
ENDOCRIN	0.0	0.0	0.0	0.0	0.0	0.0
OPHTHALMIC	11.5	10.0	12.8	8.0	6.8	9.0
OTHER complications	20.1	15.0	24.3	14.0	10.2	17.2
COMA	2.3	1.4	3.0	1.6	1.0	2.1
Complications total	**100.0**	**100.0**	**100.0**	**69.5**	**68.1**	**70.7**
Hypoglycaemia				0.0	0.0	0.0
2500B				4.1	3.8	4.3
Rest of other use				26.4	28.1	25.0
Other use				30.5	31.9	29.3
T1DM use				73.6	71.9	75.0
TOTAL use				**100.0**	**100.0**	**100.0**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B; total use = complications total + other use

5.6.2. Costs of inpatient care per patient

Table 25, and **Figure 19** in **Appendix 2** show the costs per patient in 1998 by diagnostic groups and sex. Hospital costs due to renal complications were 2.5-fold those of other complications, 4.3-fold those of ophthalmic complications and 5.7-fold those of peripheral vascular complications. Costs for treating renal complications alone were 14% higher than the costs due to other hospital use (hypoglycaemia + diabetes without complications + rest of other use), and formed almost half of the costs of all T1DM-related hospital use.

Table 25. Mean cost (€) of inpatient care per patient in 1998 by complication group and sex

	Cost per patient	Cost per female patient	Cost per male patient	Difference in costs (%) between sexes
CERVASC	11.2	21.8	2.1	959.3
CARVASC	15.3	19.3	12.0	61.2
PERVASC	39.0	29.2	47.4	62.2
NEUROL	5.8	0.3	10.5	3,366.4
RENAL	222.3	248.1	200.3	23.9
ENDOCRIN		0.0	0.0	
OPHTHALMIC	51.3	43.5	57.9	33.3
OTHER complications	89.3	64.9	110.2	69.9
COMA	10.1	6.1	13.6	123.0
Complications total	**444.4**	**433.2**	**454.0**	4.8
Hypoglycaemia	0.1	0.0	0.1	
2500B	25.9	24.2	27.4	12.8
Rest of other use	169.1	178.8	160.7	11.3
Other use	195.0	203.1	188.0	8.0
T1DM use	470.3	457.5	481.3	5.2
TOTAL use	**639.4**	**636.3**	**642.0**	0.9

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B; total use = complications total + other use

Generally, the hospital costs of all complications and the total hospital costs per patient were slightly higher for men than for women. The costs due to renal complications per patient were almost 24% higher for women than for men. The costs for treating cardiovascular complications were also higher in women. Treating other complications and peripheral vascular complications had accounted for higher costs in men. The number of users due to cerebrovascular (total 3

persons) and neurological complications (2 women) was small, and thus the differences (%) between sexes showed huge percentages.

5.6.3. Total costs of inpatient care in the cohort

The total costs in the whole cohort by complication group and sex are presented in **Table 26**. Total inpatient costs in the cohort (4,701 patients) in 1998 were a little over 3 million euros, of which costs due to treating complications accounted for over 2 million euros and those due to treating renal complications over 1 million euros. The costs of whole T1DM-related use totalled 2.2 million euros, and the costs of hospital use for other diseases than diabetes were 0.9 million euros.

Table 26. Total costs (€) of inpatient care in the cohort in 1998 by complication group and sex

	Costs in 1998 *(per 4,701 patients)*	**Costs in 1998** *(per 2,168 females)*	**Costs in 1998** *(per 2,533 males)*
CERVASC	52,574	47,351	5,223
CARVASC	72,071	41,780	30,291
PERVASC	183,486	63,367	120,119
NEUROL	27,223	656	26,567
RENAL	1,045,207	537,923	507,284
ENDOCRIN	0	0	0
OPHTHALMIC	240,954	94,231	146,723
OTHER complic.	419,893	140,661	279,232
COMA	47,699	13,230	34,469
Complications total	**2,089,106**	**939,200**	**1,149,907**
Hypoglycaemia	348	0	348
2500B	121,860	52,574	69,286
Rest of other use	794,761	387,730	407,031
Other use	916,621	440,304	476,317
T1DM use	2,210,966	991,773	1,219,192
TOTAL use	**3,005,727**	**1,379,504**	**1,626,223**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B; total use = complications total + other use

5.6.4. Costs of inpatient care per hospital user

Costs per hospital user in 1998 are presented in **Table 27,** and graphically in **Figure 20** in **Appendix 2**. Apart from treating cerebrovascular complications (very few patients), treatment of renal complications formed the highest costs calculated per hospital user (7,015 €), followed by treatment of peripheral (5,734 €) and cardiovascular (3,276 €) complications. The costs of treating renal complications were 38% higher than the costs of treating of all kinds of complications. The mean costs for hospital use due to all complications were 5,071 €, and for the total inpatient cost the figure was 5,310 €.

Table 27. Costs (€) of inpatient care per hospital user in 1998 by complication group and sex

	Cost per hospital user	Cost per hospital user, females	Cost per hospital user, males	Difference in costs (%) between sexes
CERVASC	17,525	47,351	2,611	1,713.3
CARVASC	3,276	3,482	3,029	14.9
PERVASC	5,734	3,960	7,507	89.6
NEUROL	2,094	328	2,415	636.4
RENAL	7,015	7,369	6,675	10.4
ENDOCRIN		0	0	
OPHTHALMIC	2,802	2,298	3,261	41.9
OTHER complications	2,837	2,164	3,364	55.5
COMA	1,325	1,103	1,436	30.3
Complications total	**5,071**	**4,943**	**5,180**	4.8
Hypoglycaemia	348	0	348	
2500B	2,299	2,191	2,389	9.1
Other use	3,757	3,700	3,811	3.0
TOTAL use	**5,310**	**5,128**	**5,475**	6.8

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code);
other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related);
total use = complications total + other use

There were notable differences in costs between sexes in 1998. In general, costs per hospital user were slightly higher in men than in women. The costs per male hospital user due to peripheral vascular complications were almost 90% higher than those for the corresponding female group. The costs per male user were 55% higher than those per female user in treating other complications and 42% higher in treating ophthalmic complications. The costs due to renal complications calculated per hospital user were around 10% higher in women than in men. The

numbers of hospital users due to cerebrovascular and neurological complications were too small to allow comparisons between sexes.

5.6.5. Costs of inpatient care per treatment period

Table 28, and **Figure 21** in **Appendix 2** show the costs per treatment period (discharge) in 1998. The mean costs of a treatment period for all kinds of diseases (total costs) and for that of all kinds of complications were around 2,300 euros. Hospital use due to the rest of other use (where 2500B is excluded) and cardiovascular and renal complications accounted for the highest costs per treatment period.

Table 28. Costs (€) of inpatient care per treatment period in 1998 by complication group and sex

	Cost per treatment period	Cost per treatment period, females	Cost per treatment period, males	Difference in costs (%) between sexes
CERVASC	17,525	47,351	2,611	1,713.3
CARVASC	2,669	3,214	2,164	48.5
PERVASC	1,911	2,185	1,793	21.9
NEUROL	1,296	328	1,398	326.3
RENAL	2,581	2,637	2,524	4.5
ENDOCRIN	0	0	0	0
OPHTHALMIC	2,042	1,812	2,223	22.7
OTHER complications	2,058	1,675	2,327	39.0
COMA	1,223	1,103	1,277	15.8
Complications total	**2,288**	**2,366**	**2,229**	6.2
Hypoglycaemia	348	0	348	
2500B	1,904	1,643	2,165	31.8
Rest of other use	2,703	2,638	2,769	5.0
Other use	2,560	2,460	2,661	8.2
T1DM use	2,261	2,312	2,221	4.1
TOTAL use	**2,365**	**2,395**	**2,340**	2.4

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B; total use = complications total + other use

Generally, the costs per treatment period in 1998 were slightly higher in women than in men for all kinds of complications of T1DM and for total hospital costs. Measured by this variable, costs due to renal complications were quite similar between the sexes. Men had higher costs per treatment period than women due to other (+39%) and ophthalmic (+22.7%) complications and due to diabetes without complications (+31.8%), while women's costs were more prominent for treating cardiovascular complications (+48.5%).

6. DISCUSSION

6.1. General limitations of the study

There was no non-diabetic control group. Such a control group would have given comparison data relating to hospital use, also in different age groups. Standardisation by sex and age would also have given added value to the results.

The results of this study are valid only in the Finnish population and the Finnish health care system, and certain caution is needed when generalising them to other populations and health care systems.

The main focus of this longitudinal study was to describe only inpatient hospital care and to calculate its costs, as in many studies they have proved to form a dominant share of the total treatment costs of persons with diabates. Registers were used, and according to previous studies their reliability, validity and coverage can be considered very good. Costs and use of outpatient care were omitted, as this data would have been difficult (or impossible) to get, especially during the long follow-up for this population. By conducting a survey, complimentary data of inpatient and outpatient hospital care could have given more value to the study and given more detailed information. Though, administering a survey might have required a large sample size, and it would have been more expensive and time-consuming to conduct (Keskimäki et al 1997).

Transfer payments (e.g. costs of sick leave and disability, costs of Social Insurance Institute) were omitted, as the perspective of the study was societal. Also, the costs of drugs for patients were not included in the calculations (cost of bed-day includes the costs of treatment that happens in hospital, as well as out-of-pocket payments of patients).

Indirect costs (productivity losses due to mortality and morbidity) were not included, as they are very seldom included in similar studies and are difficult to calculate, and raise debate and controversy between researchers.

In a section 6.10 of the discussion, though, costs of outpatient care and drugs were included in the national estimates of health care costs of T1DM and persons with T1DM in Finland in 2001.

Complications of pregnancies, which were excluded from this study, might have caused an excess use of hospitals for diabetic women compared with non-diabetic women. This possible incremental effect was not examined because no control group was used. Hospital use during pregnancy in diabetic women would be an interesting subject for a separate assessment. In this

study, the exclusion of complications of pregnancies may have caused an underestimation of hospital use in women. This might have partly contributed to the higher hospital use in female patients than in male patients. On the other hand, women with T1DM have been recommended to be referred to hospital for clinical evaluation while planning their pregnancies; these were included in this current assessment.

6.2. Methodological aspects

6.2.1. Finnish hospital discharge register (FHDR) and T1DM

Drug treatment for diabetes is free of charge in Finland. Patients receive reimbursement from the Social Insurance Institution after the institution has approved the patient's application based on a certificate from the treating physician. Only occasionally do the parents of a diabetic child fail to seek reimbursement for insulin costs, and would thus not be included in the nationwide Central Drug Registry. The ascertainment rate of childhood T1DM (based on the Central Drug Register) in Finland is therefore almost 100% (Tuomilehto et al 1991).

In Finland, there are better possibilities to conduct register-based health studies than in most countries, as the coverage is good and the quality for research purposes is usually excellent. It is also possible to link registers with a personal identification code (Keskimäki et al 1997). The accuracy and quality of the FHDR data for epidemiological research purposes have been estimated in a number of studies (Keskimäki and Aro 1991; Keskimäki et al 1997, Mähönen 1997, Nikiforov 1984; Salmela and Koistinen 1987, Niemi and Winell 2005). In a comparison of coded diagnoses with hospital records during the corresponding hospital stay, 95% of the principal diagnoses and 96% of the dates of admission and discharge were found to be correct in 1986, though the accuracy of the FHDR data was moderate concerning recording procedures, whereas accident types (in addition to accident location and nature) and secondary diagnoses were more often underreported (Keskimäki and Aro 1991). Virtually all hospitals in Finland are owned by communities or federations of communities and are primarily funded by local and governmental taxes. Patients only pay a fixed nominal fee for any hospitalisation. Thus, hospital charges are not an obstacle in seeking hospital care in Finland.

All persons in this study were ascertained to be patients with diabetes, as all were dependent on insulin. Thus no patients were missed. Only the main diagnoses of hospital discharges were compared, which means that the inferior accuracy of the secondary diagnoses in FHDR had no relevance. The use of primary diagnosis also prevented double counting, that can happen when

multiple diagnoses are used. All patients identified in the Finnish T1DM register were also found in the FHDR, i.e. every patient had been hospitalized at least once during the study period.

6.2.2. Inpatient care and costs

Hospitalisations after T1DM durations of 9-11 and 16-18 years were compared in both sexes. The inpatient treatment took place during 1973-1998. The inpatient treatment was considered in three-year periods to obtain steadier frequencies across years and to damp fluctuations. These three-year numbers were then divided by three to get yearly figures and to demonstrate how hospital use differs in various complication groups when T1DM has lasted on average 9.5 years compared with 16.5 years. Yearly inpatient care was calculated per 1,000 patients to adjust for different numbers of men and women and to take into account mortality during observation periods. Also, the numbers and shares of hospitalisations of each complication group were compared with the amount of hospitalisations of all complication groups, inpatient treatment due to other causes than diabetes and the amount of all hospitalisations.

ICD-8 codes were converted to correspond to ICD-9 codes, because the coding changed in January 1st, 1987. The complication groups and complications were based on the criteria of the American Diabetes Association (1998), which was considered the best 'authority' for this purpose. Cerebrovascular complications was presented as a group of its own, as was diabetic coma. Ketoacidosis and hypoglycaemia have ICD-9 codes, but they do not have ICD-8 codes, so their inclusion in complication grouping would have distorted the comparison between complication groups; they were thus excluded from the main groupings.

The length of stay (LOS) in hospital was calculated based on real treatment periods, to obtain the actual average time in hospital in each complication group. Simply diving bed-days by treatment periods would have given a slight underestimate because if a person was admitted to hospital before the calculation period (duration of diabetes 9-11 or 16-18 years), these days would have been omitted, and if a person stayed in hospital after the calculation period, these days would also have been disregarded.

In the hospitalisation data related to complications, no treatment periods had lasted longer than 365 days. This means that very long hospital periods (“outliers”) did not affect the means of the variables.

Acute hypoglycaemia was considered separately using an ICD-9 code to assess its approximate occurrence. It was not included in the complications as a group because there was no specific code for it before January 1st, 1987 (ICD-8). Had it been included, the basis for calculations

would have been somewhat different, and in this study, due to the ICD coding, there were most likely less cases due to hypoglycaemia than there were in reality. For many patients, their hospitalisations due to hypoglycaemia would not have been diagnosed as hypoglycaemia; instead, they could have been coded into complication group "other", causing an overestimation of hospital use for that group and an underestimation of inpatient hospital use due to hypoglycaemia in the younger observation group.

The validity of inpatient costs used in this study can be considered good because the average unit costs used are based on cost data from all Finnish general hospitals providing specialised somatic care. These unit costs are recommended for use in health economic cost analyses and evaluations in Finland by the National Research and Development Centre for Welfare and Health (STAKES).

Inpatient hospital care and the corresponding costs were calculated separately for patients aged under 16 years since this patient group is typically treated in paediatric wards in Finland, and the costs of treatment in these wards are higher than in many other hospital wards.

Statistical methods

This study was population based, as the study population consisted of all Finnish T1DM patients diagnosed before the age of 18 years (between 1965-1979). The rather large cohort (the number of patients was 5166) was not a random sample of T1DM patients. Thus, no statistical methods were used to test the differences. The study type was designed to be descriptive, not predictive or explanatory, and the main objective was to describe how hospital use and costs of numerous complications of T1DM changed during a long period of follow-up time by sex. The data was formed by linking registers. The register data included only few variables about the population, and the possibilities to perform multivariate analyses to control possible confounding variables were small. This is why statistical methods were not used or considered mandatory, as they might be better suited for different kind of study set-ups, variables and content, with perhaps a separate control group of non-diabetic patients.

6.3. Inpatient care of a cohort of T1DM patients during 1973-1997

The total rate of hospitalisations clearly dropped after 1987, especially among women. Since 1992, the total use remained at the same level, with 19-22% of the cohort using hospital yearly, and the difference between the sexes levelled off. The drop in the total rate after 1987 was caused by a steep decrease in diabetes-related hospitalisations. The number of yearly hospital

bed-days dropped by 50% during 1979-1997, the LOS decreased by 42% (from 9.3 to 5.4 days), but the yearly number of discharges only dropped slightly.

Men stayed in hospital on average slightly longer than women. Twice as many male patients as female patients became deceased during the follow-up (308/157). This higher mortality may also have supported the need for a longer hospital stay in male patients since they may have had more severe problems than female patients. As a general trend, the yearly numbers of hospital bed-days and discharges dropped clearly after 1987, especially among women. At the end of 1987, the mean age of the cohort was 25.6 years (min 9.1; max 40.7) and the mean duration of diabetes 15.3 years (min 8; max 23.0).

There are evidently several reasons for the decrease of hospitalisations after 1987. No changes in the national policy for hospital care (in general or for diabetic patients) took place in the late 1980s, but a new reimbursement system from government funds to local communities to cover part of the health care costs was implemented. At the same time, but largely independently of the former, many regional diabetes care programmes were implemented to organise diabetes care within local communities. In 1986, an experiment was started in Finland to examine the effect of the length of initial treatment hospital stay on the treatment balance of children with diabetes (Simell et al 1993). The results encouraged efforts to shorten the initial treatment time and may have affected the prevailing treatment practices even more widely. Human insulin was adopted in Finland nationwide in 1986-1987. To what extent the change to human insulin in the late 1980s, which required several additional contacts between patients and treating physicians, actually improved outpatient care of T1DM patients (and as a consequence reduced unnecessary hospitalisations and the LOS) cannot be determined from this study or from other data.

Any comparison of the results of this subsection of the study with those from other countries is difficult because only a few hospital utilisation studies of diabetes exist and these have generally concentrated on inpatient care due to diabetes mellitus, rather than specifically investigating patients with T1DM. In particular, population-based and longitudinal studies of T1DM-related hospital use are lacking. The different methods and study designs also make comparisons difficult.

The proportion of yearly hospital users was reported to be around 25% by Moss et al (1991) for diabetic patients diagnosed under 30 years of age. Donnan et al (2000) also reported a similar hospital admission rate (mean age 34 years, SD 15 years). In a German study, around 18% of diabetic patients were hospitalised at least once (Icks et al 2001). In a recent Finnish cross-sectional study, over 26% of T1DM patients (all ages included) used somatic hospital care in 1997 (Kangas 2001). These findings from that study are in line with the results of this study.

Aro et al (1994) examined the inpatient care of drug-treated diabetic patients in Finland in 1989. The percentage of hospital users per year with diabetes as the principal diagnosis was related to age, and it dropped first from 41% (age 0-14 years) to 24% (age 15-24 years), to 18% (age 25-44 years) and finally to 10% (age 55-64 years). Among children aged 0-14 years, the ratio of bed-days of diabetic children compared with that of children without diabetes was 10 to 1. In this cohort, the proportions of hospital users were somewhat different, averaging 23% from 1973 (mean age of patients 15 years, min/max age 2/27 years) to 1987 (mean age 25 years) and dropping after this to 9% in 1997 (mean age 36 years). One reason for the higher proportion of hospital users in the youngest group in the study by Aro et al (1994) compared with this study might be that the hospital visits related to the diagnosis of the disease (visits during the month following diagnosis, in 1973-1979) were excluded. In comparison, an Australian study reported that 5.5% of diabetic patients (excluding newly diagnosed cases) aged 0-19 years were hospitalised at least once in 1987 (Sutton et al 1989).

The LOS of diabetic patients varies between different studies, depending on the year, methods applied, patients' age, types of complications, country and initial treatment (Green and Solander 1984; Fishbein 1985; Sutton et al 1989; Jacobs et al 1991; ADA 1993a; Aro et al 1994; Hirasing et al 1996; Simell et al 1996; Icks 2001; Kangas 2001). In most studies, T1DM and T2DM are not separated. Treatment practices and funding of hospital costs differ between countries and years. Therefore, comparisons should be made with caution. On the other hand, such differences observed can be used in the evaluations of the management of diabetes between countries and over time.

In a study by Aro et al (1994) the LOS of diabetic children (0-14 years) was 5.1 days and the LOS of non-diabetic children 0.5 days in 1987. In a German study, the mean hospital stay in 1997 (excluding hospitalisations at the onset of diabetes) was seven days for diabetic patients aged under 20 years (Icks 2001). For the same age group in a Dutch study, the LOS decreased from 14.5 days to 11.9 days between 1980 and 1991 (Hirasing 1996). In this study, the LOS (due to any cause) was 6.5 days for 1987 and 5.4 days for 1997.

The length of the initial treatment and patient education, the latter in most countries starting for childhood-onset T1DM patients in hospital, varies markedly between countries (Simell et al 1996). In an Australian study, the median duration of hospital stay for diabetic patients aged 0-19 years was 12 days at the time of diagnosis and seven days after other admissions in 1987. The average LOS was four days (Sutton et al 1989). A study carried out in all hospitals in Finland in 1985 indicated that for diabetic children aged under 15 years, the overall mean initial LOS in hospital was 24 days, and that for the other admissions seven days (Simell 1994; Simell et al

1996). The length of the initial treatment affects the costs, but not necessarily the effectiveness of treatment. In a Finnish study, 4-week and 1-week initial hospital treatment periods were compared with each other, and the conclusion was that a shorter period is more cost-effective than a longer one because the effectiveness in both periods was similar (Simell et al 1993). In the present longitudinal study, the first hospital visits for diagnosing diabetes were excluded for purposes of comparison.

According to the Finnish inpatient and day surgery statistics in 1997, 15.5% of the Finnish general population used hospital services yearly and the mean LOS was 11.1 days (83% of the treatment periods were less than 10 days). For the treatment of diabetes (both T1DM and T2DM included), the average LOS was 13.0 days. The structure of resource utilisation among diabetic patients (due to diabetes) indicated that they had 75% of their bed-days and 50% of their treatment periods in wards of primary health care centres. The corresponding figures for specialised hospital use were 23% (bed-days) and 48% (treatment periods). The general population had 41% of their bed-days and 73% of their treatment periods in specialised hospitals, and 54% and 21% in primary health care centre wards (Pelanteri and Nenonen 1998).

Discharges (treatment periods) per user and bed-days per user have very rarely been reported in previous studies. In a Finnish study, T1DM patients were observed to have 2.2 discharges and 13.7 inpatient days per user and LOS of 6.2 (Kangas 2001). These figures are in accordance with the results of this study.

The amount of resources used for particular diseases can form a useful basis for cost calculations and cost-benefit comparisons of alternatives for treating the disease. This study shows interesting trends in inpatient resource use for a population-based cohort of T1DM patients during 25 years longitudinally. Hospitalisation costs constitute 60-80% of direct costs of diabetes, and diabetic patients clearly use more hospital services than the general population. A US study (Moss et al 1999) reported, that by reducing glycosylated haemoglobin level by just 1%, hospital days could be reduced by 14-20%, which would result in 4-5 billion dollars savings in direct costs alone in the US nationwide. Hypertension and especially glycosylated haemoglobin level were the most important predictors for hospitalisation. In Finland, over 50% of T1DM patients had poor average glycaemic control in the mid-1990s (Valle et al 1999). That the situation was likely even worse in the past. It is difficult to assess the extent to which improved glycaemic control and active self-monitoring of blood glucose might have influenced hospital admissions over time in this study.

In the future, it would be interesting to explore the relationships between duration of diabetes, patient's age and hospitalisation in more detail, and to investigate the effect of other

demographic variables and the presence of various diabetic complications on inpatient care and costs of care. The cost structure of T1DM should be calculated in more detail, incorporating direct, indirect (productivity) and intangible costs (e.g. loss of quality of life), to obtain a more complete description of the costs and the effects of diabetes. Most studies have not distinguished between the costs related to T1DM and T2DM diabetes, although their treatment costs do differ (Stern and Levy 1994).

6.4. Use of inpatient care by T1DM patients due to diabetes (main diagnosis 250) or other causes during 1973-1997

The proportion of patients hospitalised with diabetes as the main diagnosis (main diagnosis 250) decreased from 26% and 21% per year (1987) to 8% and 10% per year (1997) in females and males, respectively. However, when the main diagnosis was some other than diabetes-related (other than 250), the proportion of hospital users in both sexes increased steadily from 6% to 14% in 25 years, exceeding the diabetes-related use in 1992. During the entire 25-year study period, diabetes-related bed-days comprised 67% of all bed-days, and there were twice as many bed-days and hospital discharges due to diabetes-related causes than due to other causes. During the first years from 1973 to 1989, hospital use due to diabetes was three to four times more common than the use due to other causes. Bed-days due to diabetes decreased markedly towards the end of the study period, i.e. during 1980 to 1997 by 66%, while bed-days due to other causes increased, exceeding the number of diabetes-related bed-days in these patients in 1993. Discharges due to other causes than diabetes increased by 106%, the number of patients using hospital annually increased by 73% and discharges per hospital user increased from 1.3 to 1.6 between 1979 and 1997. This indicates that more patients tended to use hospital more frequently due to causes other than diabetes as the years elapsed and the patients became older.

The average LOS due to other causes than diabetes was longer than that due to diabetes (during the entire follow-up 7.9 days and 7.4 days, respectively), but there was marked variation in LOS between the years and the sexes. During the 25-year study period, the average number of yearly discharges due to diabetes increased from 1.3 to 2.0 per hospital user. However, the number of yearly discharges dropped distinctly after 1987; in female patients it decreased by 70% and in male patients by 59% during 1988-1997. Thus, fewer patients used hospital, but those who did, used it more frequently.

Females used hospital care more than males; females had 21% more bed-days, 26% more discharges due to diabetes, and 25% more bed-days and 15% more discharges due to other

causes than diabetes than males during the 25-year period. The difference in hospital use due to diabetes between female and male patients levelled off during the last 10 years.

After 1987, diabetes-related hospital use began to drop steeply. One reason for this might be that human insulin was taken into use at that time in Finland, which may have reduced the need for inpatient care. Treatment practices may also have changed in a way that encouraged outpatient care. An economic recession in Finland started in 1990-1991, resulting in the cutting of funds allocated to health care and most likely reducing diabetes-related inpatient hospital use. During the follow-up, however, the yearly number of hospital discharges and the percentage of hospital users due to reasons other than diabetes as the main diagnosis doubled in this cohort. The increase in hospital visits may be explained by the greater incidence of various chronic illnesses with advancing age and the emergence of diabetic complications.

Any comparison of the results with the findings to the results of other studies is difficult because, to my knowledge, no equivalent studies have been carried out earlier. Previous studies on utilisation of inpatient care by diabetic patients have focused on hospital use among all diabetic patients, not among T1DM patients separately. Longitudinal studies of T1DM-related hospital use are almost non-existent. Furthermore, the different methods and study designs applied in earlier studies make comparisons difficult. In a Dutch study, Hirasing et al (1996) reported a dramatic decrease in diabetes-related hospital bed-days (by 55%) between 1980 and 1991. In this study here, the decrease for this period was 36%.

In a study by the ADA, the LOS attributable to diabetes itself was 6.2 days (4.6 days for patients under 44 years of age). The LOS attributable to chronic complications of diabetes was 8.2 days, and the LOS due to other co-morbid conditions in diabetic patients was 9.5 days. Depending on age, the LOS attributable to different chronic complications ranged from 2.5 to 15.3 days. The LOS attributable to complications and other co-morbid conditions together among diabetic patients was 2.8 days longer than the LOS among non-diabetic patients (American Diabetes Association 1993a). These results indicate that hospital use by diabetic patients due to other causes than diabetes itself warrants a more detailed analysis.

There may be some underestimation of the inpatient care attributed to diabetes in this subsection of the study. Diabetes often contributes to the development or is a cause of other illnesses, which are coded as the main diagnosis for hospital admission. A recent evaluation of drug treatments for other diseases in Finnish T1DM patients showed that virtually all treatments were more common in diabetic patients than in non-diabetic control subjects (Reunanen et al 2000). When only the main diagnosis is taken into account in exploring the use of hospital care, as was done in

this analysis, the real effect of diabetes on inpatient use will be underestimated. In Sweden, it was observed that the number of discharges from somatic hospitals with diabetes as any diagnosis was 2.5 times higher than the number of discharges with diabetes as the primary diagnosis (Jönsson 1983). Furthermore, some co-morbid diseases attributed to diabetes, e.g. pneumonia, may cause more hospital days for diabetic patients than for a non-diabetic population (American Diabetes Association 1993a). In this study, such excess in hospital use related to diabetes was included in the hospital use due to other reasons than diabetes, also causing some underestimation of hospital use due to diabetes. However, it is difficult to determine which other diseases are predisposed to or caused by diabetes and which hospital admissions are longer because of diabetes.

In the future, it would be interesting to examine more closely the effect of various T1DM-related complications on the utilisation of inpatient care and costs as well as to identify the heavy users of inpatient care. By targeting interventions to these risk groups as early as possible, hospital resources and costs could be saved, not to mention the alleviation of human suffering.

6.5. Inpatient care of T1DM patients by duration of diabetes (9.5 years vs. 16.5 years) and sex

The results indicated that for hospital use due to complications, the numbers of hospital users doubled, the annual number of discharges increased 3-fold and the annual number of bed-days increased 2.8-fold when the duration of diabetes increased from an average of 9.5 to 16.5 years.

The yearly number of discharges due to other causes than complications dropped markedly (-28%), but the drop was smaller than the increase in discharges due to complications, so the total number of discharges due to any cause increased somewhat for both sexes when diabetes lasted longer. A remarkable finding is anyway that the yearly number of total discharges was 7.1-fold that of the number of discharges due to complications in the group having suffered from diabetes on average 9.5 years, but 2.4-fold in the group whose diabetes had lasted on average 16.5 years.

The yearly number of bed-days due to other causes than complications dropped considerably (-41%) when diabetes lasted longer. This figure compared with the number of bed-days due to complications was 5.8-fold when the duration of diabetes was 9.5 years, but only 1.2-fold in the older group. The drop was bigger than the increase in bed-days due to complications, causing a decline of the total number of bed-days (-10%). Notable is the increase in the share of bed-days for the treatments of complication groups, as calculated from the total numbers of bed-days (14.7% to 44.6%).

One reason for the considerable drop in the yearly number of discharges and bed-days due to other causes than complications was a prominent decrease in hospitalisations due to ICD code 25000/2500B, diabetes without complications, which dropped over 70% when diabetes lasted on average 7 years longer. More diabetic patients without complications may have been treated in outpatient care and at home as a result of a change in treatment practices. Patients may also have learned better self-management of the disease as they got older. However, hospitalisations of many complications increased manifold with the increasing duration of diabetes.

Regarding discharges, the biggest complication groups were other, ophthalmic and renal complications and coma when diabetes had lasted 9-11 years. When the duration of diabetes increased, the biggest groups were ophthalmic, other and renal complications, while the relative increase was biggest in the discharges of peripheral vascular, renal, cardiovascular and ophthalmic complications. Regarding bed-days, the biggest complication group was other complications, followed by ophthalmic and renal complications and coma. When the duration of diabetes lasted longer, the biggest groups were other, renal and ophthalmic complications, and the biggest relative increase in the amount of bed-days occurred in the treatment of cardiovascular, peripheral vascular and renal complications. A distinct drop was seen in the number of bed-days for treating coma, which may indicate better self-management of blood glucose levels as patients became older.

The length of stay decreased in all complication groups, except in cerebro-, cardio-, and peripheral vascular complications. Although the LOS in hospital generally decreased, the number of discharges per user increased, especially for the big complication groups (other, renal, ophthalmic complications); thus, patients were clearly more frequently in hospital as diabetes lasted longer. As a result, the number of bed-days per user for complication groups increased because the drop of the LOS was offset by the increase in the frequency of hospital visits.

A comparison between sexes demonstrated notable differences. Generally, women clearly used more inpatient treatment than men. By using discharges in the assessment (complications combined, other causes than diabetes, total hospital use, diabetes without complications), women used hospital around 36-55% more than men, and by using bed-days the corresponding figures showed 30-50% more inpatient treatment for women. As the duration of diabetes increased, the sex differences for these figures narrowed, but the sex difference still remained bigger for shares of discharges than for bed-days.

The finding that women used hospital so much more than men was surprising. This result may be explained, at least partly, by the fact that women may seek health care more readily than men

when a disease occurs. This kind of health behaviour has been reported earlier in Finland in a study by Kokko (1988), according to which women visited health centres 1.5 times more than men. Mens' attitude towards disease and symptoms seem to be different compared with womens', and that leads to mens' slower reaction to seek health care when they notice symptoms of a disease (Kivelä 1990).

Another Finnish study (Hujanen et al 2004) reflects this same phenomenon that women, at least in certain age groups, seem to use hospitals more than men. According to that study, per capita municipal somatic specialised care treatment costs in women aged 16-52 years were 11% higher than those in men, and costs in women aged 18-40 years were almost twice the costs in men in 2002.

As diabetes lasted longer, men had a slightly bigger increase than women in the hospital use due to all complications and in the total hospital use, as measured by number of discharges, and in the hospital use due to all complications, as measured by the number of bed-days. Women's total number of bed-days dropped slightly more than that of men (-12% vs. -7%). Women visited hospitals slightly more frequently than men, when total hospital use and hospital use due to other causes than diabetes were observed. Men, however, generally stayed during their treatment periods a bit longer in hospital than women, especially considering the group of complications combined, other hospitalisations than those due to diabetes and total hospital use, when diabetes had lasted 9.5 years or 16.5 years; the LOS decreased for both sexes by about the same amount. The yearly numbers of bed-days and discharges per user considering all complications combined increased for both sexes clearly as the duration of diabetes lasted longer.

An increase in the proportion of yearly discharges due to renal complications was notably bigger for women than for men as the duration of diabetes increased, but for ophthalmic complications, men had a clearly bigger increase. The sex difference in yearly discharges was about the same (8% points higher for women) in the 9.5-year cohort for ophthalmic complications as in the 16.5-year cohort for renal complications. Thus, women seemed to use hospital relatively more frequently due to ophthalmic causes than men when diabetes had lasted on average 9.5 years, but they visited hospital relatively more often for renal causes than men when diabetes had lasted 16.5 years. The yearly number of discharges due to other complications dropped about 10% points for both sexes.

The biggest differences between the sexes in the absolute number of discharges per 1,000 patients per year were that women had twice as much ophthalmic and over 50% more renal complication discharges when diabetes had lasted 9.5 years, and almost 40% more ophthalmic and twice as much renal complication discharges compared with men, when diabetes had lasted longer.

There were huge increases in the number of yearly discharges due to certain complications as diabetes lasted longer. For women, those due to renal complications increased 6-fold, peripheral vascular complications 5.7-fold and ophthalmic complications 3.3-fold. For men, yearly discharges due to peripheral vascular complications increased 5.8-fold, renal complications 5-fold and ophthalmic complications 4.6-fold.

The variable "discharges per user" showed that renal, ophthalmic, cardiovascular and other complications caused clearly more frequent hospital use in both sexes when the duration of diabetes increased. The number of discharges per male patient was higher than that for women in the case of peripheral vascular and other complications, but smaller due to coma, when diabetes had lasted longer. The latter finding was attributed to a notable drop in the number of women using hospital due to coma, for some unknown reason (n=45/18 women). This may indicate a better self-management of blood glucose levels as female patients became older.

The proportion of yearly bed-days of the complication group “other” dropped clearly, especially among men, but other complications still remained the biggest single complication group as the duration of diabetes was longer. In both sexes, the share of renal complications showed a considerable increase, replacing ophthalmic ones as the second biggest group with the increase in the duration of diabetes. The share of yearly bed-days of ophthalmic complications dropped in women but rose in men. Thus, the relative structure of the shares of bed-days indicated that women used clearly more bed-days for ophthalmic causes than men when diabetes had lasted on average 9.5 years, but the difference seemed to level off when diabetes had lasted on average 16.5 years.

In terms of bed-days and discharges, men had a higher proportion in the complication group “other” than women also as diabetes had lasted longer. This suggests that men were more prone to be given diagnoses "other defined" (25008/2507B) or "non-defined" complications (25009/2508B) and exact diagnoses were for some reason more seldom for men than for women.

The most striking sex differences considering the absolute number of bed-days per 1,000 patients per year were that women had twice as many ophthalmic and 60% more renal complication discharges when diabetes had lasted 9.5 years, and around 50% more ophthalmic and renal complication bed-days compared to men when diabetes had lasted longer.

There were vast increases also in the yearly number of bed-days due to certain complications as diabetes had lasted longer. For women, the number of renal complications increased 4.8-fold, peripheral vascular complications 4.3-fold, neurological complications 3.2-fold, ophthalmic complications 2.5-fold and other complications 2.3-fold. For men, the number of peripheral vascular complications increased 6.9-fold, renal complications 5-fold, ophthalmic complications

3.4-fold and other complications 2.2-fold. These figures stress the importance of good metabolic control and management, as these considerable increases in hospital use happened in only 7 years on average, and most of these complications can be life-threatening and can reduce the quality of life immensely.

It was checked that no hospital periods exceeding a duration of 365 days existed in hospital use for any complication group during the two 3-year observation periods. Certain single shorter "outliers" were observed, which raised the means of bed-days in certain groups and observation periods. On the other hand, they increase use of resources and generate costs.

In the observation period with duration of diabetes from 9 to 11 years, there were 445 male bed-days due to renal complications (n=33), one person being in hospital for 155 days . If these bed-days were disregarded, bed-days due to renal complications for men would have 7.6-folded as diabetes lasted longer, and 7-folded if also the biggest number of bed-days produced by a single male in the latter observation period (167 of 2,154 bed-days, n=107) was disregarded.

A big percentual rise of women's bed-days for the treatment of cardiovascular complications was partly attributed to one person, who used half of the bed-days as the duration of diabetes increased (n=8, 206 days in the cohort of 16-18 years duration), causing also an elevation in the LOS and bed-days per user.

Men had more bed-days and bigger LOS regarding the treatment of peripheral vascular disease than women as diabetes increased. A contributory factor for this was that one male patient used 17% of the bed-days in the latter 3-year observation period (n=53; 798 bed-days).

Hospital use due to endocrine complications was practically non-existent in this study (3 bed-days for hyperkalaemia). Intriguing is, why the American Diabetes Association classified this as a group of its own. The reason may be that endocrine complications evolve at a later age. Also surprising was the small number of cerebrovascular patients and their bed-days (0.3-1.4% of bed-days due to complications). It is evident, though, that their numbers increase as diabetes lasts longer.

The number of bed-days due to neurological complications increased in women, but decreased in men, as the duration of diabetes increaced. That is partly explained by the fact that the number of female users 3-folded while the number of male users increased by around 40%. It is odd why a larger number of men had less hospital days than women; this might be explained by the rather small number of patients.

Men had clearly more bed-days for the treatment of peripheral vascular complications as calculated per user (15.1 days vs. 7.3 days) and male patients with peripheral vascular

complications visited hospital more frequently than women (discharges per user 1.7 vs. 1.3) as diabetes lasted longer. Also women's LOS due to peripheral vascular complications was clearly shorter than that of men, which was the reason for the smaller hospital use of women.

Men had more bed-days per user due to renal complications than women when diabetes lasted longer. The reason was that LOS in women decreased distinctly. The frequency of visits was similar for both sexes as the duration of diabetes prolonged.

In comparison, the amount of bed-days due to hypoglycaemia was about the same as bed-days due to cerebrovascular complications, and the amount of discharges due to hypoglycaemia was similar to that due to cardiovascular complications (in the 16.5-year cohort). Its share of the total number of bed-days was only 0.4%, and if it was included in the complications, its share would have been 0.9% of the bed-days of all complications. Men visited hospital more frequently, but women had a longer stay in hospital due to hypoglycaemia (in the 16.5-year cohort).

Certain common diagnoses of complications of T1DM, that caused many hospitalisations according to ICD-9 codes did not have specific ICD-8 codes, e.g. ketoacidosis (ICD-9: 2501B) and microangiopathy (ICD-9: 2506B), and this may have caused an underestimation of hospitalisations in the younger observation group. The lack of ICD-8 code for microangiopathy may have caused an underestimation of peripheral vascular complications in the younger group, and therefore an overestimation of the marked growth of that group as diabetes lasted longer. Patients with microangiopathy or ketoacidosis may have been diagnosed before 1987 as non-defined complications (ICD-8: 25009), and this coding may partly explain the 2.7-fold drop in that diagnosis (non-defined complications) when diabetes had lasted 16-18 years. Also, after the year 1987, some diseases earlier classified as non-defined complications may have been classified as other defined complications, as their share 3-folded as the diabetes lasted longer.

The primary diagnosis of hospital use was used to avoid double counting. This may have caused an underestimation of hospital use, as diabetes is often a contributory cause to the main disease causing hospital use and is marked as a secondary diagnosis in hospital records.

Using a control group would have allowed the incremental effect of diabetes on hospitalisations to be shown and would have increased the value of the study. Due to difficulty in obtaining a valid and reliable control group, and due to limited resources and the scope of the study, the use of a control group was omitted.

The main reasons for these notable increases in hospitalisations (in 7 years) are evidently metabolic and indicate the severe nature of T1DM and its complications; it should be

remembered that, in addition to chronic complications, acute complications (hypoglycaemia, ketoacidosis, coma) of the disease can result in death.

There were considerable increases in bed-days for the treatment of certain complications, while bed-days for the treatment of some other complications dropped markedly when the duration of diabetes lasted longer. Generally, in the 7-year period, hospital use due to complications increased, while hospital use due to diabetes without complications dropped dramatically (e.g. bed-days: +175% vs. –72%). This was one of the major findings in this study, demonstrating a clear structural change in hospital use as diabetes lasts longer. Bed-days for treatment of nephropathy 7-folded, that for ophthalmic disorders 3-folded (glaucoma 8-folded) and for that for personality disorders doubled.

According to the findings of this study, there is really a great need for effective intervention programmes for T1DM, at least in Finland. By preventing and delaying complications, part of the resources devoted to treating persons with T1DM could be allocated to treatment of other diseases, not to mention the extra life-years and quality-of-life gains achieved for diabetic patients. The results of this study may also be relevant rather long, as there are no effective intervention methods yet available for preventing T1DM and its complications, as compared with T2DM and associated complications (e.g. interventions related to exercise, smoking, eating saturated fat, nutrition, diet).

6.6. Costs of inpatient care of T1DM by duration of diabetes

Numerous notable changes were discovered in costs of inpatient care as duration of T1DM increased on average by 7 years, from 9.5 to 16.5 years. When the duration of T1DM was 9.5 years, the share of costs of treatment of all complications was 14% and the share of costs of treatment of diabetes without complications (ICD codes 25000 and 2500B) was 60% of total costs of inpatient care. As the duration of T1DM increased to 16.5 years, the share of treatment costs of complications was almost half of the total costs, but the share of treatment costs of diabetes without complications had dropped to 16% of total treatment costs. Inpatient care of ophthalmic complications had become clearly more costly than hospital treatment of other complication groups. It was followed by inpatient care of other and renal complications; these groups incurred the vast majority of the costs of treating complications. The share of treatment costs due to ophthalmic diseases was clearly higher in women than in men when T1DM had lasted 9.5 years. This finding implies that women get eye problems at an earlier age than men.

Combined treatment costs of all complications per patient had a notable increase, as they 2.5-folded in 7 years. On the other hand, total treatment costs (all costs combined) and total T1DM-related costs per patient decreased because there was a considerable drop related to treatment costs due to diabetes without complications.

When T1DM had lasted 16.5 years, average treatment costs per patient increased substantially in all complication groups (except coma). Costs due to peripheral vascular complications diseased 5.7-folded, and those due renal and ophthalmic complications 4.6- and 2.8-folded. Ophthalmic, other and renal complications were clearly the most expensive complication groups in terms of average inpatient costs per patient, followed by peripheral vascular complications, neurological complications, cardiovascular complications, coma, cerebrovascular complications and endocrine complications, in that order.

It should be emphasised that these considerable increases in costs due to hospitalisations took place in an average of only 7 years. Complications of T1DM are typically severe in nature and often lead to premature death. Besides the growing costs to patients, the health care system and the whole society, human suffering may be immense, especially when a person with T1DM has several complications simultaneously. In this cohort, when T1DM had lasted 9.5 years, one of every eight patient had two or more complications at the same time, but when T1DM duration increased to 16.5 years, every fourth patient had two or more complications.

The comparison of average treatment costs between sexes for certain complications also yielded some intriguing findings as T1DM duration increased from 9.5 to 16.5 years. In men, treatment costs of ophthalmic and peripheral vascular complications increased clearly more than those in women, but generally, women's treatment costs predominated in practically every complication group and cost category. Women's treatment costs due to ophthalmic complications were twice those of men (T1DM 9.5 years), but as T1DM lasted longer (T1DM 16.5 years) they were still 1.5-fold. The cost difference related to treatment of renal complications remained around the same as duration of T1DM increased (i.e. women's costs were 1.5-fold those of men). In the main cost categories (complications combined, other inpatient use, T1DM use, total inpatient use) women's costs distinctly prevailed (33% - 45% bigger), regardless of wheather T1DM lasted 9.5 or 16.5 years. The cost differences between sexes remained notable as T1DM had lasted an average of 16.5 years, although they somewhat diminished. Also, it is known that when females develop diabetes, either T1DM or T2DM, their relative risk of CVD is increased more steeply than that of diabetic males (Tuomilehto et al 2004).

Total inpatient treatment costs in the cohort were 7.2 million euros (T1DM 9.5 years), but they dropped to 5.6 million euros (T1DM 16.5 years). The main contributor to this was the decrease in the treatment costs of diabetes without complications (-3.5 million €). On the other hand, as the costs of all complications combined increased by 1.5 million euros, costs due to T1DM declined by 2 million euros when T1DM duration increased to 16.5 years. Remarkably that treatment costs of ophthalmic complications (T1DM 16.5 years) became almost as high as the costs of all 9 complication groups combined when T1DM had lasted 9.5 years, around one million euros. It is evident that special attention should be paid to preventing especially eye complications by administering effective care, as the treatment costs of ophthalmic complications alone contributed to over 40% of the growth of costs of all complications with T1DM increased by 7 years. Naturally, loss of vision also causes numerous problems in everyday life (at work and home, in leisure) and may cause other health problems.

A comparison of treatment costs per hospital user gives different kinds of results. As the duration of T1DM increased, inpatient treatment costs of all complications increased by one-third because treatment costs and number of bed-days 2.5-3.5-folded, but at the same time the number of users (due to complications) increased by 'only' 85%. Many patients (around every fourth) had more than two complications simultaneously, when T1DM had lasted 16.5 years; thus, the severity and treatment costs of T1DM obviously can vary notably between patients. In the future, complications in these patients, their treatment costs and hospital use should be further followed up, and preventive interventions targeted to these patient groups, before complications start to evolve.

As T1DM duration increased to 16.5 years, the most expensive treatments per hospital user were due to other, renal and cardiovascular complications. The equivalent costs per user due to ophthalmic complications remained the same (5,800 €) since the treatment costs and number of users both 2.8-folded as T1DM duration increased in that group. Treatment costs per user due to neurological complications dropped by one-quarter; the costs rose by 50%, but this was offset by the fact that the number of users doubled. Treatment costs per user due to peripheral vascular complications rose slightly, as the costs of treatment 6-folded and the number of users 5-folded. Treatment costs related to renal costs per user increased by almost one-third since although the number of users 3.5-folded, the equivalent treatment costs 4.6-folded. Generally, the rise in both costs of treatment and numbers of users that occurred in an average in 7 years of increased T1DM was remarkable.

Costs of treatment due to cardiovascular complications became clearly the most expensive complication group in women (around 9,000 €/user/year) as the duration of T1DM increased to

16.5 years; however, number of users was small (n=8). In men, renal complications became the most expensive complication group (7,000 €/user/year) and the costs per user increased more in men than in women (+45% vs. +21%). In general, treatment costs per user related to all complications increased somewhat more in men than in women as T1DM lasted on average 7 years longer.

In terms of inpatient costs per treatment period, certain consistent changes seemed to occur. As the duration of T1DM increased to 16.5 years, costs per treatment period in every 'cost group' (except for cerebrovascular, cardiovascular and peripheral vascular complications) decreased around 17%-50%. The main reason for this was the distinct drop in LOS in hospital. In addition, as patients got older, use of the paediatric ward, which has higher bed-day costs than e.g. the internal medicine ward, naturally diminished. Changing treatment practices and improved medical treatments (e.g. treatments of ophthalmic complications) most likely contributed to the decline in costs per treatment period.

When the duration of T1DM increased to 16.5 years, costs per treatment period due to renal complications in women dropped by one-quarter, while in men the costs remained at the same level. An explanation for this is that women visited hospital more frequently, but stayed there shorter periods than men, whose costs per treatment period were now 22% higher than those of women (T1DM 16.5 years).

Moreover, the costs per treatment period due to peripheral vascular complications clearly became higher in men than in women as duration of T1DM increased to 16,5 years, the reason being that men had more bed-days and longer LOS in hospital.

Hospital use of patients under 16 years of age had a different effect on the costs in certain complication groups, when T1DM had lasted on average 9.5 years (**Table 13 in Appendix 1**). Every third bed-day due to complications, every sixth bed-day due to total hospital use and half of the bed-days due to diabetes without complications were caused by patients aged under 16 years, but there were no bed-days due to cerebrovascular, cardiovascular, peripheral vascular and neurological complications in this younger patient group. The percentages of bed-days due to other, ophthalmic and renal complications and coma were 27, 9, 6 and 18, respectively. Female patients had more bed-days than men due to ophthalmic and renal complications and coma when T1DM had lasted 9.5 years and the patients were under 16 years of age. In conclusion, ophthalmic and renal complications (and naturally coma) emerge earlier in life than the rest of the complications, especially in female patients, and this affects the costs, as paediatric care is more expensive than hospital care in many other wards.

6.7. Inpatient care of T1DM in 1998

In 1998, when the duration of T1DM was on average 25 years, there were 566 hospital users due to any cause. This represents 12% of the whole cohort (N=4,701). Due to complications of T1DM, around 9% (412 persons) of the cohort used hospital. Of the complications, renal, other and ophthalmic complications were clearly the dominating ones. Patients with these complications formed 93% of hospital users due to all complications and two-thirds of all hospital users. Users due to renal and other complications alone formed almost 75% of all users due to complications in 1998.

In terms of hospital discharges, the share of discharges due to renal complications was considerable, accounting for around 45% of all complication discharges and almost one-third of total discharges. Of total discharges, the share of all complications was slightly over 70%, but diabetes without complications (ICD code 2500B) formed only 5% of all discharges.

There were on average 2.2 discharges per hospital user in 1998 due to all complications and due to total hospital use (in renal complications, the figure was 2.7). Generally, men used hospital slightly more frequently than women.

Regarding bed-days in 1998, the share of bed-days due to renal complications turned out to be predominant compared with other complication groups (over half of bed-days of all complications and almost 40% of total bed-days). Interesting also is that the number of bed-days due to ophthalmic complications was now at about the same level as that of diabetes without complications, ICD code 2500B (5% of total bed-days). In addition, the number of bed-days due to peripheric vascular complications was higher than that of ophthalmic complications (in both sexes).

In women, the share of bed-days due to renal complications was noteworthy (60% of bed-days of all complications and over 40% of total bed-days). Women also had 25% more renal bed-days than men per 1,000 patients. On the other hand, men had 33% more bed-days due to ophthalmic complications, twice the amount of bed-days due to coma and distinctly more bed-days due to peripheric vascular and other complications than women per 1,000 patients in 1998. The reason for these differences is unclear; perhaps women have better glycaemic control and self-monitoring of blood sugar than men, leading to a smaller risk of these complications. Also, in earlier stages of T1DM, women may have been more active in seeking health care, and thus, may have had different health behaviour than men (e.g. relating to smoking, exercise, nutrition). However, women seem to be more sensitive to developing renal complications than men at this stage of the disease. In general, men had more bed-days than women in 1998, but the difference was very small.

In terms of LOS in hospital in 1998, besides cerebrovascular complications (only a few patients), LOS due to cardiovascular and renal complications was longest (7.7 and 7.4 days), but their standard deviations (SD) were widest. The SD of renal complications in women was notably larger than in men (15 vs. 8.9), which was reflected as a wider variation in total LOS (all complications and total use). In general, the average LOS in 1998 was 6.2 days.

In 1998, diabetic nephropathy was the single diagnosis causing overwhelmingly the most hospital use. Of all diagnoses, diabetic nephropathy caused over 7 times more bed-days than diabetes without complications (ICD code 2500B) or diabetic microangiopathy (which ranked 3rd and 4th, respectively, on the 'top diagnoses' list), and 15 times more bed-days than e.g. diabetic retinopathy (6th on the 'top diagnoses' list). This stresses the importance of good glycaemic self-control and regular check-ups by physicians and nurses to avoid and postpone especially renal disease, which is a common cause of hospital use and mortality among T1DM patients.

6.8. Costs of inpatient care of T1DM in 1998

In 1998, T1DM-related treatment costs accounted for almost three-quarters of total costs of hospital use. The share of costs due to the treatment of complications was approximately 70%. Costs for treating renal complications caused half of the treatment costs of all complications (women 57%, men 44%), and over one-third of total inpatient treatment costs. Treatment costs due to other complications (20% of treatment costs of all complications), ophthalmic (11.5%) and peripheral vascular complications (around 9%) were the next highest.

In 1998, treatment costs due to renal complications per hospital user were highest (over 7,000 €/hospital user). This cost was around 33% higher than the cost of total use and 2.5-fold that of e.g. ophthalmic complications. Men had over 40% higher treatment costs per hospital user than women due to ophthalmic complications, but in renal complications the cost difference between sexes was small. The numbers of hospital users due to hypoglycemia (n=1) and cerebrovascular (n=3), neurological (n=13) and cardiovascular (n=22) complications were quite small.

In terms of costs per treatment period in 1998, (apart from those due to cerebrovascular complications, where the number of patients was very small), costs per treatment period due to cardiovascular and renal complications were the highest (about 2,600 €). Men's costs per treatment period due to ophthalmic complications were again somewhat higher than those of women (20% higher), but in renal complications the difference was negligible.

The average inpatient treatment costs due to renal complications were 222 € per patient in 1998, and they totalled over one million euros in the whole cohort. These costs were 4-6 fold those of, for instance, ophthalmic and peripheral vascular complications. In general, men's treatment costs per patient were slightly higher than those of women, but the difference was negligible. Women's treatment costs due to renal complications were around 25% higher than those of men, while men, in turn, had higher treatment costs due to other, peripheral vascular and ophthalmic complications and coma. Women's treatment costs due to cardiovascular and cerebrovascular complications were higher than those of men, but the number of patients was quite small.

In 1998, the total average inpatient treatment costs per patient with T1DM were 640 € (636 € women, 642 € men), and due to complications of T1DM they were 444 €. To put these figures into wider perspective and to estimate the size of the burden of treatment costs of T1DM on society, a comparison with the national treatment costs may be enlightening. The average inpatient cost of municipal somatic specialised care per person in Finland in 1998 was 345 € (Hujanen et al 2004). The costs for men aged 18-40 years were 117 € and for men aged 41-64 years 332 €. The corresponding costs for women were 243 € (in age group 18-40) and 302 € (in age group 41-64). These costs were inflated from the original 2002 price level to the 1998 price level by using the price index of municipal health services (Hujanen 2003; www.tilastokeskus.fi/tk/hp/kui_kust.html).

In 1998, the average age of persons in this study was 35 years (min 19, max 51), and around two-thirds of persons were aged from 18-40 years. Thus, the younger age group in the study by Hujanen et al (2004) forms a better comparison group than the older one (41-64 years) when comparing with the national inpatient costs. Inpatient treatment costs per male T1DM patient in 1998 were 5.5 times higher than the average costs of somatic specialised inpatient care of men aged 18-40 years in Finland (642 € vs. 117 €). Those costs were double the average equivalent costs of inpatient care of all age groups of men in Finland (642 € vs. 326 €). Respectively, inpatient treatment costs per female T1DM patient in 1998 were 2.6 times higher than the average costs of somatic specialised care of women aged 18-40 years in Finland (636 € vs. 243 €). Those costs were 1.7-fold the average equivalent costs of inpatient care of all age groups of women in Finland (636 € vs. 364 €). Inpatient treatment costs per T1DM patient in 1998 were almost twice as high as than the average costs of somatic specialised care in Finland (640 € vs. 345 €).

As mentioned earlier, the youngest patients in 1998 were 19 and the oldest 51 years of age. Thus, the treatment costs do not contain the initial treatment costs, costs related to the period shortly after T1DM was diagnosed and treated in the paediatric department, and when the patient and

his/her parents were counselled about treatment of T1DM. Many patients had not yet developed complications, especially complications involving the most expensive treatments.

Generally, comparing costs between different studies is often impossible or very difficult because different methods have been used, and patients, their ages, severity of diseases, follow-up periods differ and studies have been conducted in different years. Countries also differ in respect to age structure, incidence of various diseases, availability and relative prices of health care resources and medicines, price levels, clinical practices and incentives to health care professionals and institutions (Drummond and McGuire 2001).

Comparison of treatment costs presented in different studies in Finland can also be really difficult. In a recent study, Punnonen (2005) explored the costs of 27 common treatments in specialised care. All central hospitals and almost all local hospitals participated and provided their pricing information of various treatments. The results revealed that there was large cost variation in treatments of the same diseases across hospitals. The costs of treatment of the same disease were often manyfold depending on the hospital. For example, the 'packet price' for the treatment of T1DM varied between 1,457 € and 2,520 € (in 17 hospitals using DRG pricing).

6.9. Comparison of costs of inpatient care of T1DM patients when duration of T1DM was on average 9.5 years vs. 16.5 years vs. 25 years

Various complications of T1DM develop at a differing pace over time. It is therefore essential to study hospitalisations and costs longitudinally to determine the use of physical and monetary resources required to treat complications of T1DM. Apart from this study, few longitudinal studies have thus far been conducted on hospital use and costs of T1DM complications.

Interesting and considerable changes were discovered when the costs of treatment of T1DM having lasted on average 9.5 years (range 9-11 years) or 16.5 years (range 16-18 years) were compared with the costs of treatment of T1DM in 1998, when T1DM had lasted on average 25 years (range 19-33 years). It should be taken into account, though, that the basis of cost calculations (and hospital use) in 1998 was cross-sectional. This may have caused some bias.

Costs per patient

In terms of average annual costs per patient by duration of T1DM (**Table 10** in **Appendix 1** and **Figures 22** and **23** in **Appendix 2**), there was a marked increase in treatment costs due to renal complications. When the duration of T1DM increased from 9.5 years to 16.5 years, the costs of treating renal complications 4.5-folded, and when the duration increased to 25 years (16.5 to 25

years), these costs doubled. Thus, in around 15 years (T1DM duration 9.5 years vs. 25 years) the costs of treating renal complications 9-folded. It would be interesting to see how these costs develop over an even longer duration of T1DM. Would they still continue to rise and at what speed? As the average age in the cohort in 1998 was 35 years (min 19, max 51) and the average age at diagnosis was 10 years, the treatment costs due to renal complications would presumably continue to rise, but perhaps not at the same speed as before 25 years of T1DM duration.

Generally, as the duration of T1DM increased from 9.5 years to 16.5 years, all treatment costs due to complications, except those due to coma, rose clearly. When these costs were compared in the next duration range (16.5 vs. 25 years), there was an increase in treatment costs due to cerebrovascular, cardiovascular, peripheral vascular and renal complications and coma. Notably, treatment costs of ophthalmic complications first had an almost 3-fold increase (9.5 vs. 16.5 years), but dropped almost three-quarters as diabetes lasted longer (16.5 vs. 25 years). One reason for this may have been the increasing use of outpatient hospital care and the developments in treatment practices and medical technology. For example, laser photocoagulation has proved to be an effective treatment for diabetic retinopathy, and retinal photography is a cost-effective screening method to prevent visual impairment (Pajunpää 1999). Also, many ophthalmic patients had most likely become blind, and this fact naturally would have decreased hospital use and treatment costs in that complication group. As the duration of T1DM increased by 7 years (from 16.5 to 25 years), the treatment costs of all complications combined had a slight decrease, but those of total hospital use and especially diabetes without complications (code 2500B) had a clear drop. In around 15 years (T1DM duration 9.5 vs. 25 years), treatment costs due to code 2500B had a considerable drop, well over 90%. This was the single main contributor to treatment costs of total hospital use dropping around over 50% in that period, as did the costs due to T1DM-related use. During the same period, the treatment costs of all complications combined more than doubled.

Costs per treatment period

The average annual costs per treatment period for separate complication groups in differing durations of T1DM (9.5/16.5/25 years) are compared in **Table 11** in **Appendix 1** and in **Figures 24** and **25** in **Appendix 2**. The costs per treatment period due to total use, T1DM-related use, renal complications, coma and especially those due to T1DM without complications dropped more in the earlier duration period of T1DM (9.5/16.5 years) than in the later one (16.5/25 years).

In general, despite a few exceptions, average annual costs per treatment period dropped when 9.5/16.5/25 years of T1DM duration were compared. Comparing the costs when duration of

T1DM increased by around 15 years (9.5 to 25 years) is most interesting, as costs per treatment period dropped notably (by 20%-50%) in each cost category (except for cerebrovascular, cardiovascular and endocrine complications, where the numbers of patients were rather small). Costs per treatment period due to total use, T1DM-related use and all complications combined declined by one-third as the duration of T1DM increased by 15 years.

Striking was the decline in costs per treatment period due to ophthalmic complications. When T1DM had lasted 9.5 years, the costs due to ophthalmic complications per treatment period were the highest of all groups (4,400 €/period), but when T1DM lasted on average 15 years longer, the costs per period dropped by over one-half. The reason for this was the marked decreases in bed-days, LOS and numbers of hospital users. These decreases were obviously due to the reasons mentioned earlier (development of treatment practices, technical advancement).

Costs per hospital user

Another picture is obtained when average annual treatment costs per hospital user in each complication group are compared between different durations of T1DM (9.5/16.5/25 years). These figures are presented in **Table 12** in **Appendix 1** and in **Figure 26** in **Appendix 2**. Total costs per user due to all hospitalisations decreased continuously as the duration of T1DM increased (by one-quarter between 9.5/16.5 years and 16.5/25 years) because total costs diminished more than did the number of hospital users. On the other hand, costs per user due to all complications combined first increased by around one-third (between 9.5 and 16.5 years of T1DM duration), and then decreased by about the same amount as T1DM lasted on average 25 years (range 16.5/25 years). Thus, these costs remained at the same level of over 5,000 € per user during a 15-year period (9.5/25 years of T1DM).

A lot of fluctuation was observed in the costs per user in different complication groups, as T1DM lasted longer. Treatment costs per hospital user due to ophthalmic complications were the highest of all treatment costs for complications when T1DM had lasted 9.5 years (5,800 € per user). When the T1DM duration increased from 16.5 to 25 years, these costs dropped by 50%, and the costs per user were now the 6th highest of the 9 complication groups. The main reasons for this drop were the considerable decline in hospital bed-days and the decrease in LOS (from 5.4 to 3.2 days). Again, not surprisingly, costs per user due to treatment of renal complications continued to rise as the duration of T1DM increased from 9.5 to 25 years (increase around 50%). These costs became the second highest of treatment costs of all complication groups (7,000 €/user). Although LOS of renal complications declined somewhat when the duration of T1DM increased from 9.5 to 25 years (9.1 to 7.4 days), the frequency of hospital visits (discharges/user

1.5 to 2.7) and the number of hospital users increased at the same time. Because the increase in bed-days, and thus, the increase in treatment costs of renal complications, was bigger than the increase in hospital users, costs per hospital user due to renal complications rose clearly.

Treatment costs per user due to peripheral vascular complications also increased as T1DM duration increased to 25 years. An essential reason for this was growth in the amount of use due to microangiopathy (ICD 2506B), which in 1998 ranked fourth of all diagnoses causing bed-days (at the same level as diabetes without complications, ICD 2500B). A direct comparison of the treatment costs of peripheral vascular complications over time is impossible because microangiopathy did not have a specific ICD code before 1987. This means that the treatment costs due to peripheral vascular complications when T1DM had lasted 9.5 years were underestimated. Treatment costs due to other complications of T1DM were most likely somewhat overestimated as microangiopathy was possibly coded in that group.

6.10. Health care costs of persons with T1DM and of T1DM in Finland in 2001

Costs of inpatient hospital care of T1DM are notable. In this study, the costs of outpatient care and medicines were not included. To give a wider picture of this disease, the following calculations are informative:

Health care costs of persons with T1DM in Finland

Health care costs (all) for a person with T1DM were 22,095 FIM (3,717 €) in Helsinki in 1997 (Kangas 2002). The total cost was over four times higher than for the control group (22,095 FIM vs. 5,315 FIM). As the health care costs were 10.4% higher in Helsinki in 1997 than in Finland overall (Kangas 2002), the costs for a person with T1DM in Finland would be:

- 22,095 FIM / 1.104=20,013 FIM (3,366 €).

This figure is next inflated to the 2001 price level using the price index of municipal health care (Hujanen 2003, www.tilastokeskus.fi/tk/hp/kui_kust.html):

- 2001 index 116.4 / 1997 index 104.6 =1.113
- 20,013 FIM* 1.113 = 22,375 FIM (3,764 €), which is the total cost of a person with T1DM in 2001.

There were around 45,000 persons with T1DM in Finland in 2000 (Reunanen 2006), so when multiplied: 45,000 * 22,375 FIM = 1,007 billion FIM, or 169 million euros.

- In 2001, the health care costs of all persons with T1DM in Finland were around *170 million euros.*

Health care costs of T1DM in Finland

The excess cost of a person with T1DM compared with the cost of a person without T1DM in Helsinki in 1997 was 16,780 FIM (2,823 €) (Kangas 2002). Using the same methodology as above, the excess costs of a person with T1DM in Finland in 2001 would be:

- 16,780 / 1.104 = 15,199 FIM (2,557 €).
- 15,199 FIM* 1.113 = 16,916 FIM (2,845 €), which is the (excess) cost of T1DM per person in 2001.
- 45,000 * 16,916 = 761 million FIM, or 128 million euros
- In 2001, the health care costs of T1DM in Finland were around *130 million euros*.

7. CONCLUSIONS

1. The length of stay in inpatient care and the total number of yearly bed-days of T1DM patients decreased notably with ageing of the patients from 1973 to 1997, but hospital visits became more frequent. In nearly all stages of diabetes, women used more hospital bed-days than men.

2. The use of bed-days of T1DM patients due to diabetes (main diagnosis ICD-9 code 250.xx) was 3- to 4-fold that due to other diagnoses (main diagnosis other than 250), as shown by the results during the period from 1973 to 1987. After this period, the use due to diabetes decreased steadily, while the use due to other diagnoses increased, reaching the level of use due to diabetes in the early 1990s. Increases in the numbers of hospital users and discharges contributed to this increase. During the total follow-up period of 25 years, the use of bed-days due to diabetes was twice as high as the use due to other diagnoses.

3. When the duration of T1DM increased on average from 9.5 to 16.5 years with ageing of patients, the yearly numbers of bed-days due to all complications of diabetes increased almost 3-fold, while the yearly numbers of bed-days due to T1DM without complications dropped considerably. The number of bed-days due to renal complications, peripheral vascular diseases and ophthalmic complications in particular increased markedly. At this stage of diabetes, women consumed clearly more bed-days than men, especially due to renal and ophthalmic complications.

   In 1998, when T1DM had lasted on average 25 years, the proportion of bed-days due to renal complications constituted almost 40% of total bed-days, while the share of bed-days due to ophthalmic complications was now only 5% of total bed-days. Among the T1DM patients having suffered from diabetes for 25 years, male patients used slightly more total bed-days and bed-days due to diabetes than female patients.

   It can be concluded that women use inpatient care more than men during the earlier stages of T1DM and obviously get many complications earlier than men, but as T1DM lasts longer, male patients catch up to female patients in terms of bed-days consumed.

4. As the duration of T1DM increased from 9.5 to 16.5 years with ageing of the patients, the yearly costs of inpatient care due to diabetic complications 2.5-folded and their share of the costs rose to almost half of total costs of inpatient care. Average treatment costs per patient for all complication groups (except coma) increased substantially; a vast majority of these costs were incurred due to ophthalmic and renal complications and complications

classified as other complications. Women's treatment costs were higher than those of men in practically every complication group and cost category, although the differences between sexes somewhat diminished as duration of T1DM increased (by these 7 years). Treatment costs of ophthalmic complications contributed almost half of the growth of costs of treatments of all complications at this stage of diabetes.

In 1998 (T1DM duration on average 25 years), the yearly costs for treating renal complications accounted for half of the treatment costs of all complications of diabetes, and the costs of treating renal complications were higher in female patients. At this stage of diabetes, the total yearly treatment costs per patient were about the same for both sexes. In comparison with the average inpatient costs of municipal somatic specialised care per person in Finland in 1998, the inpatient treatment costs per T1DM patient were considerably higher (roughly 1.7-5.5 times higher, depending on age and sex).

5. Besides the notable inpatient costs of T1DM calculated in this study, T1DM obviously causes considerable outpatient costs as well as loss of quality and lenght of life. These costs and losses should be addressed in future studies.

6. The results of this study showed that in the early phases of T1DM, T1DM without complications causes a considerable amount of inpatient bed-days. The use of inpatient care increases with ageing of patients; an important cause of this increase is the development of complications of diabetes. These results combined with the high incidence of T1DM in Finland indicate that the economic burden of inpatient care of T1DM is substantial. Measures to prevent T1DM and its complications and treatments focused on complications of T1DM should be developed.

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APPENDIX 1. TABLES IN APPENDIX 1

Table 1. Number of bed-days and discharges, and mean length of stay (LOS) of diseases (by diagnoses) causing most inpatient care in each complication group (ranked by amount of bed-days) and for total use in the two observation period of three years of duration of T1DM.

	T1DM duration 9-11 years				T1DM duration 16-18 years				
ICD-8/ICD-9	**Bed-days**	**Discharges**	**LOS**	**Diagnosis**	**ICD-8/ICD-9**	**Bed-days**	**Discharges**	**LOS**	**Diagnosis**
Total hospital use									
25000/2500B	28,045	3,856	7.3	Diabetes, sine complicatione	25000/2500B	7,711	1,539	5.0	Diabetes, sine complicatione
25008/2507B,X	1,801	229	7.9	Complicatione alia (definita)	25008/2507B,X	5,707	644	8.9	Complicatione alia (definita)
25002/2504B/3620B	1,345	185	7.3	Complicatione oculi (+retinopathia)	25004/2503B	4,262	537	7.9	Nephropathia diabetica
30040-41/3004A	1,048	20	52.4	Neurotico-depressiva/depressiva	25002-3/2504B+3620A,B	4,012	756	5.3	Complicatione oculi (+retinopathia)
25009/2508B	749	76	9.9	NUD/complicatione non descripta	295.xx/295	1,978	6	329.7	Schizophrenia.
25007/2502B	696	106	6.6	Coma diabeticum	301.xx/301.x	1,310	43	30.5	Perturbationes personalitatis
295.xx/295	643	9	71.4	Schizophrenia	../2501B	609	141	4.3	Ketoacidosis. Icd-9 only
25004/2503B	609	74	8.2	Nephropathia diabetica	../2506B	551	111	5.0	Microangiopathia diab. Icd-9 only
301.xx/301	602	15	40.1	Perturbationes personalitatis	34099/3400A	431	25	17.2	Sclerosis multiplex, MS
../2501B	347	72	4.8	Ketoacidosis. Icd-9 only	25005/2505B	385	59	6.5	Neuropathia diabetica
296.xx/296	345	4	86.3	Perturb. mentis affectivae graves.	71238/7148X	317	13	24.4	Arthritis rheumatoides alia def.
					25007/2502B	312	65	4.8	Coma diabeticum
Cerebrovascular complications									
43499	30	1	30.0	Embolia cerebri	433.xx/4340A	96	5	19.2	Thrombosis cerebri
435/4351A	19	2	9.5	Ischaemia cerebralis transitoria (TIA)	4374A	38	1	38.0	Alii morbi cerebrovasc.
4311A	16	1	16.0	Haemorrhagia intracerebralis	4351A,4359X	13	3	4.3	Ischaemia cerebralis transitoria (TIA)
Cardiovascular complications									
42792	8	3	2.7	Fibrillatio auricularis	410.xx/4100B,X	133	13	10.2	Infarctus myocardii acutus
41291	7	2	3.5	Status post infarctum cordis	4289X	75	2	37.5	Insufficientia cordis
42798	4	3	1.3	Alia arrhythmia definita	41201-91/4120X	72	8	9.0	Status post infarctum cordis
					42700	24	2	12.0	Incompensatio cordis. Oedema cardiale
					4110B	31	2	15.5	Instabil angina pectoris

T1DM duration 9-11 years					T1DM duration 16-18 years				
ICD-8/ICD-9	**Bed-days**	**Discharges**	**LOS**	**Diagnosis**	**ICD-8/ICD-9**	**Bed-days**	**Discharges**	**LOS**	**Diagnosis**
Peripheral vascular complications									
../2506B	90	11	8.2	Microangiopathia. Icd-9 only	../2506B	547	109	5.0	Microangiopathia. Icd-9 only
70708-09	58	7	8.3	Ulcus chronicum cutis. Alii defin.+ NUD	7078X	131	6	21.8	Ulcus chronicum cutis. Loco alio definito
88510	23	3	7.7	Amputatio traumatica pollicis (thumb)	7070A	117	7	16.7	Ulcus chronicum cutis.
44390	16	1	16.0	Alii morbi vascularum peripheric.	25006	73	10	7.3	Gangraena diabeticum
45100	16	2	8.0	Phlebitis et thrombophlebitis	70709/7079X	84	3	28.0	Ulcus chronicum cutis. NUD
					7071A	70	5	14.0	Ulcus extremitatis inferioris
Neurological complications									
25005/2505B	273	36	7.6	Neuropathia diabetica	25005/2505B	385	59	6.5	Neuropathia diabetica
					3540A	28	20	1.4	Syndroma canalis carpi
					35701	10	4	2.5	Morbi nervorum periph. Nervi mediani
Renal complications									
25004/2503B	609	74	8.2	Nephropathia diabetica	25004/2503B	4,262	537	7.9	Nephropathia diabetica
59010/5901A	199	19	10.5	Infectio renis. Pyelonephritis acuta	59010/5901A	301	54	5.6	Infectio renis. Pyelonephritis acuta
59000	124	9	13.8	Infectio renis. Pyelonephritis chronica	59902/5990B	164	14	11.7	Alii morbi tractum urinariorum
59099	27	4	6.8	Infectio renis. NUD	59000/5900A	64	6	10.7	Infectio renis. Pyelonephritis chronica
58099	26	2	13.0	Nephritis acuta	58200	43	8	5.4	Nephritis chronica cum uraemia
Endocrine complications									
-					2767	3	1	3.0	Hyperkalaemia

	T1DM duration 9-11 years					T1DM duration 16-18 years			
ICD-8/ICD-9	**Bed-days**	**Discharges**	**LOS**	**Diagnosis**	**ICD-8/ICD-9**	**Bed-days**	**Discharges**	**LOS**	**Diagnosis**
Opthalmic complications									
25002/3620B	1,174	153	7.7	Retinopathia diabetica	25002/3620A,B	3,143	566	5.6	Retinopathia diabetica
2504B	171	32	5.3	Complicatione oculi. Icd-9 only	2504B	739	174	4.2	Complicatione oculi. Icd-9 only
25001/3664A	93	12	7.8	Cataracta diabetica	375.xx/365.x	250	50	5.0	Glaucoma
36400/3640A	41	9	4.6	Iridocyclitis acuta	25001/3664A	137	27	5.1	Cataracta diabetica
374.xx	66	9	7.3	Cataracta	25003	95	6	15.8	Complicatio oculi alia sive NUD
375.xx/365.x	31	8	3.9	Glaucoma	374.xx/366.x	80	22	3.6	Cataracta
36402	27	3	9.0	Iridocyclitis, uveitis chronica	37700	72	10	7.2	Haemorrhagia corporis vitrei
Other complications									
25008/2507B	1,640	230	7.1	Complicatione alia definita	25008/2507.x	5,689	642	8.9	Complicatione alia definita
25009/2508B	872	78	11.2	Complicatione non descripta, NUD	25009/2508B	277	57	4.9	Complicatione non descripta, NUD
681.xx/x,682.xx/x	115	13	8.8	Cellulitis. Infectiones cutis/subcutis	7301G	66	6	11.0	Osteomyelitis chronica
72010	77	3	25.7	Osteomyelitis chronica	682.xx	17	4	4.3	Cellulitis. Infectiones cutis/subcutis
Coma									
25007/2502B	702	107	6.6	Coma diabeticum	25007/2502B	313	66	4.7	Coma diabeticum
Hypoglycaemia									
Only ICD-9	-				2510B	86	26	3.3	Coma hypoglycaemicum
					2512B,X	71	15	4.7	Hypoglycaemia alia and NUD

ICD= International classification of diseases

Table 2. Shares (%) of the annual costs of complication groups of total inpatient costs and shares (%) of the annual costs of complication groups of the costs of all complications, by duration of T1DM

	Shares (%) of total costs		Shares (%) of complication costs	
	T1DM 9.5 yrs.	**T1DM 16.5 yrs.**	**T1DM 9.5 yrs.**	**T1DM 16.5 yrs.**
CERVASC	0.1	0.3	0.8	0.7
CARVASC	0.0	0.8	0.3	1.8
PERVASC	0.4	2.6	2.5	5.6
NEUROL	0.4	0.8	3.1	1.9
RENAL	1.8	10.3	12.4	22.5
ENDOCRIN	0.0	0.0	0.0	0.0
OPHTHALMIC	4.8	17.4	34.2	38.1
OTHER complicat.	5.3	12.7	37.7	27.9
COMA	1.3	0.7	9.1	1.4
Complications total	**14.2**	**45.7**	**100.0**	**100.0**
Hypoglycaemia	0.0	0.3	0.0	0.8
2500B/25000	60.9	15.7	428.7	34.4
Rest of other use	25.0	38.6	175.8	84.4
OTHER use	85.8	54.3	604.5	118.8
T1DM use	75.0	61.4	528.7	134.4
TOTAL use	**100.0**	**100.0**	**704.5**	**218.8**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes); other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B/25000

Table 3. Average annual costs (€) per patient in the cohort by complication group and by duration of T1DM and changes (%) in costs with the increased duration of diabetes.

	Costs per patient T1DM 9.5 yrs	Costs per patient T1DM 16.5 yrs	Change in costs (%) 9.5/16.5 yrs
CERVASC	1.5	3.6	131.4
CARVASC	0.6	9.2	1406.4
PERVASC	5.0	28.6	472.2
NEUROL	6.2	9.4	51.5
RENAL	24.5	114.2	365.4
ENDOCRIN	0.0	0.1	
OPHTHALMIC	67.8	193.2	184.8
OTHER complicat.	74.8	141.3	88.8
COMA	18.0	7.3	59.8
Complications total	**198.6**	**506.9**	**155.2**
Hypoglycaemia		3.8	
2500B/25000	851.4	174.5	79.5
Rest of other use	349.2	427.6	22.5
OTHER use	1,200.6	602.1	49.9
T1DM use	1,050.1	681.3	35.1
TOTAL use	**1,399.2**	**1,109.0**	**20.7**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes); other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B/25000

Table 4. Annual costs (€) per treatment period by complication group, duration of T1DM and sex, and differences between sexes

	Costs per female treatment period, T1DM 9.5 yrs.	Costs per male treatment period, T1DM 9.5 yrs.	Difference in costs (%) between sexes 9.5 yrs.	Costs per female treatment period, T1DM 16.5 yrs	Costs per male treatment period, T1DM 16.5 yrs	Difference in costs (%) between sexes 16.5 yrs
CERVASC	3,133	5,570	77.8	5,614	2,901	93.5
CARVASC	348	967	177.8	4,482	2,228	101.2
PERVASC	2,511	2,605	3.8	1,930	3,053	58.2
NEUROL	1,803	2,587	43.5	1,740	1,488	16.9
RENAL	3,293	3,068	7.3	2,460	3,000	21.9
ENDOCRIN					1,044	
OPHTHALMIC	4,487	4,350	3.1	3,397	3,220	5.5
OTHER complicat.	3,357	3,716	10.7	2,930	2,913	0.6
COMA	2,679	2,469	8.5	1,578	1,712	8.5
Complications total	**3,523**	**3,461**	1.8	**2,864**	**2,941**	2.7
Hypoglycaemia	0	0		2,147	736	
2500B/25000	3,294	3,515	6.7	1,692	1,723	1.9
Rest of other use	3,555	3,771	6.1	2,806	3,062	9.1
OTHER use	3,360	3,592	6.9	2,344	2,517	7.4
T1DM use	3,336	3,494	4.8	2,421	2,500	3.3
TOTAL use	**3,383**	**3,573**	5.6	**2,556**	**2,694**	5.4

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

Table 5. Numbers of hospital users in 1998 by complication group and sex

	Number of users, total	Number of users, females	Number of users, males
CERVASC	3	1	2
CARVASC	22	12	10
PERVASC	32	16	16
NEUROL	13	2	11
RENAL	149	73	76
ENDOCRIN	0	0	0
OPHTHALMIC	86	41	45
OTHER complications	148	65	83
COMA	36	12	24
Complications total	**412**	**190**	**222**
Hypoglycaemia	1	0	1
2500B	53	24	29
Other use	244	119	125
TOTAL use	**566**	**269**	**297**
Total N in the cohort	4,701	2,168	2,533

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); total use = complications total + other use

Table 6. Number of inpatient discharges per 1000 patient in 1998 by complication group and sex

	Discharges per 1,000 patients, total	Discharges 1,000 patients, females	Discharges 1,000 patients, males
CERVASC	0.6	0.5	0.8
CARVASC	5.7	6.0	5.5
PERVASC	20.4	13.4	26.5
NEUROL	4.5	0.9	7.5
RENAL	86.2	94.1	79.4
ENDOCRIN	0.0	0.0	0.0
OPHTHALMIC	25.1	24.0	26.1
OTHER complications	43.4	38.7	47.4
COMA	8.3	5.5	10.7
Complications total	**194.2**	**183.1**	**203.7**
Hypoglycaemia	0.2	0.0	0.4
2500B	13.6	14.8	12.6
Rest of other use	62.5	67.8	58.0
Other use	76.2	82.6	70.7
T1DM use	208.0	197.9	216.7
TOTAL use	**270.4**	**265.7**	**274.4**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B; total use = complications total + other use

Table 7. Number of discharges per hospital user in 1998 by complication group and sex

	Discharges per user, total	Discharges per user, females	Discharges per user, males
CERVASC	1.0	1.0	1.0
CARVASC	1.2	1.1	1.4
PERVASC	3.0	1.8	4.2
NEUROL	1.6	1.0	1.7
RENAL	2.7	2.8	2.6
ENDOCRIN	0.0		
OPHTHALMIC	1.4	1.3	1.5
OTHER complications	1.4	1.3	1.4
COMA	1.1	1.0	1.1
Complications total	**2.2**	**2.1**	**2.3**
Hypoglycaemia	1.0	0.0	1.0
2500B	1.2	1.3	1.1
Other use	1.5	1.5	1.4
TOTAL use	**2.2**	**2.1**	**2.3**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); total use = complications total + other use

Table 8. Number of bed-days per 1000 patients in 1998 by complication group and sex

	Bed-days per 1,000 patients, total	Bed-days per 1,000 patients, females	Bed-days per 1,000 patients, males
CERVASC	32.1	62.7	5.9
CARVASC	44.0	55.4	34.3
PERVASC	112.1	83.9	136.2
NEUROL	17.7	0.9	32.0
RENAL	638.6	712.6	575.2
ENDOCRIN	0.0	0.0	0.0
OPHTHALMIC	81.0	68.7	91.6
OTHER complications	256.5	186.3	316.6
COMA	29.1	17.5	39.1
Complications total	**1,211.2**	**1,188.2**	**1,231.0**
Hypoglycaemia	0.2	0.0	0.4
2500B	74.5	69.6	78.6
Rest of other use	394.2	417.0	374.7
Other use	468.6	486.6	453.2
T1DM use	1,285.9	1,257.8	1,309.9
TOTAL use	**1,679.9**	**1,674.8**	**1,684.2**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease; neurol = neurological complications; renal = renal complications; endocrin = endocrine complications; ophthalmic = ophthalmic complications; 2500B = T1DM without complications (ICD-9 code); other use = hypoglycaemia + 2500B + rest of other use (any inpatient use other than T1DM-related); T1DM use = complications total + 2500B; total use = complications total + other use

Table 9. Single diagnoses causing most inpatient care (bed-days, discharges, LOS's) in 1998, when duration of T1DM was on the average 25 years (19-33 years)

ICD-9 code	Number of bed-days	Number of discharges	LOS	Diagnosis
Total hospital use				
2503A,B	2,917	389	7.5	Nephropathia diabetica
2507A,B,X	972	175	5.6	Complicatione alia (definita)
2500A,B	405	77	5.3	Diabetes, sine complicatione
2506A,B	394	76	5.2	Microangiopathia diabetica
2501A,B	232	44	5.3	Ketoacidosis
3620A,B	194	64	3.0	Retinopathia diabetica
2961A	142	2	71.0	Depressio mentis gravis
2502A,B	137	39	3.5	Coma diabeticum
4340A	136	1	136.0	Thrombosis cerebri
2504A	126	29	4.3	Cum complicatione oculi
2508A,B	120	20	6.0	Complicatione non descripta, NUD
5678X	103	12	8.6	Peritonitis alia definita
5672A	99	16	6.2	Peritonitis suppurativa diffusa
4140X, 4148B,X	82	8	10.3	Morbi cordis ischaemici alii.
4402A	79	11	7.2	Atherosclerosis
6951C	67	2	33.5	Casus erythematodes syndroma Lyell
2505A,B	66	10	6.6	Neuropathia diabetica
4100B,X	65	5	13.0	Infarctus myocardii acutus.
2961E	60	1	60.0	Depressio mentis gravis
0388X	58	3	19.3	Septichaemia alia definita
3101A	55	1	55.0	Perturbatio mentis per laesionem cerebri
6819X	54	2	27.0	Cellulitis
7870A	53	12	4.4	Symptomata organorum digestionis. Nausea et emesis
0350X	47	6	7.8	Erypipelas alia definita seu NUD
3000A	37	3	12.3	Neuroses

ICD-9 code	Number of bed-days	Number of discharges	LOS	Diagnosis
Cerebrovascular complications				
4340A	136	1	136.0	Thrombosis cerebri
4318X	9	1	9.0	Haemorrhagia intracerebralis
4360A	6	1	6.0	Morbus cerebrovascularis alius sive non definitus.
Cardiovascular complications				
4140X	44	5	8.8	Morbi cordis ischaemici alii.
4100B	40	2	20.0	Infarctus myocardii acutus
4100X	25	3	8.3	Infarctus myocardii acutus
4148B	24	2	12.0	Morbi cordis ischaemici alii.
4289X	21	1	21.0	Insufficientia cordis.
4148X	14	1	14.0	Morbi cordis ischaemici alii.
4254A	12	2	6.0	Cardiomyopathia

ICD-9 code	Number of bed-days	Number of discharges	LOS	Diagnosis
Peripheral vascular complications				
2506B	356	65	5.5	Microangiopathia diabetica
4402A	79	11	7.2	Atherosclerosis
2506A	38	11	3.5	Microangiopathia diabetica
4518X	24	2	12.0	Phlebitis, thrombophlebitis et trombosis phlebarum
4438X	20	2	10.0	Alii morbi vascularis peripherici.
Neurological complications				
2505A	37	2	18.5	Neuropathia diabetica
2505B	29	8	3.6	Neuropathia diabetica
7135A	9	8	1.1	Arthropathia reactiva alia cum morbo systematis nervosi.
Renal complications				
2503B	2,214	294	7.5	Nephropathia diabetica
2503A	703	95	7.4	Nephropathia diabetica
5901A	36	8	4.5	Infectio renis
5850B	21	2	10.5	Insufficientia renis chronica.
Endocrine complications				
…				
Opthalmic complications				
3620B	173	59	2.9	Retinopathia diabetica
2504A	116	24	4.8	Cum complicatione oculi
3664A	37	21	1.8	Cataracta diabetica
3620A	21	5	4.2	Retinopathia diabetica
3682A	16	1	16.0	Diplopia.
2504B	10	5	2.0	Cum complicatione oculi
Other complications				
2507B	896	160	5.6	Cum complicatione alia
2508B	88	17	5.2	Cum complicatione non descripta
2507A	59	12	4.9	Cum complicatione alia
6819X	54	2	27.0	Cellulitis
2508A	32	3	10.7	Cum complicatione non descripta
6829X	27	2	13.5	Cellulitis
2507X	17	3	5.7	Cum complicatione alia
6828X	17	2	8.5	Cellulitis
5589X	16	3	5.3	Gastroenteritis seu colitis alia noninfectiosa
Coma				
2502B	129	36	3.6	Coma diabeticum
2502A	8	3	2.7	Coma diabeticum

Table 10. Average annual costs (€) in the cohort per patient by duration of T1DM (9.5/16.5/25 years) and by complication group

	Costs per patient. T1DM 9.5 yrs	Costs per patient. T1DM 16.5 yrs	Costs per patient. T1DM ~25 yrs (19-33 yrs) in 1998	Change in costs (%) by duration of T1DM 9.5/16.5 yrs	Change in costs (%) by duration of T1DM 9.5/25 yrs	Change in costs (%) by duration of T1DM 16.5/25 yrs
CERVASC	1.5	3.6	11.2	131.4	626.7	214.0
CARVASC	0.6	9.2	15.3	1,406.4	2,400.1	66.0
PERVASC	5.0	28.6	39.0	472.2	679.5	36.2
NEUROL	6.2	9.4	5.8	51.5	6.3	38.2
RENAL	24.5	114.2	222.3	365.4	805.8	94.6
ENDOCRIN	0.0	0.1				
OPHTHALMIC	67.8	193.2	51.3	184.8	24.4	73.4
OTHER complic.	74.8	141.3	89.3	88.8	19.3	36.8
COMA	18.0	7.3	10.1	59.8	44.0	39.3
COMPLICATIONS TOTAL	**198.6**	**506.9**	**444.4**	155.2	123.8	12.3
Hypoglycaemia		3.8	0.1			
2500B/ 25000-codes	851.4	174.5	25.9	79.5	97.0	85.2
Rest of other use	349.2	427.6	169.1	22.5	51.6	60.5
OTHER use	1,200.6	602.1	195.0	49.9	83.8	67.6
T1DM use	1,050.1	681.3	470.3	35.1	55.2	31.0
TOTAL use	**1,399.2**	**1,109.0**	**639.4**	20.7	54.3	42.3

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

Table 11. Average annual costs (€) in the cohort per treatment period by duration of T1DM (9.5/16.5/25 years) and by complication group

	Costs per treatment period, T1DM 9.5 yrs.	Costs per treatment period, T1DM 16.5 yrs.	Costs per treatment period. T1DM ~25 yrs (19-33 yrs) in 1998	Change in costs (%) by duration of T1DM 9.5/16.5 yrs	Change in costs (%) by duration of T1DM 9.5/25 yrs	Change in costs (%) by duration of T1DM 16.5/25 yrs
CERVASC	3,946	4,874	17,525	23.5	344.1	259.5
CARVASC	855	3,012	2,669	252.5	212.4	11.4
PERVASC	2,562	2,531	1,911	1.2	25.4	24.5
NEUROL	2,320	1,621	1,296	30.1	44.1	20.0
RENAL	3,195	2,670	2,581	16.4	19.2	3.3
ENDOCRIN		1,044				
OPHTHALMIC	4,435	3,315	2,042	25.3	54.0	38.4
OTHER complic.	3,537	2,922	2,058	17.4	41.8	29.6
COMA	2,587	1,651	1,223	36.2	52.7	25.9
COMPLICATIONS TOTAL	**3,494**	**2,900**	**2,288**	17.0	34.5	21.1
Hypoglycaemia		1,313	348			
2500B/25000-codes	3,392	1,710	1,904	49.6	43.9	11.3
Rest of other use	3,659	2,919	2,703	20.2	26.1	7.4
OTHER use	3,466	2,423	2,560	30.1	26.1	5.7
T1DM use	3,409	2,460	2,261	27.9	33.7	8.1
TOTAL use	**3,472**	**2,622**	**2,365**	24.5	31.9	9.8

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

Table 12. Average annual costs (€) per hospital user by duration of T1DM (9.5/16.5/25 years) and by complication group

	Costs per hospital user, T1DM 9.5 yrs.	Costs per hospital user, T1DM 16.5 yrs.	Costs per hospital user, T1DM ~25 yrs. (19-33 yrs) in 1998	Change in costs (%) by duration of T1DM 9.5/16.5 yrs.	Change in costs (%) by duration of T1DM 9.5/25 yrs.	Change in costs (%) by duration of T1DM 16.5/25 yrs.
CERVASC	4,735	5,361	17,525	13.2	270.1	226.9
CARVASC	1,044	6,024	3,276	476.8	213.7	45.6
PERVASC	3,341	3,808	5,734	14.0	71.6	50.6
NEUROL	3,280	2,474	2,094	24.6	36.1	15.4
RENAL	4,712	6,131	7,015	30.1	48.9	14.4
ENDOCRIN		1,044				
OPHTHALMIC	5,758	5,796	2,802	0.7	51.3	51.7
OTHER complic.	4,913	6,437	2,837	31.0	42.3	55.9
COMA	3,335	2,179	1,325	34.7	60.3	39.2
COMPLICATIONS TOTAL	**5,361**	**7,255**	**5,071**	**35.3**	**5.4**	**30.1**
Hypoglycaemia		1,864	348			81.3
2500B/25000-codes	6,089	2,832	2,299	53.5	62.2	18.8
OTHER use	7,327	4,842	3,757	22.4	48.7	22.4
TOTAL use	**7,881**	**6,991**	**5,310**	**24.0**	**32.6**	**24.0**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

Table 13. Number of bed-days of patients under and over 16 years of age, when T1DM duration was 9.5 years on average

	Bed-days <16, female	Bed-days >16, female	Bed-days < 16, male	Bed-days >16 male	Bed-days total, fem	Bed-days total, male	Bed-days Total	% of bed-days < 16 of all fem. total	% of bed-days < 16 of all male. total	Bed-days <16, total	Share of bed-days <16 of total.
CERVASC	0	36	0	32	36	32	68	0 %	0 %	0	0 %
CARVASC	0	2	0	25	2	25	27	0 %	0 %	0	0 %
PERVASC	0	101	1	118	101	119	220	0 %	1 %	1	0 %
NEUROL	0	77	0	213	77	213	290	0 %	0 %	0	0 %
RENAL	48	541	18	427	589	445	1,034	8 %	4 %	66	6 %
ENDOCRIN	0	0	0	0	0	0	0			0	
OPHTHALMIC	121	901	31	595	1,022	626	1,648	12 %	5 %	152	9 %
OTHER complic.	358	940	385	1,070	1,298	1,455	2,753	28 %	26 %	743	27 %
COMA	108	274	18	302	382	320	702	28 %	6 %	126	18 %
COMPLIC.Total	**635**	**2,872**	**453**	**2,782**	**3,507**	**3,235**	**6,742**	**18 %**	**14 %**	**1,088**	**16 %**
Hypoglycaemia	0	5	0	4	5	4	9	0 %	0 %	0	0 %
2500B/25000	6,785	8,672	6,249	6,225	15,457	12,474	27,931	44 %	50 %	13,034	47 %
Rest of other use	1,253	4,354	1,642	4,064	5,607	5,706	11,313	22 %	29 %	2,895	26 %
OTHER use	8,038	13,026	7,891	10,289	21,064	18,180	39,244	38 %	43 %	15,929	41 %
T1DM use	7,420	11,544	6,702	9,007	18,964	15,709	34,673	39 %	43 %	14,122	41 %
TOTAL use	**8,673**	**15,898**	**8,344**	**13,071**	**24,571**	**21,415**	**45,986**	**35 %**	**39 %**	**17,017**	**37 %**

cervasc = cerebrovascular disease; carvasc = cardiac disease; pervasc = peripheral vascular disease;
neurol = neurological complications; renal = renal complications; endocrin = endocrine complications;
ophthalmic = ophthalmic complications; 2500B/25000 = T1DM without complications (ICD-9/ICD-8 codes);
other use = hypoglycaemia + 2500B/25000 + rest of other use (any inpatient use other than T1DM-related);
T1DM use = complications total + 2500B/25000

APPENDIX 2. FIGURES IN APPENDIX 2

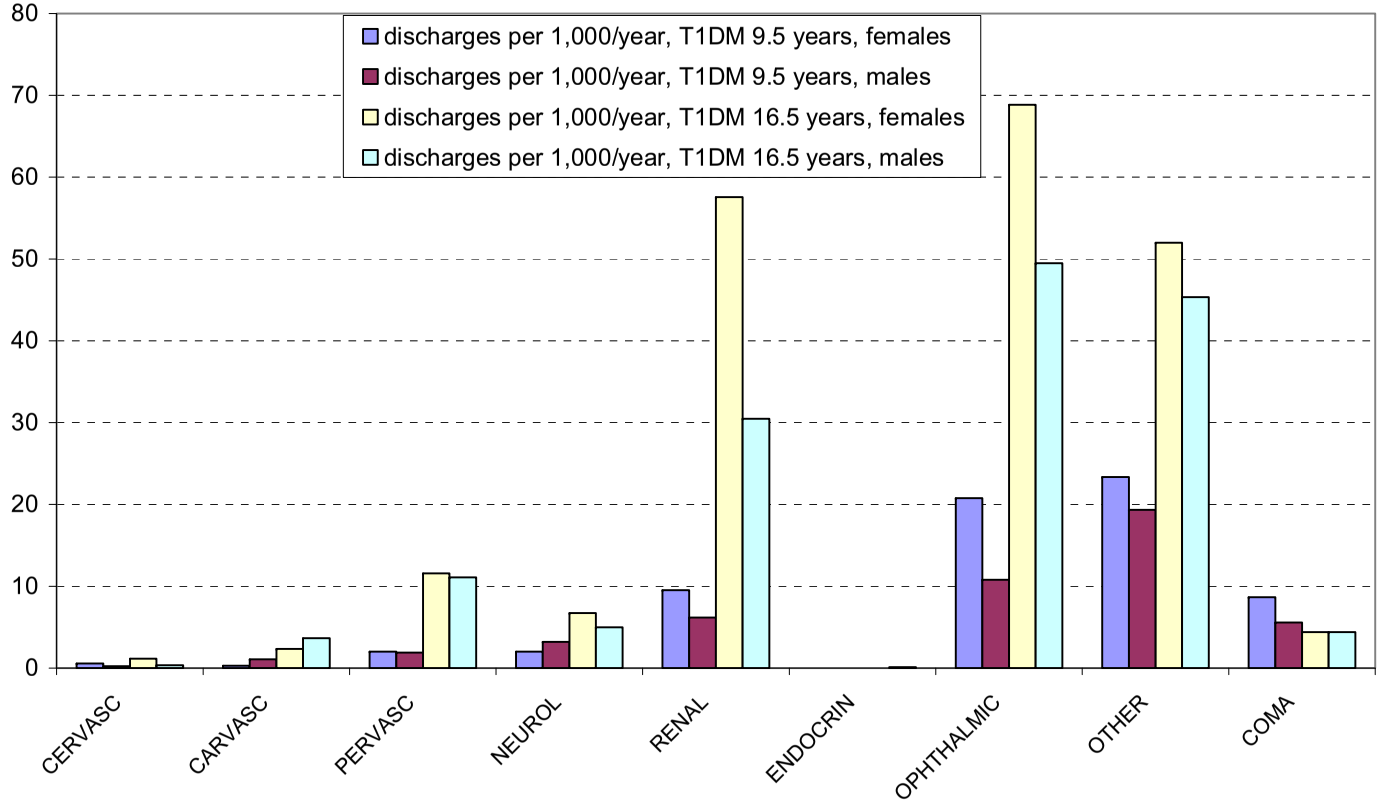

Figure 1. Mean number of yearly discharges per 1,000 patients by complication group, duration of T1DM and sex

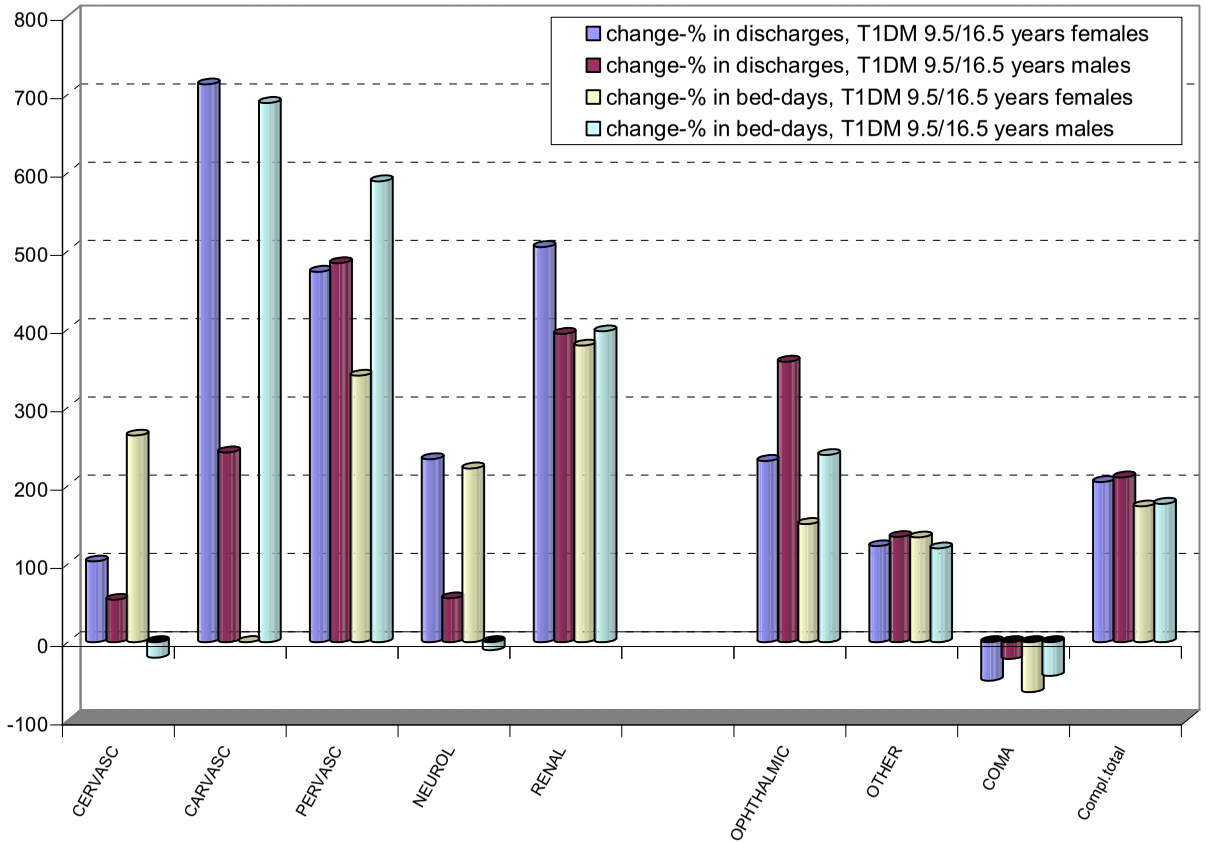

Figure 2. Proportional change (%) in mean yearly discharges and bed-days during the follow-up (T1DM 9.5 to 16.5 years) by complication group and sex

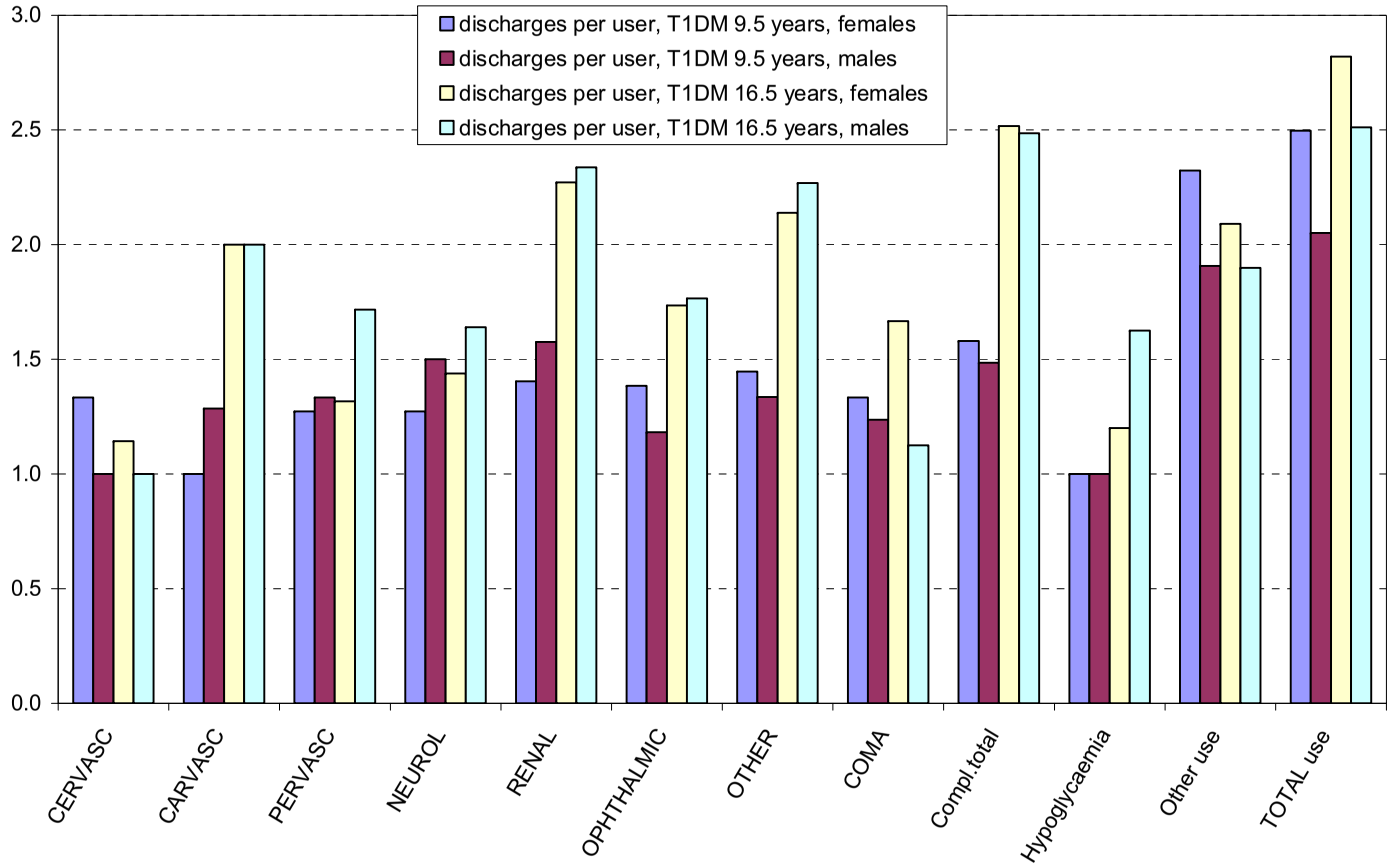

Figure 3. Mean number of yearly discharges per hospital user in each complication group and for other use and total use by duration of T1DM and sex

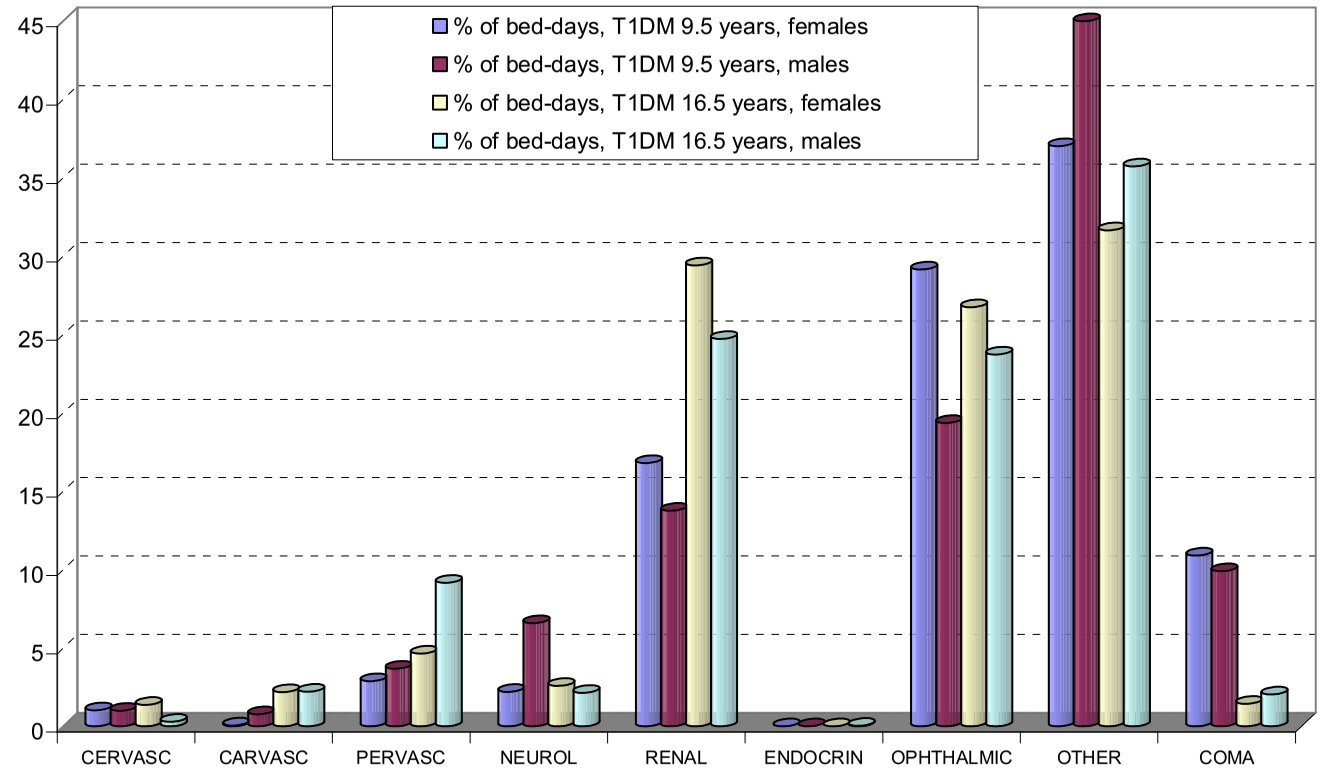

Figure 4. Percentages of yearly bed-days due to complications out of all bed-days due to complications by complication group, duration of T1DM and sex

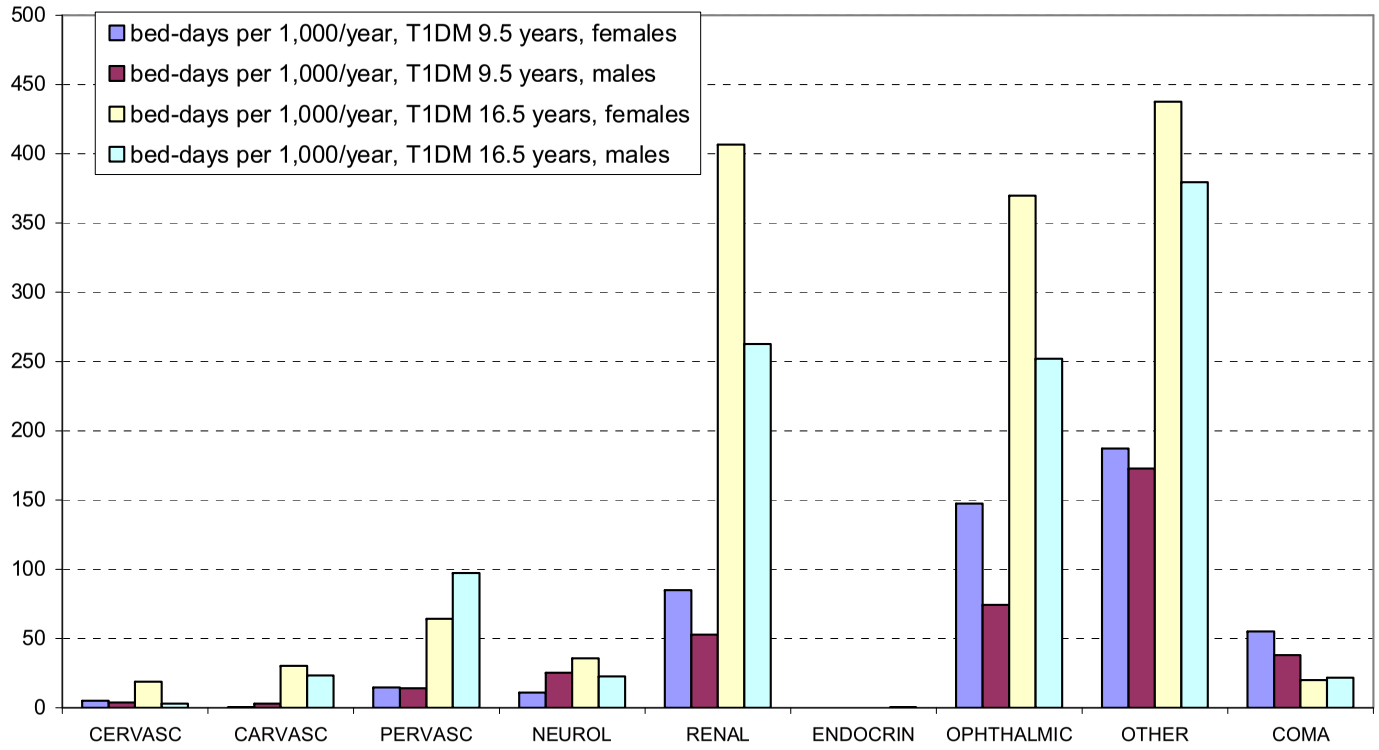

Figure 5. Mean number of yearly bed-days per 1,000 patients by complication group,duration of T1DM and sex

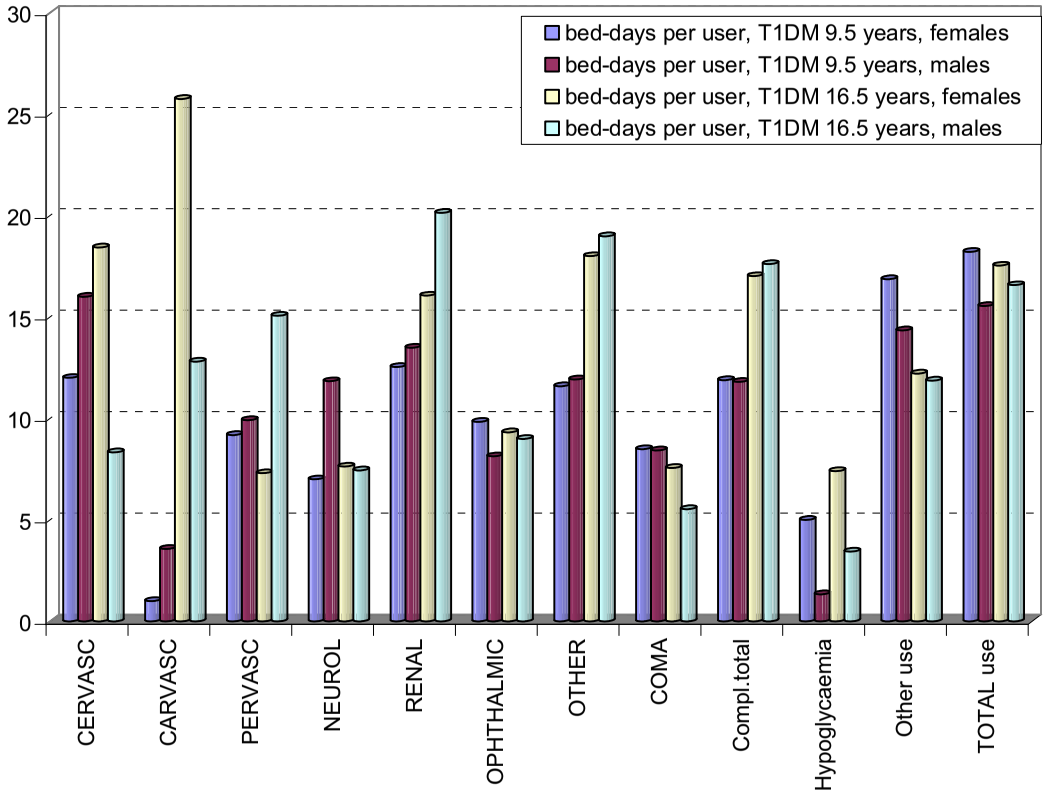

Figure 6. Mean yearly number of bed-days per hospital user in each complication group and for other use and total use by duration of T1DM and sex

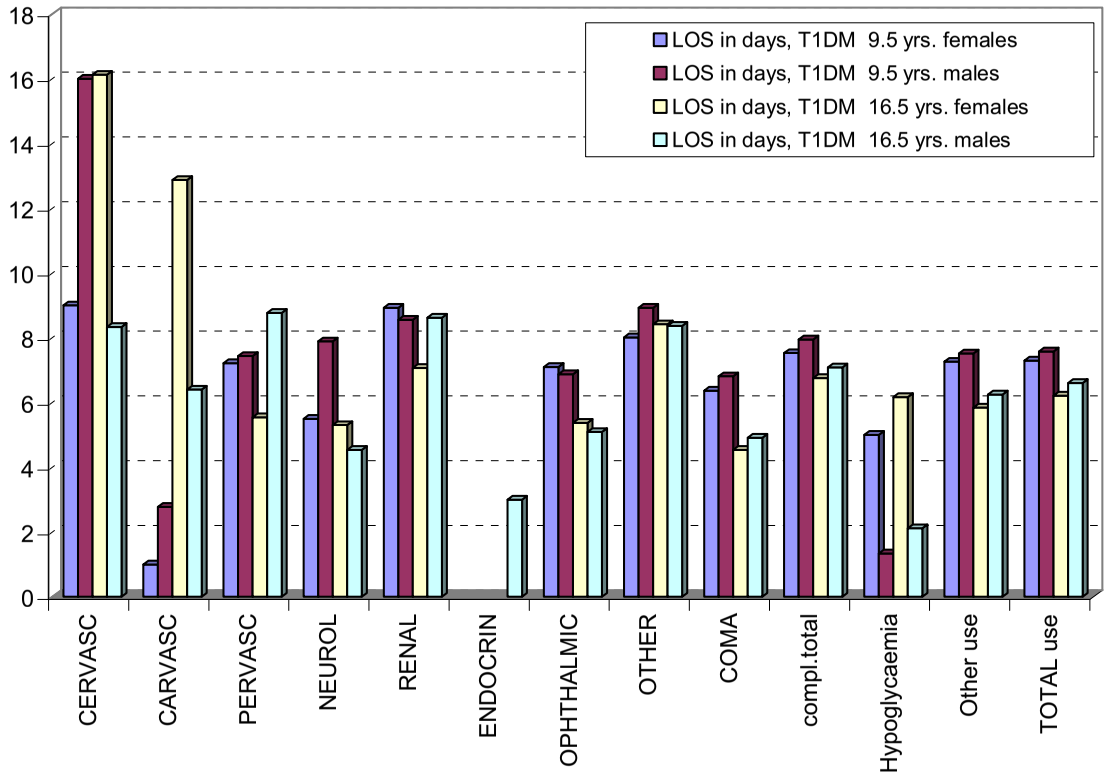

Figure 7. Mean length of stay (LOS) in hospital in each complication group and for other use and total use by duration of T1DM and sex

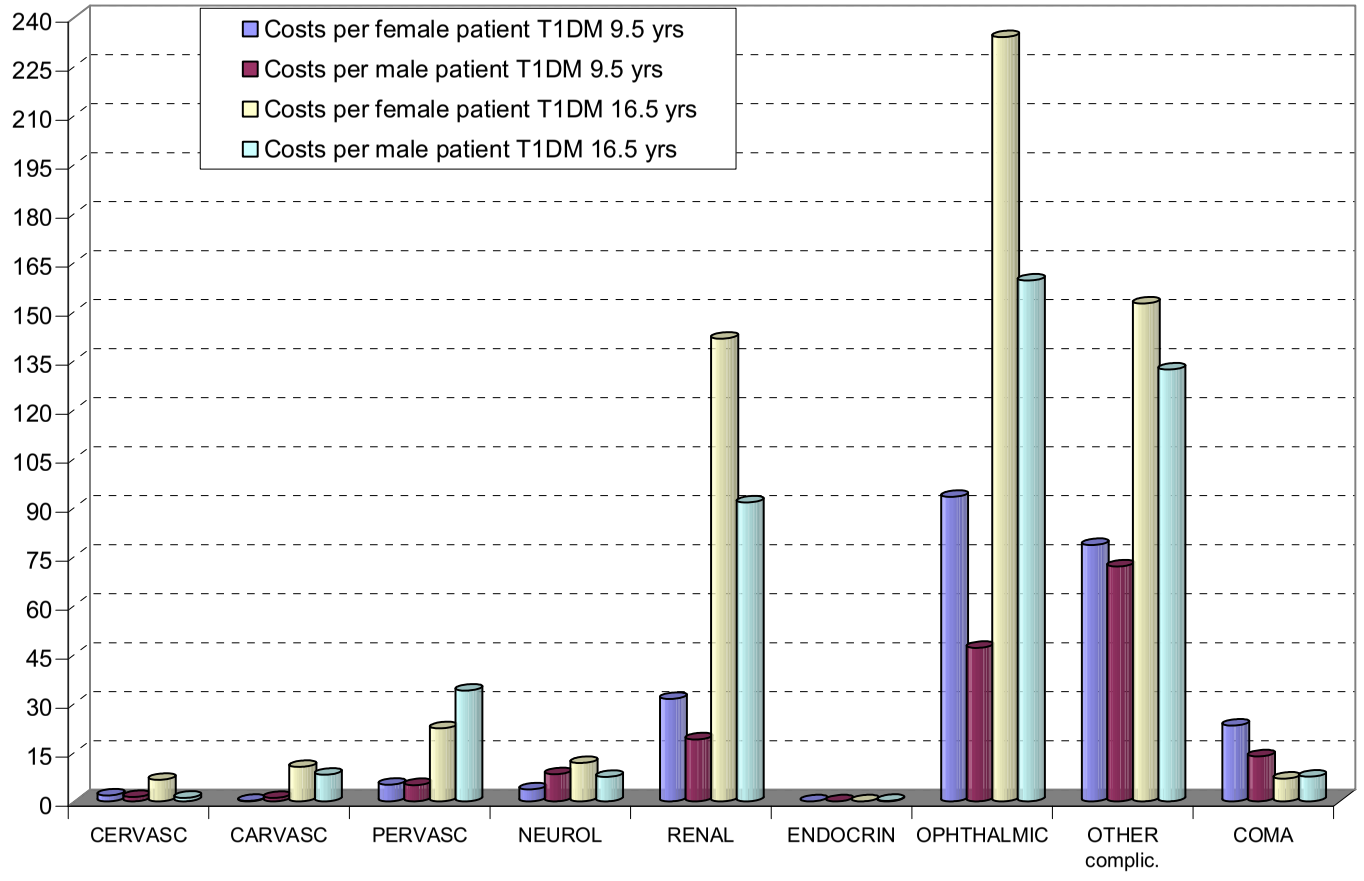

Figure 8. Average annual costs (€) per person by complication group, duration of T1DM and sex

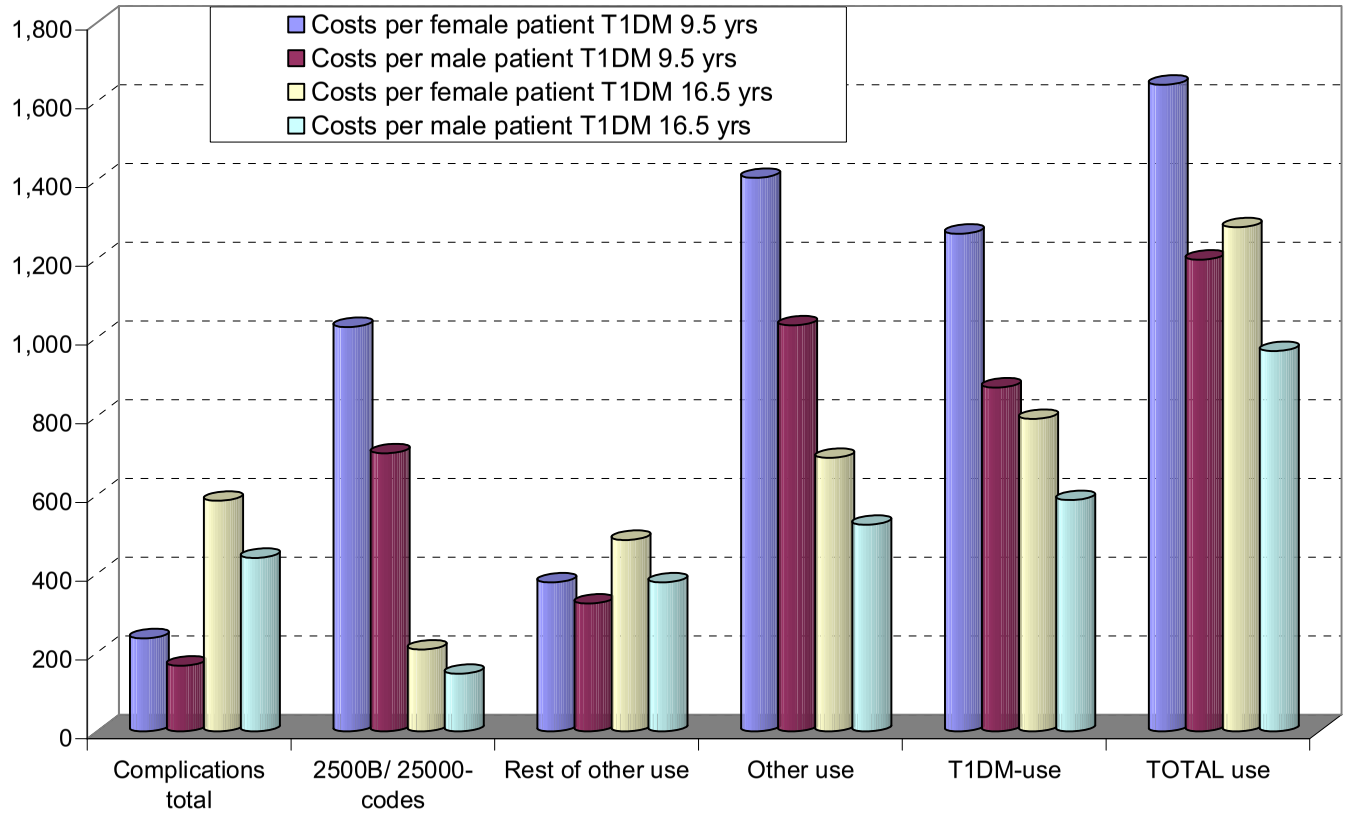

Figure 9. Average annual costs (€) per person by duration of T1DM and sex for all complications, T1DM without complications, other inpatient hospital use, T1DM related use and total use

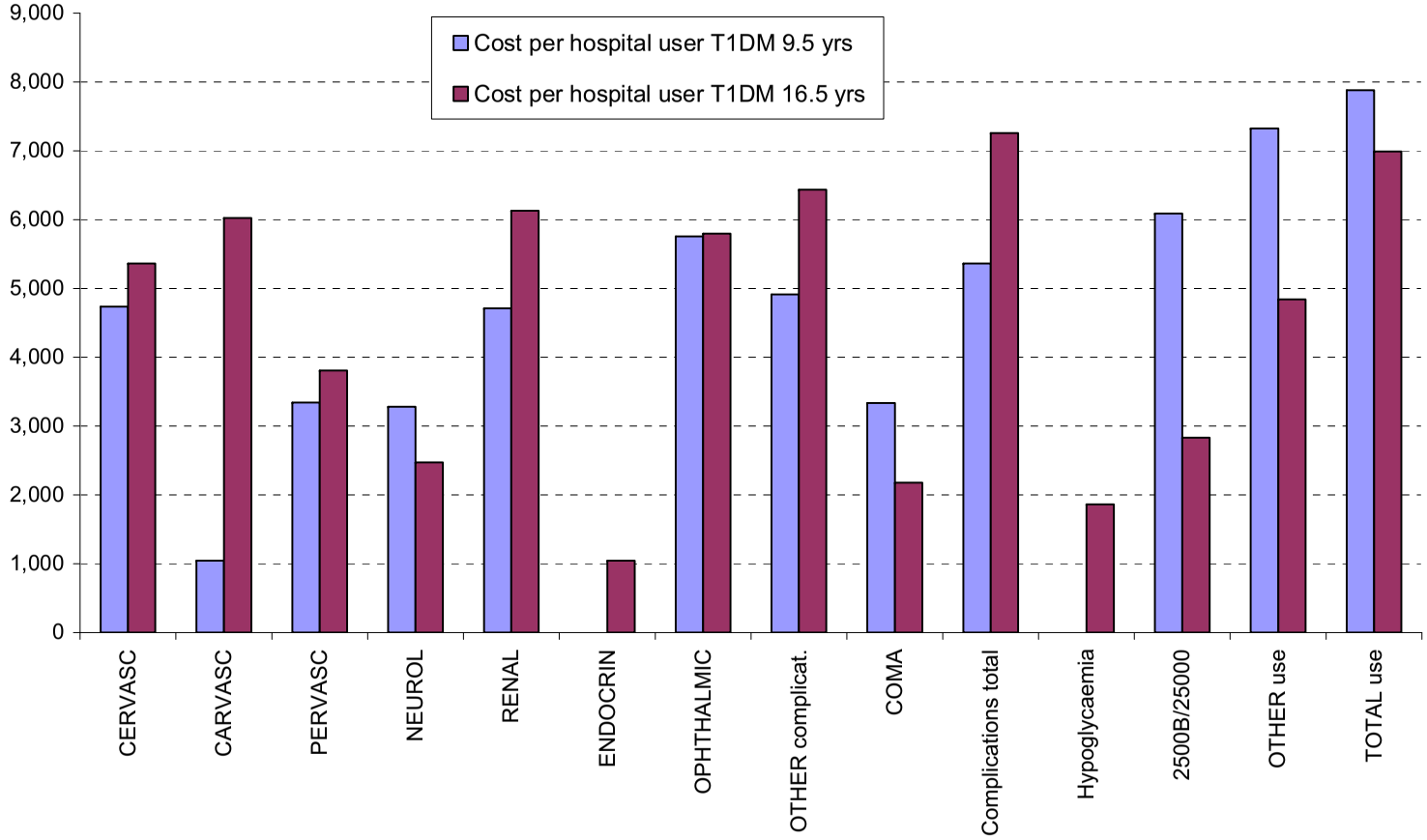

Figure 10. Annual costs (€) per inpatient hospital user by complication group and duration of T1DM

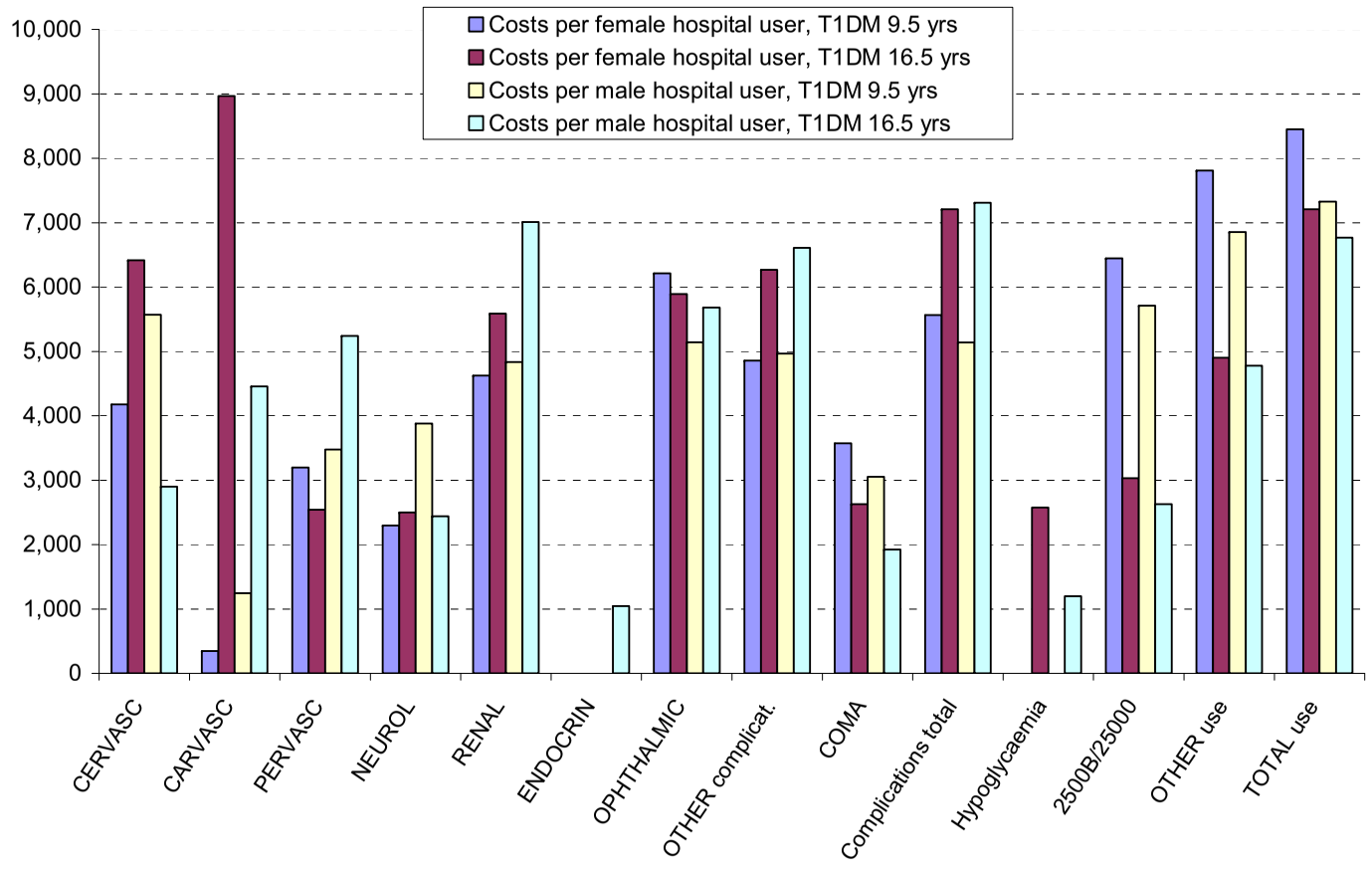

Figure 11. Annual costs (€) per inpatient hospital user by complication group, duration of T1DM and sex

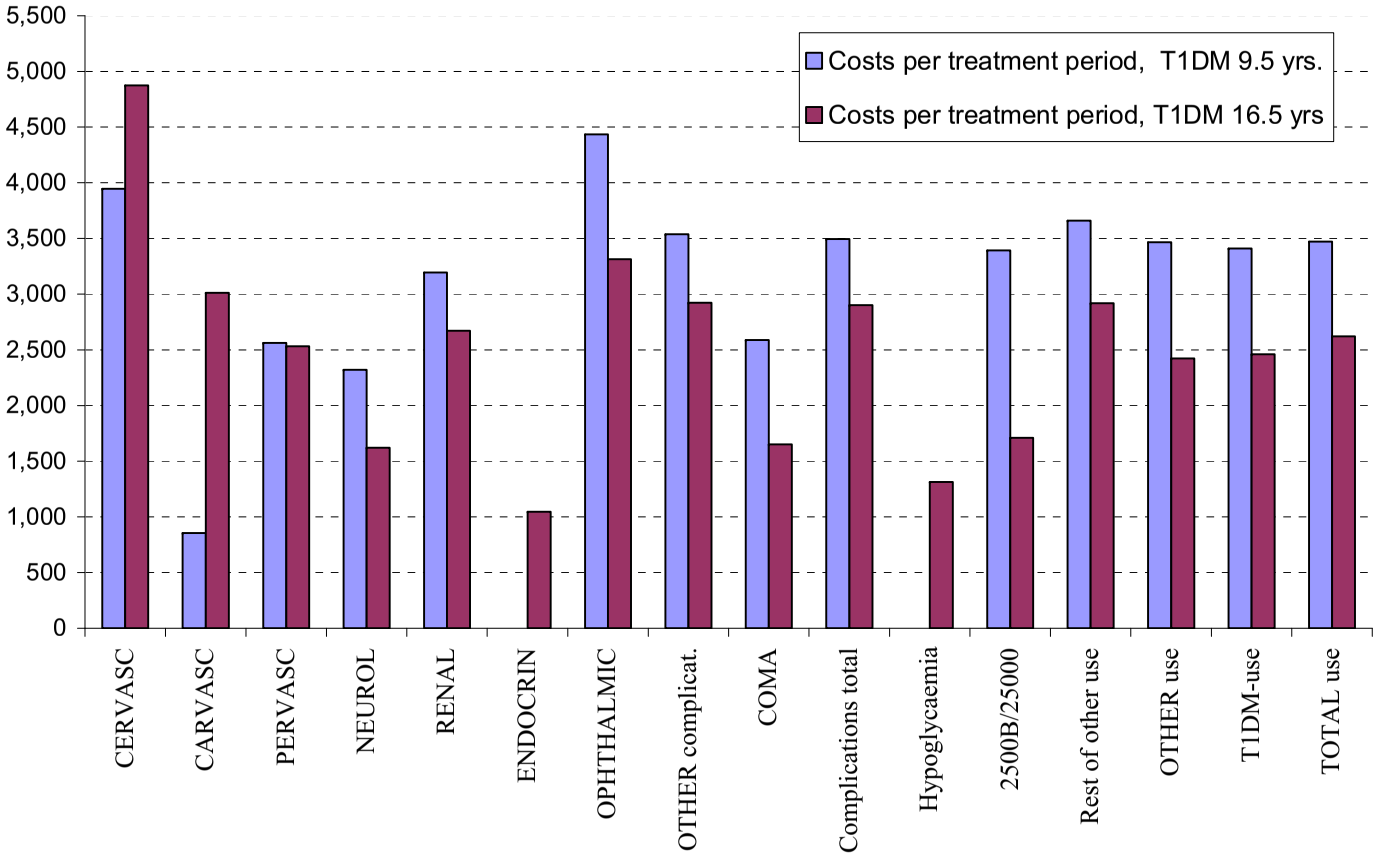

Figure 12. Annual costs (€) per treatment period by complication group and duration of T1DM

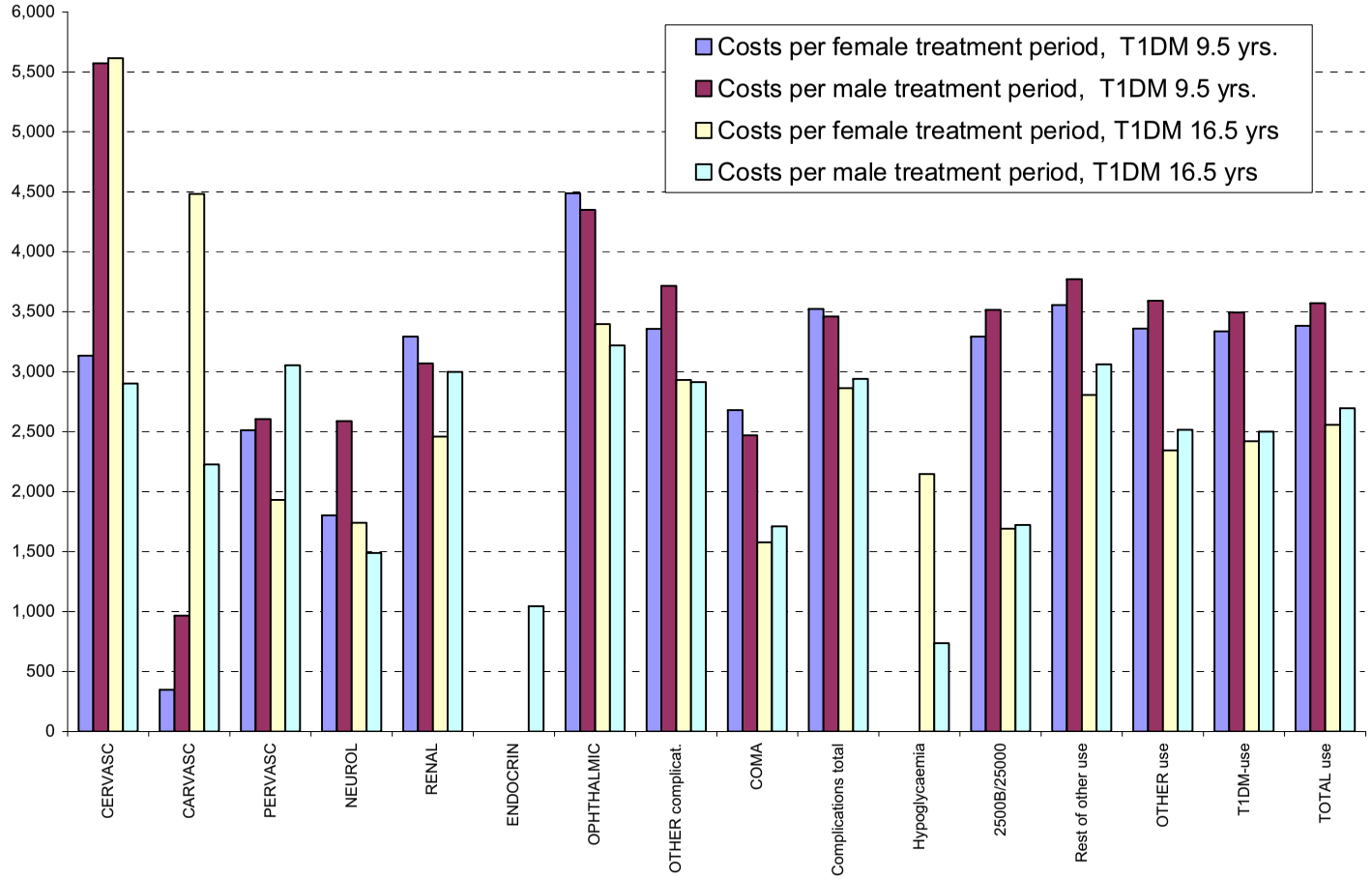

Figure 13. Annual costs (€) per treatment period by complication group, duration of T1DM and sex

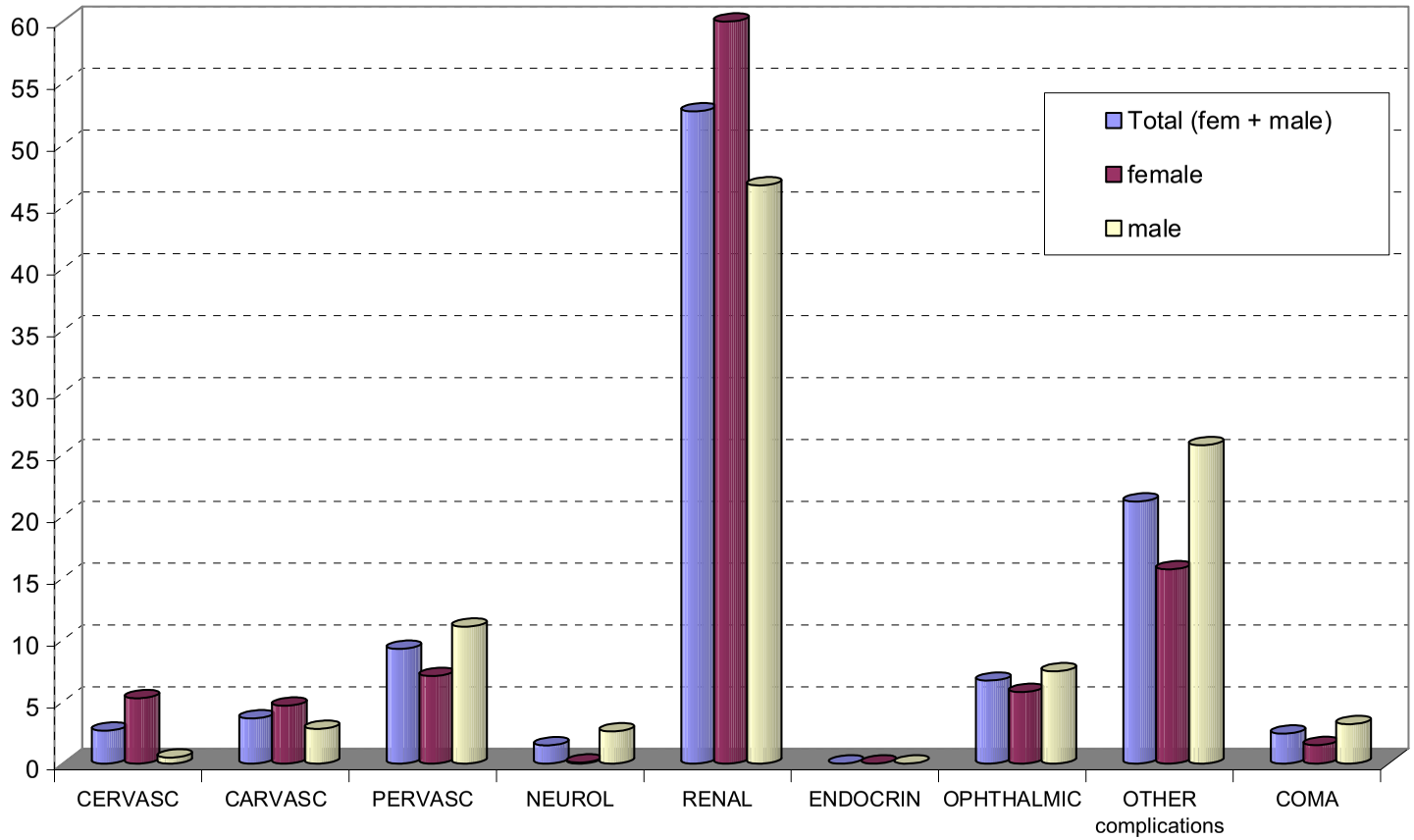

Figure 14. Shares (%) of bed-days due to complications and all bed-days in 1998 by complication group and sex

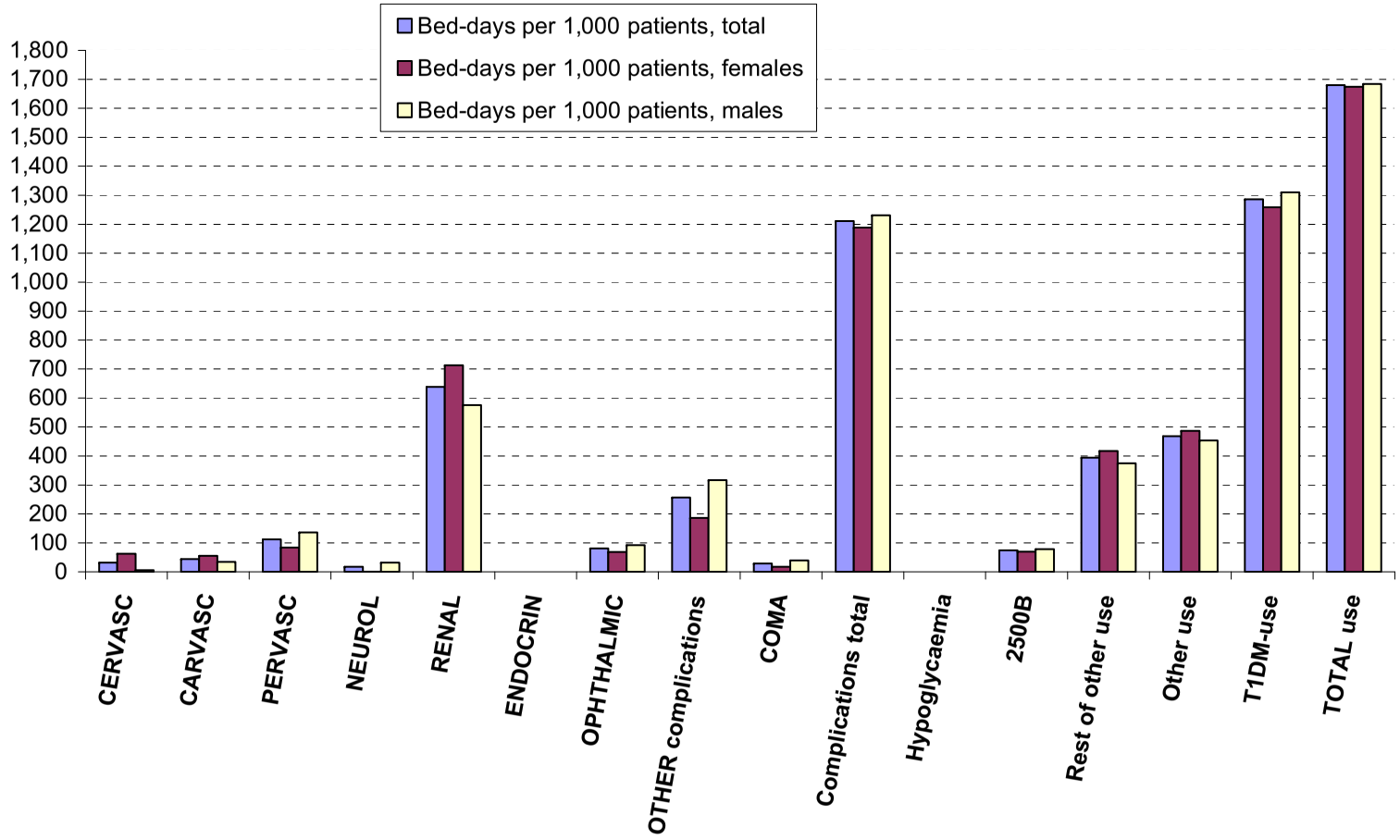

Figure 15. Number of bed-days per 1,000 patients in 1998 by complication group and sex

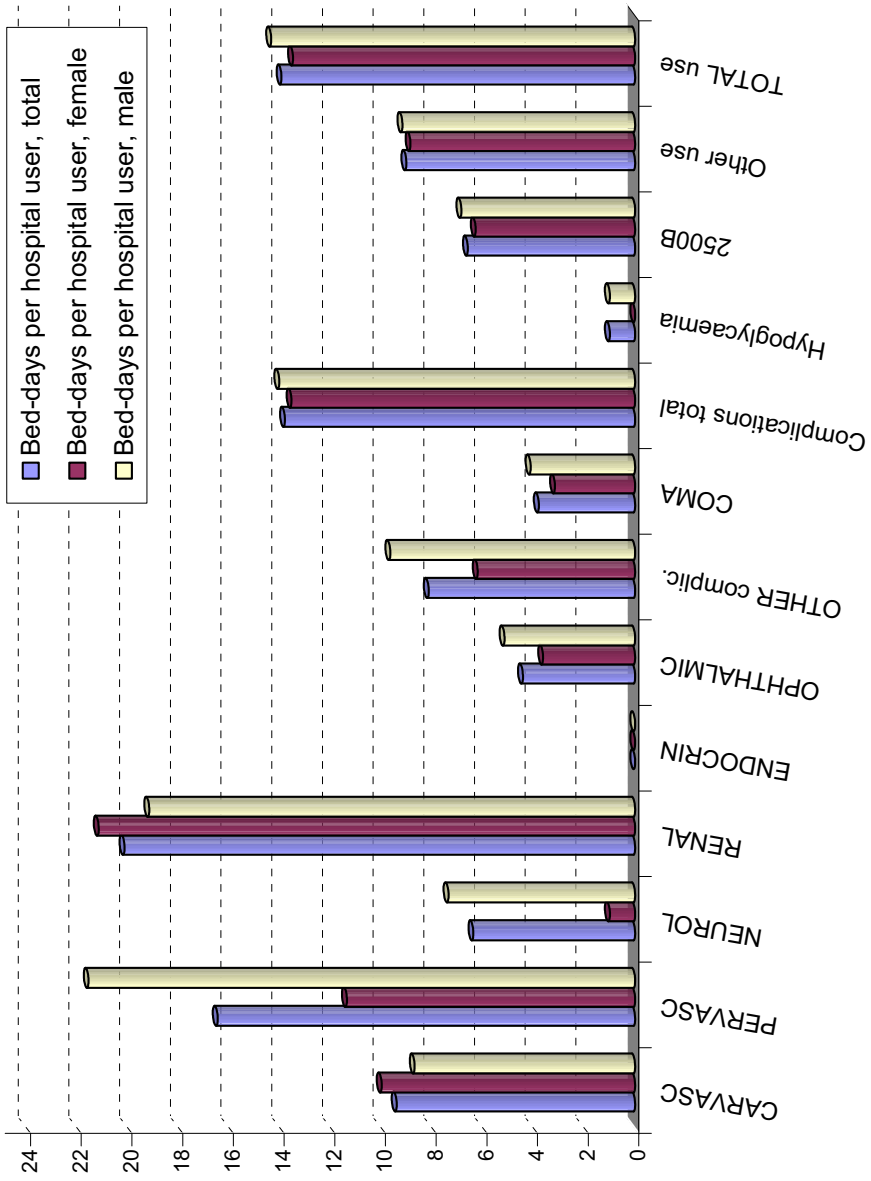

Figure 16. Number of bed-days per hospital user in 1998 by complication group and sex

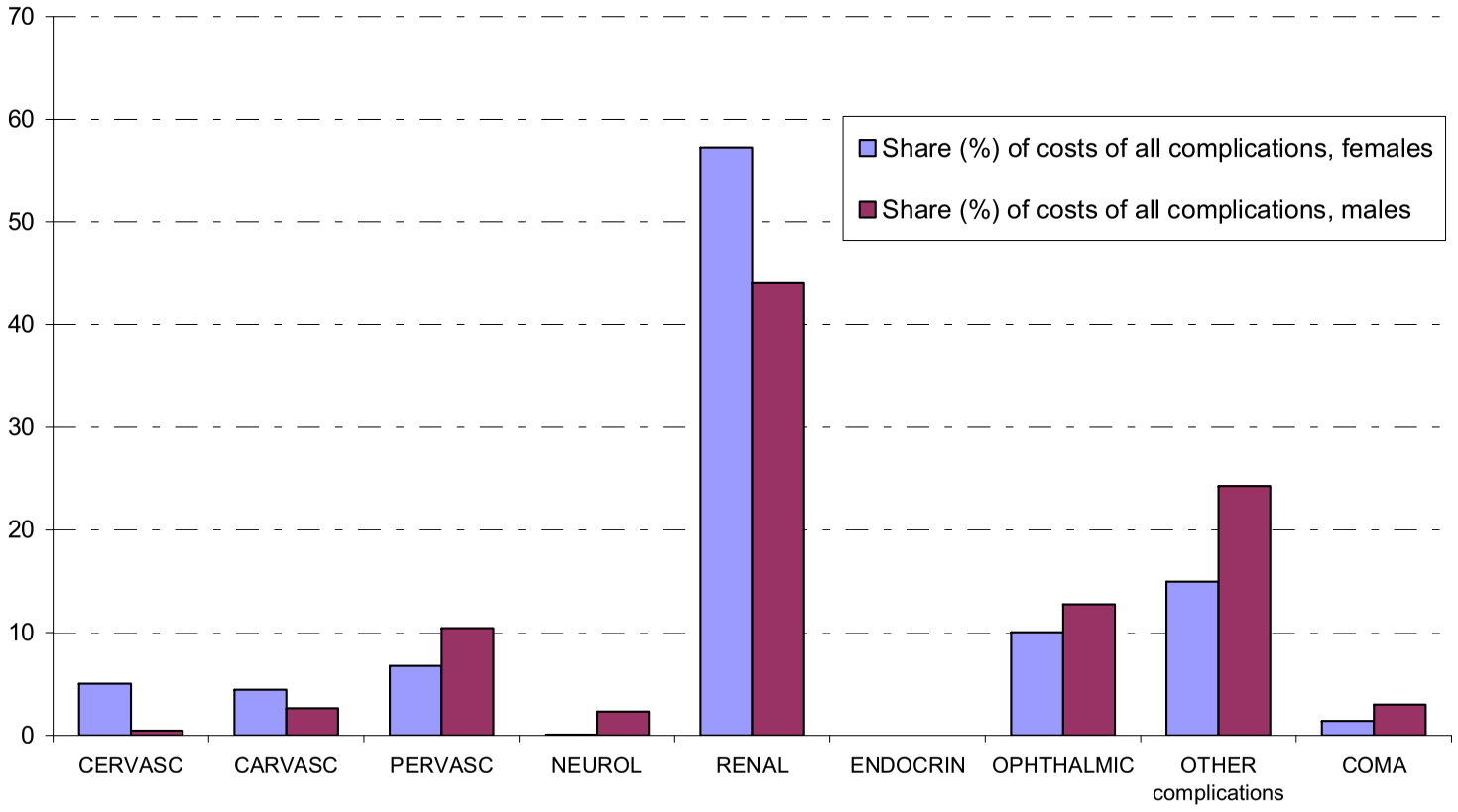

Figure 17. Shares (%) of the costs of inpatient care due to complications in 1998 by sex

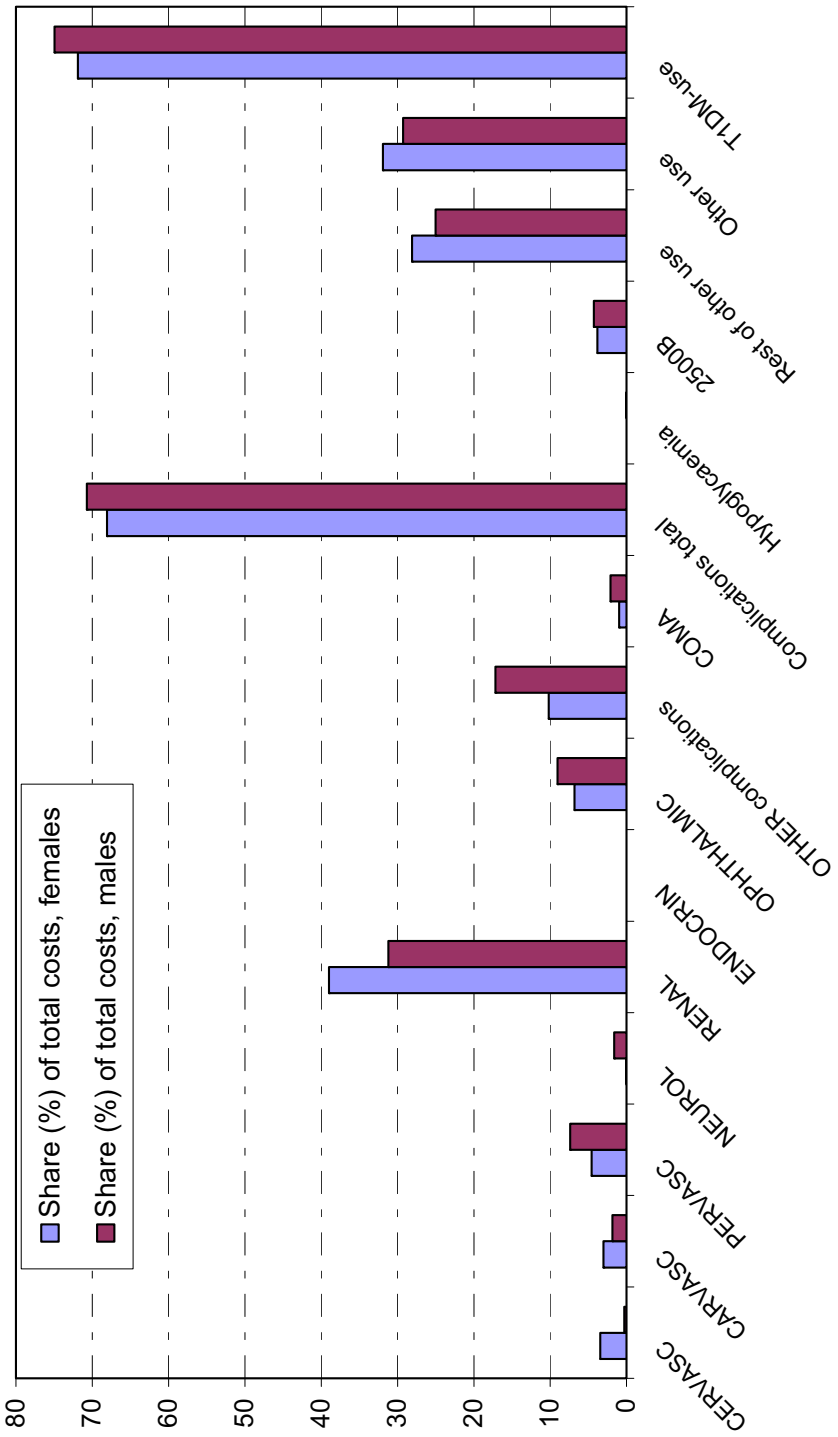

Figure 18. Shares (%) of the costs of total inpatient care in 1998 by sex

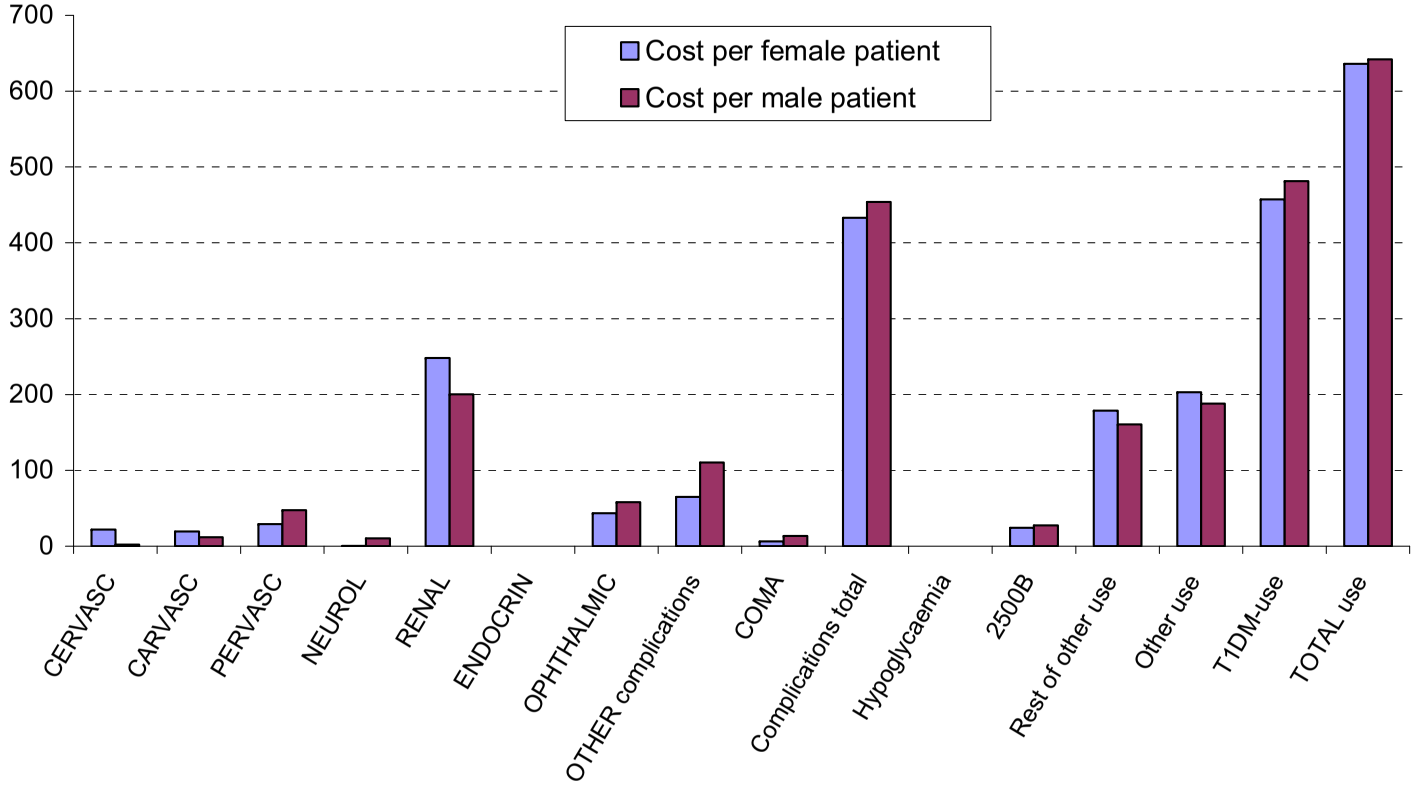

Figure 19. Mean cost (€) of inpatient care per patient in 1998 by complication group and sex

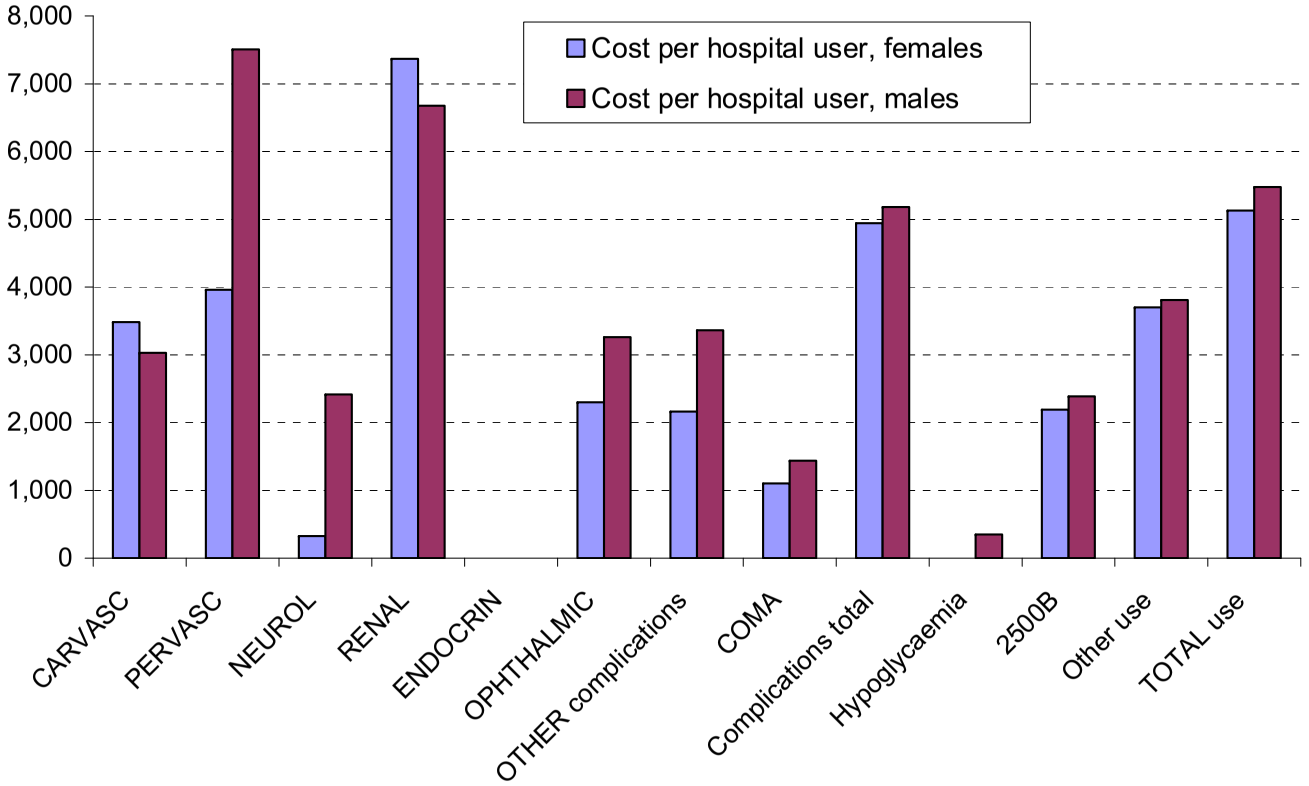

Figure 20. Costs (€) of inpatient care per hospital user in 1998 by complication group and sex

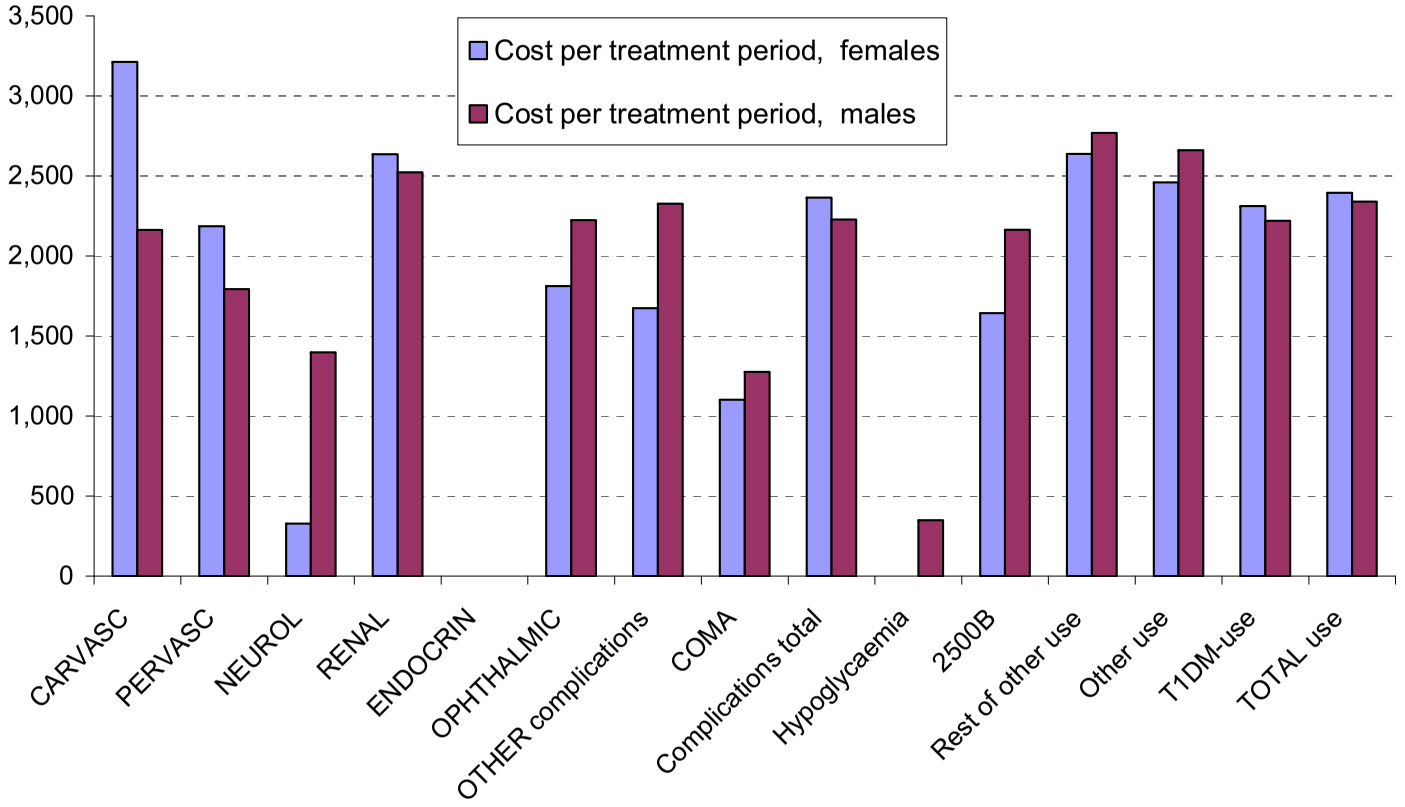

Figure 21. Costs (€) of inpatient care per treatment period in 1998 by complication group and sex

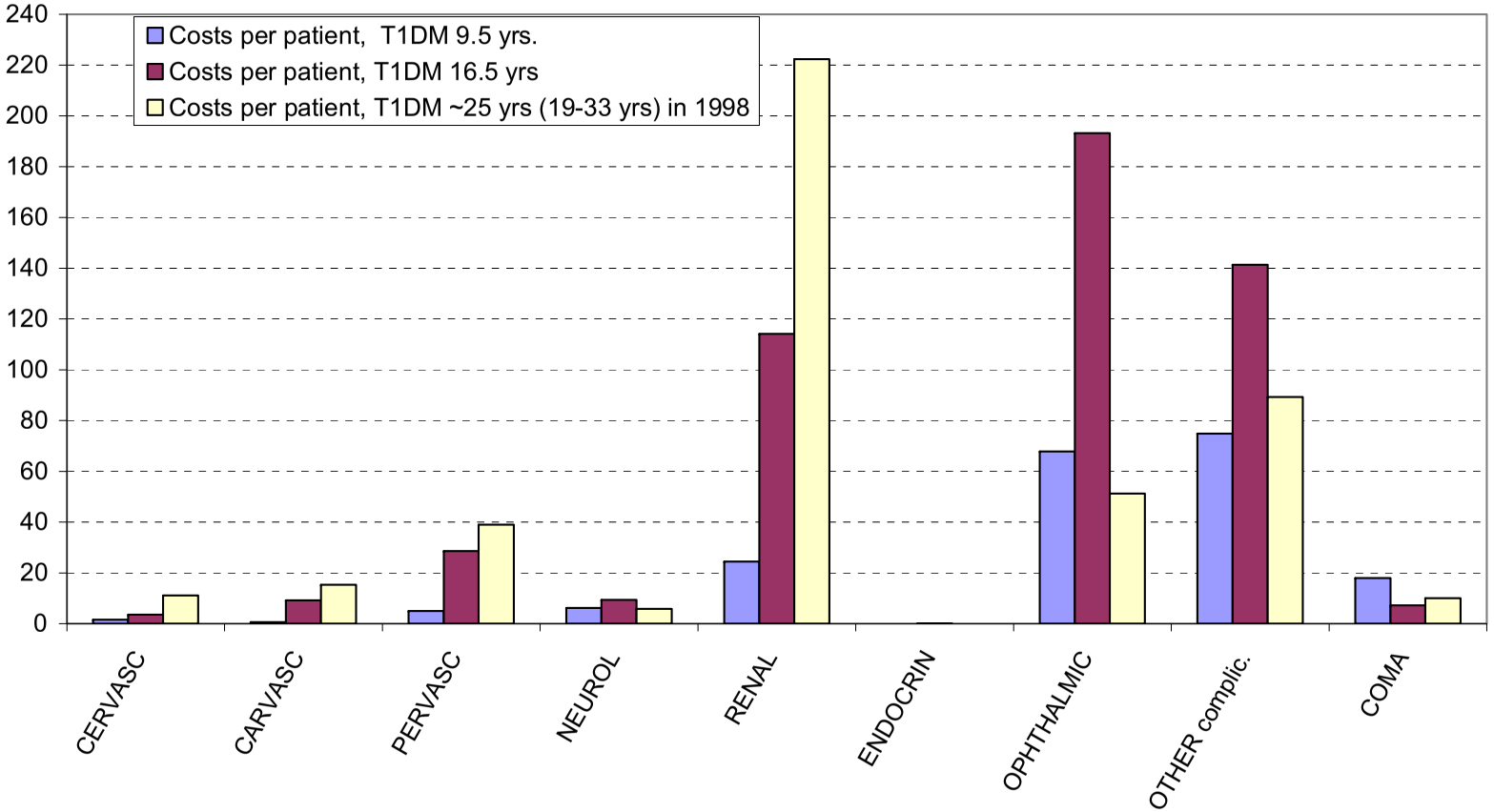

Figure 22. Average inpatient costs of complications per patient, when duration of T1DM is 9.5, 16.5 or 25 years

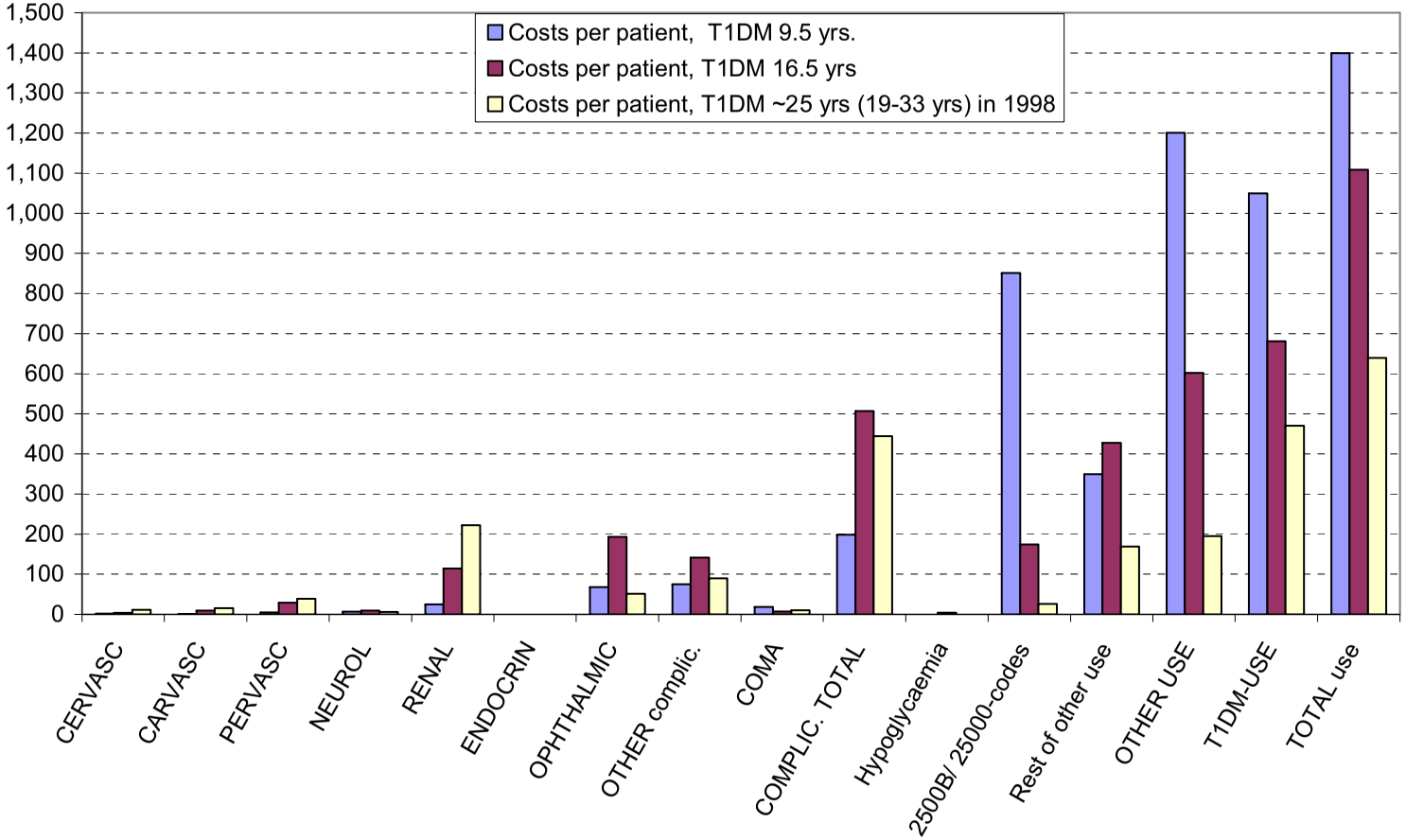

Figure 23. Average inpatient costs per patient, when duration of T1DM is 9.5, 16.5 or 25 years

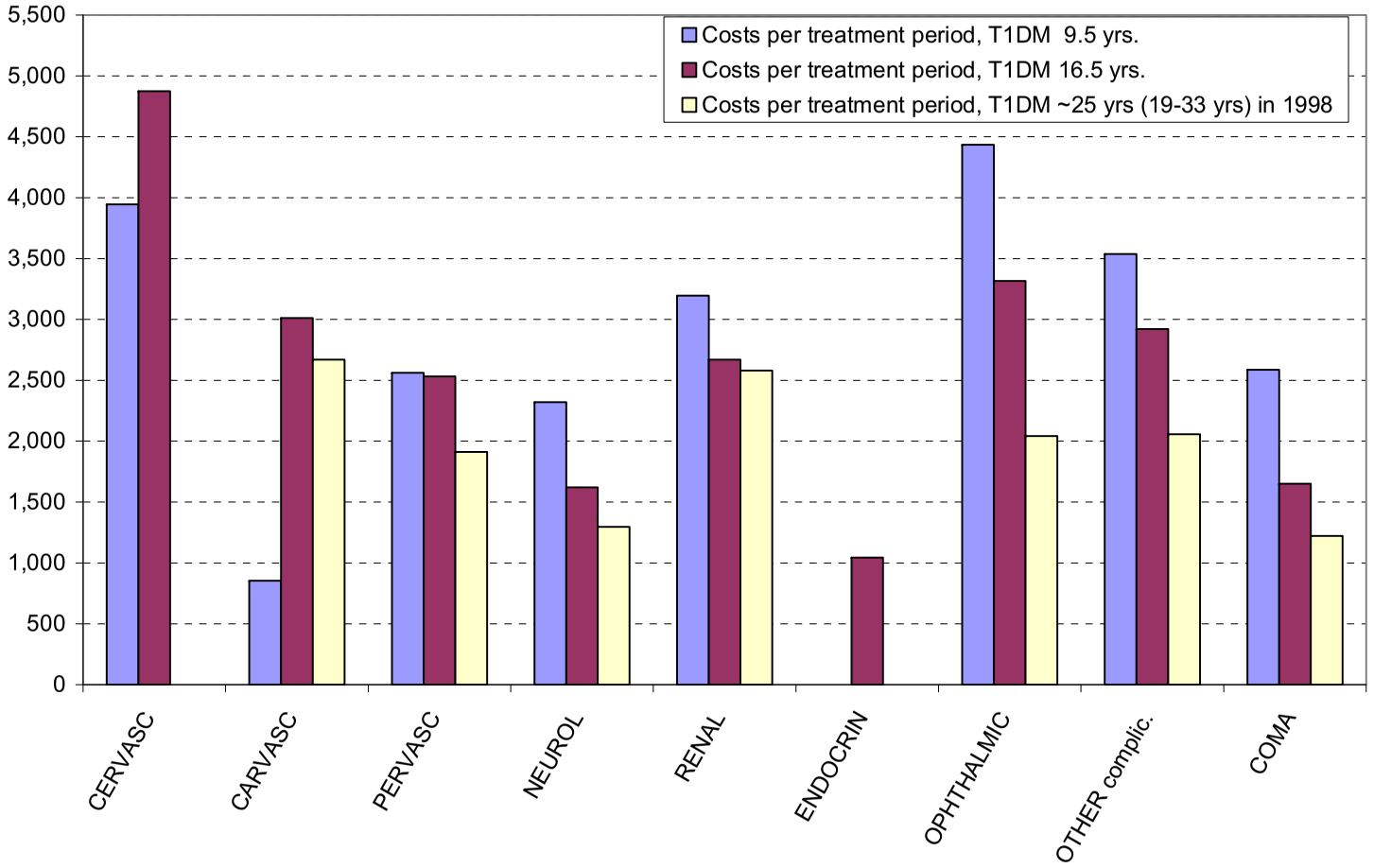

Figure 24. Average annual inpatient costs (€) per treatment period due to complications, when duration of T1DM is 9.5, 16.5 or 25 years

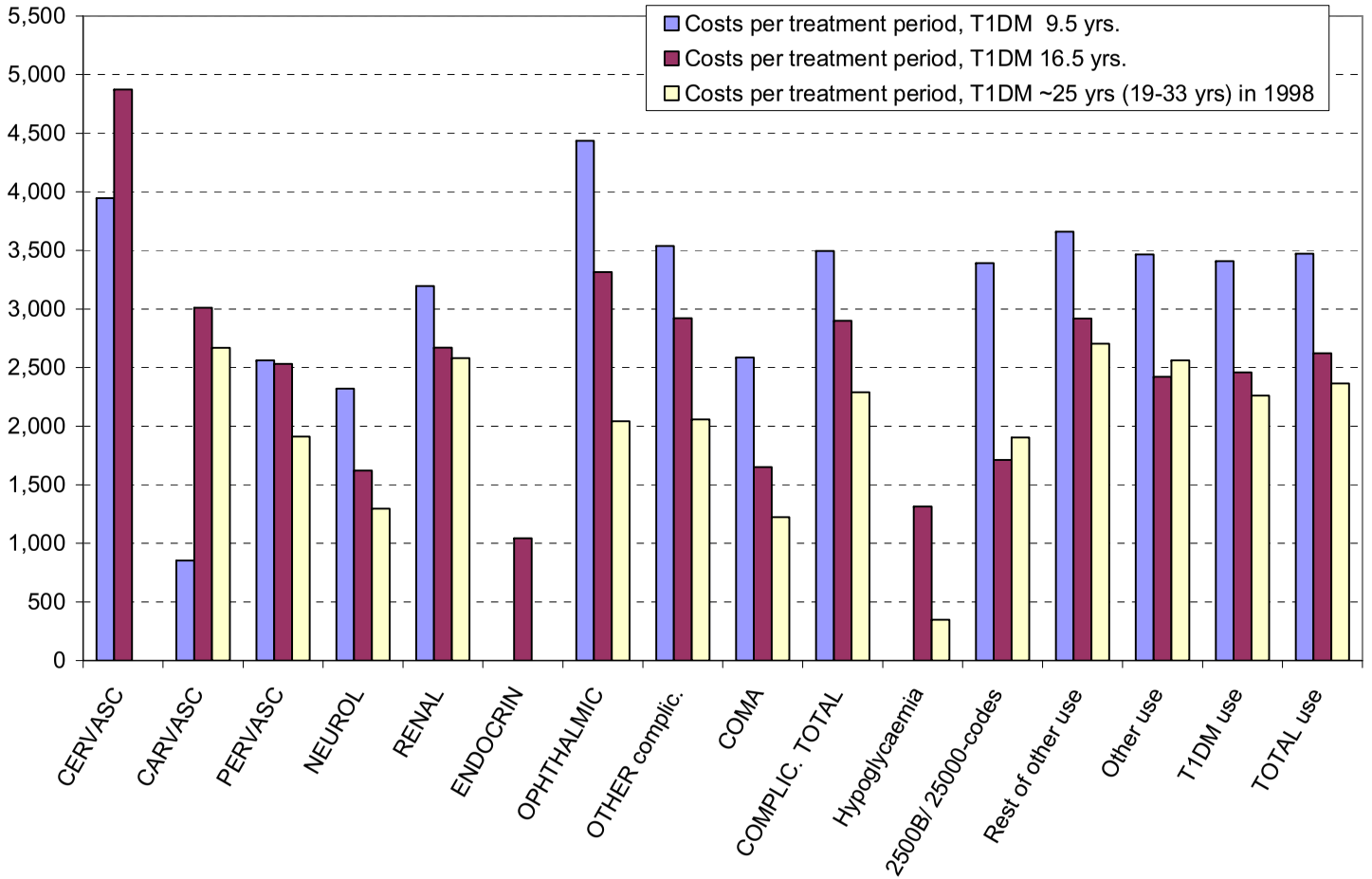

Figure 25. Average annual inpatient costs (€) per treatment period, when duration of T1DM is 9.5, 16.5 or 25 years

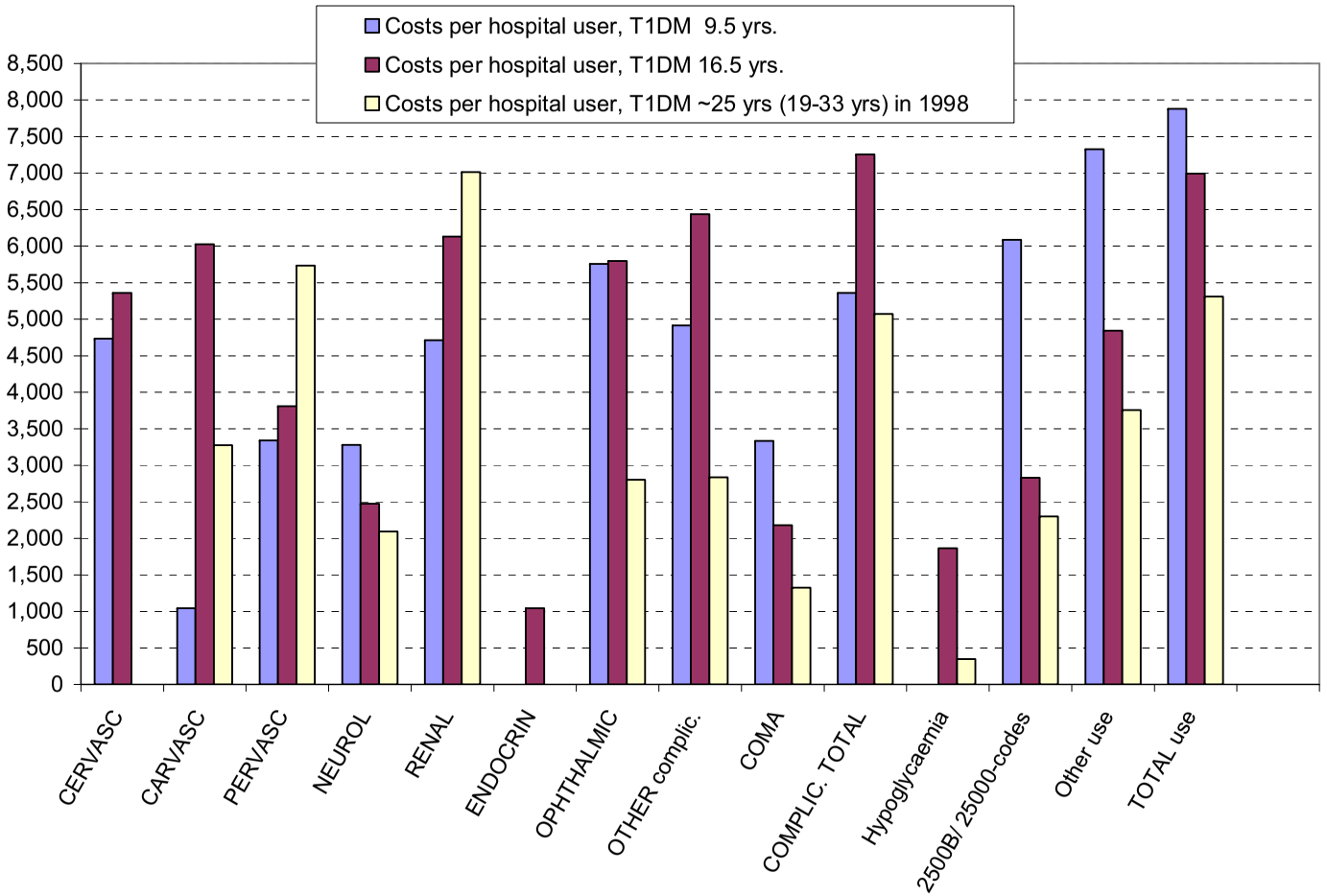

Figure 26. Average annual inpatient costs (€) per hospital user, when duration of T1DM is 9.5, 16.5 or 25 years

APPENDIX 3. LIST OF COMPLICATION GROUPS INCLUDING CORRESPONDING DISEASES.

ICD-250 codes and chronic complications of diabetes (ADA 1998) used in this study sorted by ICD-8 and ICD-9 codes. ICD-9 CM codes were translated to correspond with Finnish ICD-codes.

ICD-8	ICD-9
Diabetes mellitus	**Diabetes mellitus (B type I)**
250,00 Sine complicatione	2500- Sine complicatione
250,01 Cataracta diabetica 250,02 Retinopathia diabetica 250,03 Complicatio oculi alia sive NUD	2504- Cum complicatione oculi 3664A Cataracta diabetica 3620 Retinopathia diabetica
250,04 Nephropathia diabetica.	2503- Nephropathia diabetica
250,05 Neuropathia diabetica. Polyneuritis diabetica	2505- Neuropathia diabetica
250,06 Gangraena diabetica	2506- Microangiopathia diabetica
250,07 Coma diabeticum	2502- Coma diabeticum
250,08 Complicatio alia definita	2507- Cum complicatione alia
250,09 NUD	2508- Cum complicatione non descripta
(788,60 Acetonaemia) (789,60 Ketonuria (acetonuria))	2501- Cum ketoacidosi 7916A Ketonuria
medic.nr + E 939	2510A Hyperinsulinaemia iatrogenea seu factitia + E-koodi e.g. E932D
(780,01 Coma)	2510B Coma hypoglycaemicum
(251 diabetes insulin treatment excluded)	(2511A Hyperinsulinaemia alia 2512A Hypoglycaemia reactiva 2512X Hypoglycaemia NUD 2513A Hypoinsulinaemia postoperativa

2514A Hyperglucagonaemia
2515A Hypergastrinaemia
2518X Alia definita
2519X NUD)

Chronic complications of diabetes (ADA 1998)

ICD-8	ICD-9

Neurological symptoms

(348,29 Atrophia musculorum progressiva NUD 348,98 Alii definiti 733,10?)	3588A Myasthenic syndromes in diseases classified elsewhere (amyotrophy) Syndroma myasthenicum secundarium e.g.. amyotrophia diabetica (2505-)
(357,08 Morbi nervorum periphericorum alii,autonomis exceptis alterius nervi? 358,08 Polyneuritis et polyradiculitis aliae definitae?)	3568X Other specified idiopathic peripheral neuropathy / extraocular muscle palsy? Polyneuropathia nervorum periphericorum hereditaria et idiopathica alia definita
357	Mononeuritis of upper and lower limb 354 Mononeuropathia extremitatis superioris et mononeuropathia multiplex 355 Mononeuropathia extremitatis inferioris
(714,91 Arthritis neuropathica, diabetic excluded)	7135A Arthropathy associated with neurological disorders (Charcot's arthropathy) Arthropathia reactiva alia cum morbo systematis nervosi (e.g. Charcot's joint)
358 Morbi systematis nervosi peripherici autonomi	3371A Peripheral autonomic neuropathy Neuropathia autonomica peripherica secundaria + code of basic disease
250,05	3578A Polyneuropathy in diabetes Polyneuropathia alia secundaria + code of basic disease
Neuralgia et neuritis alia sive non definita 355,08 Alia definita 355,09 NUD	Neuralgia, neuritis, and radiculitis, unspecified 7292A Neuralgia NUD (3539X Morbi radiculares et plexus nervorum, NUD)

250,05	Neuropathia diabetica.Polyneuritis diabetica.	2505	Diabetes with neurological complications
433 434	Thrombosis cerebri Embolia cerebri	434	Occlusion of cerebral arteries Occlusio et stenosis arteriae cerebralis
430 431	Haemorrhagia subarachnoidalis Haemorrhagia cerebri		Hemorrhagic stroke 430 Haemorrhagia subarachnoidalis 431 Haemorrhagia intracerebralis 432 Haemorrhagia intracranialis alia
344	Paralysis cerebralis alia	438	Late effects of cerebrovascular disease Sequelae morbi cerebrovasculares
432	Occlusio arteriae praecerebralis	433	Occlusion and stenosis of pre-cerebral arteries Occlusio et stenosis arteriae praecerebralis
438	Morbi cerebro-vasculares alii sive non definiti	437	Other and ill-defined cerebrovascular disease Morbus cerebrovascularis alius sive non definitus
436	Morbus cerebrovascularis acutus non definitus	436	Acute, but ill-defined, crebrovascular disease Morbus cerebrovascularis acutus non definitus
435	Ischaemia cerebralis transitoria	435	TIAs Ischaemia cerebralis transitoria
437	Morbus cerebrovascularis ischaemicus generalisatus	437?	

Peripheral vascular disease

440	Arteriosclerosis	440	Atherosclerosis Arteriosclerosis
			Embolism and thrombosis, stricture of artery
444	Embolia et thrombosis arteriarum	444	Embolia seu trombosis arteriarum
(447	Alii morbi arteriae et arteriolae ,08 Alii definiti)	4471	Strictura arteriae
443	Alii morbi vascularum peripheriarum	443	Other peripheral vascular disease Alii morbi vascularis peripherici

458	Alii morbi systematis circulationis except 458,00 ---458
451	Phlebitis et thrombophlebitis Thrombosis venae portae
453	Alia embolia et trombosis venarum
454	Varices venarum extremitatum inferiorum
(445	Arteriosclerosis cum gangraena - no DM) 885-887, 895-897 Amputatio traumatica...
707	Ulcus chronicum cutis
(250,06	gangraena diabeticum)

459	Other disorders of circulatory system Alii morbi systematis circulationis
	Phlebitis and thrombophlebitis, portal vein thrombosis and thrombolism 452 and venous embolism
451	Phlebitis, thrombophlebitis et trombosis phlebarum
452	Thrombosis venae portae
453	Other venous embolism and thrombolism Alia embolia et thrombosis venarum
454	Varicose veins of lower extremities Varices venarum extremitatum inferiorum
	Gangrene and amputations (445 not in Finnish classicication)
7854	Gangraena
885-887, 895-897	Amputatio traumatica...
707	Chronic ulcer of skin Ulcus chronicum cutis
	Diabetes with peripheral circulatory disorders
2506	Microangiopathia diabetica

Cardiovascular disease

441	Aneurysma aortae
442	Aliud aneurysma
458,00	Hypotonia
413	Angina pectoris
427,20-427,99	Adams-Stokes, Dissociatio cordis, SVT + VT, FA, Functio laesa cordis NUD

	Aortic and other aneurysms
441	Aneurysma seu dissecatio aortae
442	Aneurysma arteriae alia
458	Hypotension Hypotonia
413	Angina Angina pectoris
	Conduction disorders and cardiac dysrhythmias
426	Dissociatio atrioventricularis et intraventricularis cordis
427	Dysrhythmiae cordis

(414 Morbus cordis ischaemicus asymptomaticus)	ASCVD (429,2 no) (4140 Atherosclerosis arteriarum coronarium cordis)
(429,99 Morbus cordis NUD)	4293A Cardiomegaly Cardiomegalia NUD
425 Cardiomyopathiae	425 Cardiomyopathy Cardiomyopathia
411 Alii morbi cordis ischaemici acuti et subacuti	411 Other acute and subacute forms of ischemic heart disease Alii morbi cordis ischaemici acuti et subacuti
428,99 Aliae insufficientiae myocardiae 427,00 Incompensatio cordis. Oedema cardiale (427,10 Oedema pulmonum acutum) 782,40 Insufficientia cordis acuta	428 Heart failure Insufficientia cordis (4148 Alia definita, iskeem.insuff.)
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410 Infarctus myocardii acutus 412 Morbi cordis ischaemici chronici ,01 St.post inf.cordis, cum hypertonia ,91 St.post inf.cordis, hypertonia non indicata	Myocardial infarction 410 Infarctus myocardii acutus 412 Infarctus myocardi inveteratus
412 Morbi cordis ischaemici chronici ,09 NUD, cum hypertonia ,99 NUD, hypertonia non indicata	414 Other chronic ischemic heart disease Morbi cordis ischaemici alii
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Renal complications

590 Infectio renis	590 Infection of kidney Infectio renis
596 Alii morbi vesicae urinariae 786,00-786,51 eg. incontinentia urinae	596 Other disorders of bladder Alii morbi vesicae urinariae

595 Cystitis

584,99 Sclerosis renalis NUD
(excluded pyelonefr-kihtiin-benigniin)

580,99 Nephritis acuta
581,99 Nephrosis
582 Nephritis chronica
583,99 Nephritis NUD

789,00 Proteinuria (albuminuria)
(ortost.excl.)
593,22 Albuminuria orthostatica

593,10 Nephrosis acuta tubularis
593,00 Rachitis renalis, nanosomia renalis
(265,20 Osteomalacia)
273,81 Diabetes insipidus nephrogenicus

593,20 - 593,58 Morbi renis et ureteris alia

599,02 Infectiones tractuum urinarium NUD
(599,00 Caruncula urethrae)

250,04

Endocrine/metabolic complications

271,00 Glycogenosis generalisata Gierke

595 Cystitis

587 Renal sclerosis, unspecified
Sclerosis renalis secundaria NUD
(excl. nefroskleroosi)

Glomerulonephritis, nephrotic syndrome, nephritis, and nephropathy
580 Glomerulonephritis
581 Syndroma nephroticum
582 Glomerulonephritis chronica
583 Nephritis alia et NUD
Proteinuria
7910A Proteinuria posturalis
7910X Proteinuria NUD

Renal failure and its sequelae
584 Insufficientia renis acuta
(586 missing)
588 Morbi metabolici causa insufficientia renum et morbi tubulares renum

593 Other disorders of kidney and ureter
Morbi alii renis et ureteris

Urinary tract infection
5990A Bacteriuria asymptomatica
5990B Infectio viarum urinarium acuta
5990C Infectio viarum urinarium recidivans
5990D Pyuria
5990X Alia definita seu NUD

2503 Diabetes and renal complications

Chronic renal failure (ESRD)
585 Insufficientia renis chronica

2594A Dwarfism-obesity syndrome

Glycogenosis and galactosemia

271,10 Glycogenoses aliae	2710A Glycogenosis
271,20 Galactosaemia	2711A Galactosaemia
	Disorders of iron metabolism
273,20 Haemochromatosis	2750A Haemochromatosis
	2750X Defectio metabolica ferri alia
272,00 Hypercholesterolemia essentialis sive familiaris	2720 Hypercholesterolaemia
279,00 Hypercholesterolaemia non familiaris seu NUD	
	2723A Hyperchylomicronaemia
	2767A Hyperkalaemia
	2721 Hypertriglyceridaemia
275,50 Macroglobulinaemia Waldenström	2733 Macroglobulinemia Macroglobulinaemia Waldenström
268,99 Marasmus e malnutritionis	261 Lancereaux's disease Marasmus e malnutritione
	2727 Lipidoses
258,98 Dysfunctio polyglandularis et morbi systematis endocrini alii definiti	2598X Other specified endocrine disorders Alii morbi systematis endocrini, alia definita
279,01 Hyperlipaemia, hyperglyceridaemia non familiaris NUD	2724X Other and unspecified hyperlipidemia Hyperlipoidaemia alia
(272,01 Hyperlipaemia hereditaria)	2722A Mixed hyperlipidemia Hyperlipoidaemia combinata
273,80 Glycosuria renalis	2714A Renal glycosuria Glucosuria renalis

Ophthalmic complications

377 Alii morbi retinae et nervi optici ,01 - ,19, , 98	362 Other retinal disorders Alii morbi retinae
250,02 Retinopathia diabetica	

364,00	Iridocyclitis acuta
	Vascular diseases of the iris and ciliary body
3640A	Iridocyclitis acuta
3644A	Morbi vasculares iridis et corporis ciliaris
377,90	Atrophia (et degeneratio) nervi optici (tabica exc.)
377,91	Papilloedema. Stasis papillae.
377,99	Morbi nervi optici alii sive NUD
377	Disorders of the optic nerve and visual pathways Morvi nervi optici et radiationum opticarum
(250,01, 250,02), 250,03	
250,01	
374	Cataracta
2504	Diabetes with ophthalmic complications
366	Cataract Cataracta 3664A diabetica
375	Glaucoma
365	Glaucoma
379	Amaurosis, amblyopia gravis
377,20	Amblyopia NUD
377,30	Achromatopsia
377,31	Hemeralopia ?
	Visual disturbance, low vision, blindness
368	Visual disturbances
369	Blindness and low vision

Other complications

	Bacteremia, bacterial infection, Coxsackie virus
7907A	no-specific
(0,79.2	missing - coxsackie? e.g.. 0470A, 0748X, 0741A, 0740A, 0742A, 0743A)
112,99	Moniliasis
1123A	Candidiasis of skin and nails Intertrigo et paronychia
720,10	Osteomyelitis chronica
7301G	Chronic osteomyelitis of the foot Osteomyelitis chronica, ancle and foot
560	Gastro-enteritis et colitis non ulcerosa, causa non infectiosa ,08 alia definita ,09 NUD
5589X	Other and unspecified noninfectious gastroenteritis and colitis Gastroenteritis seu colitis alia noninfectiosa
	6078B Impotence of organic origin
380	Otitis externa
3801	Infective otitis externa Otitis externa

(709,08 Morbi cutis alii definiti)	
112 Moniliasis	1121A Candidiasis of vulva and vagina Vulvovaginitis
681, 682 Cellulitis	681, 682 Cellulitis
250,08	2507 Diabetes with other specified manifestations
250,09	2508 Diabetes with unspecified complications
(723,98 Alii morbi ossium definiti)	Other bone involvement in diseases classified elsewhere (731,8 no) (7339X Alii morbii ossis et cartilaginis, alia definita seu NUD)
	Degenerative skin disorders (7093?) ADA -93 Necrobiosis lipoidica: 7098 no-diabetic, 2506-diabetic

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