Socioeconomic Consequences of Childhood Onset Type 1 Diabetes – a case study of the impact of an early life health shock

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2017

Document Version:
Publisher's PDF, also known as Version of record

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LUND
UNIVERSITY

DOCTORAL DISSERTATION
by due permission of the Faculty of Medicine, Lund University, Sweden.
To be defended at School of Economics and Management, EC3:210, on 8 June 2017 at 13.00.

Faculty opponent
Professor Jes Søgaard

Organization	Document name
LUND UNIVERSITY	DOCTORAL DISSERTATION
	Date of issue 2017-06-08
Author: Sofie Persson	Sponsoring organization

Title and subtitle: Socioeconomic Consequences of Childhood Onset Type 1 Diabetes – a case study of the impact of an early life health shock

Abstract

Type 1 diabetes is a lifelong, chronic disease, that generally has a sudden onset early in life, which changes the conditions for the affected child and the child's family. The overall purpose of this thesis was to explore the socioeconomic consequences of childhood onset type 1 diabetes and through this investigate how an early life health shock can affect adult socioeconomic status. The four included papers aim to capture the overall effect of type 1 diabetes on socioeconomic outcomes, such as education, employment and earnings, during different stages in life, including adolescence, young adulthood, and midlife. The thesis also explores potential pathways through which type 1 diabetes may ultimately lead to detrimental labor market outcomes.

The analyses were performed using data from the Swedish Childhood Diabetes Register, a Swedish national research register for childhood incidence of type 1 diabetes, that has been linked to other national health data registers and socio-economic databases. Using a control group of four unique population controls, matched by year of birth and municipality of residence at the time of the diagnosis, the effect of type 1 diabetes was studied in birth cohorts born between 1962 and 1993, analyzing outcomes in ages 16 to 50 years.

The results show that the onset of type 1 diabetes, before the age of 15, negatively affects educational achievements, in both compulsory schooling and upper secondary school, as well as the final level of education. Despite developments in treatment and educational changes over time, the data indicate a persistent negative effect of type 1 diabetes on school performance also in later birth cohorts. In a longer perspective, the results show that childhood onset type 1 diabetes negatively affects employment and earnings for both women and men. The magnitude of the effect, however, depends on individual characteristics, such as gender, age at diagnosis, and disease duration. The results suggest that adult health contributes to a large proportion of the total labor market effect of type 1 diabetes, but other important factors, related to occupation, education, and family formation, also explain part of the impact on employment and earnings.

In conclusion, the findings of this thesis show that childhood onset type 1 diabetes negatively impacts socioeconomic outcomes, both early in life and in adulthood, and represents a burden that is borne both by the individual and the society. In a broader perspective, the results provide insights to how a distinct and definable shift in childhood health may translate into working life consequences.

Key words: Type 1 diabetes, health, socioeconomic outcomes, education, employment, earnings

Classification system and/or index terms (if any): JEL Classification: I10, I12, I21, J24, J31

Supplementary bibliographical information		Language: English
ISSN 1652-8220 Lund University, Faculty of Medicine Doctoral Dissertation Series 2017:95		ISBN 978-91-7619-475-1
Recipient's notes	Number of pages: 76	Price
	Security classification	

Signature  Date 2017-05-03

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Lund University, Faculty of Medicine Doctoral Dissertation Series 2017:95
ISBN 978-91-7619-475-1
ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University
Lund 2017

To Cornelia

Content

Abstract

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Sammanfattning på svenska

Typ 1-diabetes är en livslång kronisk sjukdom, som oftast utvecklas tidigt i livet och förändrar förutsättningarna för det drabbade barnet och barnets familj. Det övergripande syftet med denna avhandling var att undersöka de socioekonomiska konsekvenserna av typ 1-diabetes och att genom detta även undersöka hur en hälsochock tidig i livet kan påverka socioekonomisk status som vuxen. De fyra studierna som ingår i avhandlingen syftar till att fånga den totala effekten av typ 1-diabetes på socioekonomiska utfall, såsom utbildning, sysselsättning och inkomst, under olika stadier i livet. Avhandlingen undersöker också möjliga förklaringsfaktorer till hur insjuknandet i typ 1-diabetes under barndomen påverkar utfall på arbetsmarknaden.

Analyserna baseras på data från det Svenska Barndiabetesregistret, ett svenskt nationellt incidensregister för typ 1-diabetes under barndomen som har kopplats till andra nationella register och databaser för hälso- och sjukvård och socioekonomiska faktorer. Genom att använda en kontrollgrupp med fyra unika populationskontroller, matchade på födelseår och bosättningskommun vid tidpunkten för diabetesdiagnosen, studeras effekten av typ 1-diabetes bland personer födda 1962–1993, från 16 till 50 års ålder.

Den första studien undersöker effekterna av typ 1-diabetes på utbildningsresultat för barn i grund- och gymnasieskolan i en kohort född 1972–1978 och med diabetesdebut innan 15 års ålder. I den andra studien utökas analysen av denna kohort till att undersöka hur det går för individerna på arbetsmarknaden i åldrarna 19–38 år. Studierna visar att typ 1-diabetes har en negativ påverkan på genomsnittliga slutbetyg från grundskolan och från teoretiska program i gymnasieskolan. Dessutom visar resultaten på lägre sysselsättning och inkomst bland personer med typ 1-diabetes. Den tredje studien undersöker effekten av typ 1-diabetes i senare födelsekohorter och finner att även personer med typ 1-diabetes födda under 1980-talet och början av 1990-talet har lägre skolbetyg. Studien diskuterar hur detta kan tolkas i ljuset av att senare födelsekohorter tidigt i sjukdomsförloppet haft tillgång till modern diabetesbehandling men där det också skett förändringar i skolbetygssystemet parallellt. Resultaten visar på behovet av fortsatt arbete för att förbättra situationen i skolan för barn med typ 1-diabetes. Den fjärde studien undersöker möjliga förklaringsfaktorer till hur insjuknandet i typ 1-diabetes under barndomen påverkar arbetsmarknadsutfall hos unga vuxna och medelålders. Resultaten visar att hälsa bidrar till en stor del av den totala effekten

men det finns också andra viktiga faktorer relaterade till val av yrke, utbildning och familjebildning som förklarar delar av den negativa effekten av typ 1-diabetes på sysselsättning och inkomst.

Sammantaget visar resultaten från denna avhandling att ett tidigt insjuknande i typ 1-diabetes har negativ inverkan på socioekonomiska faktorer, både tidigt i livet och som vuxen, och utgör en börda som bärs av individen såväl som av samhället. I ett bredare perspektiv illustrerar resultaten hur ett tydligt och definierbart skifte i barns hälsa kan påverka arbetsmarknadsutfall senare i livet.

Abbreviations and terms

Abbreviations

ATT	average treatment effect of the treated
CI	confidence interval
COI	cost of illness
HbA1c	glycated hemoglobin
EUR	Euro
KHB (method)	Karlson, Holm, and Breen (method)
LISA	Longitudinal Integration Database for Health Insurance and Labor Market Studies
OLS	ordinary least square
OR	odds ratio
PSM	propensity score matching
SCDR	Swedish Childhood Diabetes Register
SE	standard error
SEK	Swedish krona
T1DM	type 1 diabetes mellitus, also referred to as “type 1 diabetes”
WHO	World Health Organization

Terms

albuminuria	limitations in kidney function
cardiovascular disease	disorders of the heart and blood vessels
etiology	the cause of a disease
human capital	skills, talents, and productivity that the labor force possesses, and the resulting productivity
hyperglycemia	high blood sugar
hypoglycemia	low blood sugar
microvascular complication	complications that affect small blood vessels
retinopathy	damage to the retina of the eyes

List of papers

This thesis is based on the following original papers referred to in the text by their Roman numerals:

I. Persson S, Dahlquist G, Gerdtham U-G, Steen Carlsson K (2013) Impact of childhood-onset type 1 diabetes on schooling: a population-based register study. Diabetologia 56: 1254-1262

II. Persson S, Gerdtham U-G, Steen Carlsson K, Swedish Childhood Diabetes Study Group (2016). Labor market consequences of childhood onset type 1 diabetes. Economics and human biology 23: 180-192

III. Persson E, Persson S, Gerdtham U-G, Steen Carlsson K, Swedish Childhood Diabetes Study Group. Effect of type 1 diabetes on school performance in a dynamic world: new analysis exploring Swedish register data (Submitted)

IV. Persson S, Dahlquist G, Gerdtham U-G, Steen Carlsson K. Why does childhood-onset type 1 diabetes impact labour market outcomes? – A mediation analysis (Submitted)

Introduction

Dating back as far as the 19th century, researchers have investigated the relationship between health and socioeconomic status, which is often referred to as the "gradient" (see, e.g., Cutler et al. (2011) for a review). This area of research documents a strong correlation between health and socioeconomic factors, such as education and income, which has been explained by three types of mechanisms: (1) socioeconomic factors impact health; (2) health impacts socioeconomic factors; and (3) other factors impact both socioeconomic factors and health (Grossman, 2015, Deaton, 2002, Gerdtham and Johannesson, 2000, Gerdtham et al., 2016, Baker and Stabile, 2011, Case and Paxson, 2010). The first mechanism would imply that level and distribution of the socioeconomic factors may explain the level and (socioeconomic) distribution of health. This also implies that socioeconomic policies directed at education and income, such as school reforms, and tax reforms and subsidies, indirectly impact health through people's health-related behavior. The second mechanism would imply that health has wider welfare consequences beyond the health-related consequence within the health sector, such as human capital accumulation and labor productivity. Thus, health policies, and health care interventions, may impact, for example, also on schooling and income. The third mechanism would imply that the correlation between health and the socioeconomic factors is not necessarily causal, meaning that health policies may have no impact on socioeconomic outcomes and socioeconomic policies may have no impact on health outcomes. Consequently, further knowledge about the complex relationship between health and socioeconomic factors is needed to understand how policy interventions can be developed to improve health and socioeconomic factors in society.

The studies included in this thesis focus on the second mechanism, running from health to socioeconomic status and in the analyses the onset of type 1 diabetes mellitus (hereafter referred to as "type 1 diabetes" or "T1DM") during childhood is used as an example of how and why an early life health shock can impact human capital accumulation and labor market outcomes later in life. The results show that childhood onset type 1 diabetes represents socioeconomic burden that is borne both by the individual and the society.

These findings are of interest from many perspectives and contribute both to the economic and medical literature. Using type 1 diabetes as an indicator of health provides a clearly identified shift in health, with well-described risks of medical

complications and a lifelong, daily disease management that is time-consuming and restrictive (Sparud-Lundin et al., 2013, Wennick and Hallström, 2007, Wennick et al., 2009). Another advantage of using type 1 diabetes, compared to other health indicators, is that it is less likely to suffer from endogeneity problems due to its specific etiology (Maahs et al., 2010, Åkerblom et al., 2002, Dahlquist et al., 1999, Dahlquist et al., 1989, Gan et al., 2012).

From a welfare perspective, it is important to understand the burden of a disease. Costs related to the impact on socioeconomic outcomes accounts for one potentially important component of that burden, particularly concerning chronic diseases that remain with the affected individual throughout life.

The direct negative health effects of type 1 diabetes are well known and well documented in the medical literature. However, the literature on the socioeconomic consequences of the disease is limited and there is little knowledge about how the disease impacts educational and labor market prospects. The sudden onset of type 1 diabetes can be life-changing for the affected child and may also impact on other family members (Sparud-Lundin et al., 2013, Wennick and Hallström, 2007, Wennick et al., 2009). While individuals with well-controlled diabetes may be fairly unaffected by the disease in terms of health, managing the disease requires permanent changes in daily life routines. To keep the levels of blood glucose within a target range, the management of type 1 diabetes requires a lifelong, daily treatment including monitoring of blood glucose levels and injections of insulin, as well as strict routines concerning food and exercise. If blood glucose levels are not sufficiently controlled, type 1 diabetes is associated with both short- and long-term diabetic complications, including hypoglycemia (low blood sugar), cardiovascular disease, and nerve, kidney, and eye disease (The Diabetes Control Complications Trial/Epidemiology of Diabetes Interventions Complications Study Research Group, 2005).

The papers included in this thesis uses prospectively recorded, longitudinal, individual-level data from national population registers to: (1) explore the effect of type 1 diabetes on educational outcomes in upper secondary school and on the total educational level in adulthood; (2) estimate labor market consequences of childhood onset type 1 diabetes in different gender, age, disease duration, and socioeconomic groups; (3) investigate if the effect on educational outcomes has been reduced in later cohorts; and (4) explore possible pathways in which the effect may operate.

Background

Health and socioeconomic status

Previous studies on the relationship between health and socioeconomic status commonly defines socioeconomic status as an individual's or family's economic and social position in relation to others and is often measured as a combination of education, income and occupation (Baker, 2014, Cutler et al., 2011). The concept can also include other factors, such as physical assets, social class, ethnicity, etc. Most economic research in this area, however, focuses on education, income, and occupation, which is also the focus of the studies included in this thesis. Recent evidence suggests that these indicators of socioeconomic status should not be considered as a unified concept but, rather, a set of different dimensions that relate to health in their own specific way (Cutler et al., 2011).

Health is a broad concept and no standard measure exists (Ware Jr et al., 1981). The World Health Organization (WHO) defines health as "a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity" (World Health Organization, 2002). In studies assessing the causal link between health and socioeconomic outcomes, various indicators of health shocks or general measures of health during childhood have been used (Currie and Hyson, 1999, Black et al., 2007, Case and Paxson, 2010, Case et al., 2005, Currie, 2009, Behrman and Rosenzweig, 2004, Conley and Bennett, 2001). Several studies have used low birth weight as an indicator of a fetal health shock (see, e.g., Currie and Hyson (1999), Black et al. (2007), Behrman and Rosenzweig (2004)), while others have used height or body mass index as later indicators of childhood health (e.g., Case and Paxson (2010)). Currie and Hyson (1999), for example, found that low birth weight has long-term effects on health status, educational attainments, and labor market outcomes in adulthood. Behrman and Rosenzweig (2004) show that increasing birthweight increases both adult schooling attainment and adult health among women, and Black et al. (2007) report long-term effects of low birth weight on cognitive and educational outcomes as well as on earnings. Case and Paxson (2010) examined the role of height as a marker for childhood health and found that height is positively associated with higher education, health, and cognitive outcomes. However, as these health measures are rather broad it may be difficult to know what aspects of health are actually being picked up and what underlying mechanisms are channeling their long-term consequences (Baker, 2013). Furthermore, a concern with using birth weight as a measure of early childhood health, as is commonly done, is that many health problems may not emerge until after birth and important dimensions of child health may therefore not be reflected (Lundborg et al., 2014).

Some studies use self-reported, retrospective measures of childhood health (Haas et al., 2011, Smith, 2009) or specific health conditions, such as asthma, injuries, and congenital anomalies (Currie et al., 2010, Lundborg et al., 2014, Lundborg et al., 2016). Smith (2009) has shown that poor self-reported childhood health has a quantitatively large effect on education and labor market outcomes and Lundborg et al. (2014) found similar results regarding employment and earnings when analyzing the impact of adolescent health using physician-assessed general health and specific health conditions. In a later study, however, Lundborg et al. (2016) found no effect of adolescent health on educational attainment, using similar health indicators.

A methodological disadvantage of many of the health indicators used previously is that they are often associated with a number of endogeneity issues as the mechanisms causing the health problem may also have an effect on adult socioeconomic status. For example, a health condition such as asthma in childhood may be caused by the parent's lifestyle choice of smoking (Gonzalez-Barcala et al., 2013), which in itself could be associated with the child's socioeconomic status in the future (Hiscock et al., 2012). To prevent such issues from biasing the results, several econometric approaches have been used, including instrument variable approaches (Brown et al., 2005, Minor, 2011), and different fixed effects approaches, accounting for time and sibling or twin fixed effects (Lovén, 2017, Lundborg et al., 2014, Lundborg et al., 2016, Black et al., 2005).

Contribution to the literature

Why is it important to study socioeconomic effects of an early life health shock, such as the onset of type 1 diabetes? This question can be answered in many ways depending on the point of view and the papers included in this thesis contribute to several areas of research, of which three are discussed below.

Contributions to the literature on the relationship between health and socioeconomic status

Further understanding of the complex relationship between health and socioeconomic status is of importance to understand how policy interventions can be developed to improve health and socioeconomic factors in the society. This thesis contributes to this area of literature by using the onset of type 1 diabetes as an example of an early life health shock with longstanding consequences. This indicator of childhood health has two major advantages over previously used indicators. First, it provides a clearly identified start of a lifelong shift in health that is associated with well-described risks of medical complications and indicators daily disease management which can be time-consuming and restrictive (Sparud-Lundin et al., 2013, Wennick and Hallström, 2007, Wennick et al., 2009). Compared to

many previously used health measures, such as birth weight, this enables a greater understanding of what is being measured and of the underlying mechanisms at play. Secondly, the specific etiology of type 1 diabetes implies that, compared to other disease-specific indicators of health, such as type 2 diabetes and asthma, it suffers from fewer endogeneity problems, which facilitates using more straightforward methods when analyzing the effect of childhood health on labor market outcomes as it reduces the risk of bias due to confounding.

Contributions to the burden of disease literature

From a welfare perspective, it is important to understand the economic burden of a disease. In cost of illness (COI) studies, with the purpose of assessing the economic burden of a disease by identifying all relevant costs, the cost related to socioeconomic factors is one important component (Drummond, 1992, Bolin et al., 2009). In the traditional approach of these studies, costs are divided into direct costs, which refers to all direct medical and direct non-medical costs, and indirect costs, which refers to losses in productivity due to morbidity and mortality (Drummond, 1992, Hodgson and Meiners, 1982).

In the case of diabetes, most cost studies are prevalence-based and estimate the total cost to society for diabetes, without distinguishing between the different types of diabetes, or focus only on the more common type 2 diabetes. The American Diabetes Association estimated the total cost of diagnosed diabetes in the US in 2012 to $245 billion (EUR222 billion, $1 = EUR 0.904 in 2016), including $176 billion (EUR159 billion) in direct medical costs and $69 billion (EUR62 billion) due to reduced productivity (The American Diabetes Association, 2013). In Sweden, the costs of diabetes were, in 2005, estimated to EUR920 million, with 37% of the costs related to health care (Bolin et al., 2009).

Few studies have estimated the costs associated with type 1 diabetes specifically, which could differ substantially from the total diabetes cost as the two types of diabetes differ in several respects, particularly concerning age at onset. A study from 2012 estimates the costs, in the UK, separately for type 1 and type 2 diabetes (Hex et al., 2012). Regarding type 1 diabetes, the study estimates the present costs to £1 billion (EUR1.2 billion in 2016 rates, £1 = EUR 1.225) in direct costs and £0.9 billion (EUR1.1 billion) in indirect costs and by the year 2035/2036, the costs are predicted to increase to £1.8 billion (EUR2.2 billion) and £2.4 billion (EUR2.9 billion), respectively. However, as little is known about the indirect costs of type 1 diabetes specifically, most data used for the estimation of indirect costs were based on studies of both types of diabetes combined. There is also a US study from 2010, where the yearly costs of type 1 diabetes were estimated to be $14.4 billion (EUR13 billion). The authors argued that the costs due to lost income were disproportionately high considering the number of individuals with type 1 compared to type 2 diabetes (Tao et al., 2010). According to the authors, the results suggest

that combining the two types of diabetes is not appropriate when estimating the costs of diabetes.

The papers included in this thesis contribute to this line of literature by estimating the size of the loss of productivity attributed to type 1 diabetes and to other, related, intangible aspects such as level of education and employment.

Contributions to the literature on type 1 diabetes and socioeconomic outcomes

In the medical literature, the direct negative health effects associated with type 1 diabetes are well known and vastly studied. Knowledge about how the disease impacts other aspects of life is important for decision makers in health care, as well as in the education system and labor market, to understand the need for additional measures to improve the situation for the affected individuals.

Most previous studies exploring the effect of type 1 diabetes on socioeconomic outcomes are based on small sample surveys (often including fewer than 100 individuals with diabetes) lacking longitudinal data and/or the possibility to distinguish between type 1 and type 2 diabetes (Milton et al., 2006, Minor, 2011, Maslow et al., 2011, Tunceli et al., 2005, Brown et al., 2005, Brown et al., 2011, Bastida and Pagan, 2002, Fletcher and Richards, 2012, Seuring, Goryakin et al., 2015, Latif, 2009, Wennick et al., 2011). There are a few large-scale studies from both the medical and the economic disciplines that have focused on the specific effect of type 1 diabetes on education, employment, and earnings; however, these have reached conflicting results. For instance, Dahlquist and Källén (2007) compare school grades from compulsory school among children with type 1 diabetes and children in the general population born in 1973–1986. After controlling for potential confounders, the authors found a negative effect on school grades, particularly among those diagnosed before age 2 years. In 2014, Cooper and colleagues studied the effect of type 1 diabetes on school performance in 7–14-year-olds in Australia born in 1994–2003, with regard to changes over time and the impact of clinical factors (Cooper et al., 2014). They found no association between type 1 diabetes and school performance, and speculated that the introduction of new treatment technologies may have closed the educational gap in later cohorts of children. Poorer glycemic control was, however, associated with lower test scores.

Steen Carlsson et al. (2010) explored the labor market consequences of the onset of type 1 diabetes during young adulthood (onset at age 15–34 years). Their study found that women and men diagnosed early in their labor market career on average have 8% and 4% lower earnings, respectively. The study identified labor market consequences of type 1 diabetes onset after educational choices have been made and did not explore any underlying mechanisms other than employment status. Minor (2011, 2013) studied the labor market effect of both type 1 and type 2 diabetes, and concluded that the effect of diabetes was driven mostly by type 2 diabetes as they found no statistically significant effect of type 1 diabetes. Lundborg et al. (2014) explored the effect of adolescent health on labor market outcomes using

a number of major health conditions and found negative earnings effects among men reporting having diabetes at the age of 18 years, an effect that appeared fairly robust to sibling fixed effects and unobserved factors at the family level. Nielsen et al. (2016) used cross-sectional survey data from 2,415 adults with type 1 diabetes and 48,511 general population controls to study the effect on health-related quality of life, occupational status (level of employment, working hours and sick leave) and level of education. Their results showed that adults with type 1 diabetes had lower health-related quality of life, were more frequently unemployed, had more sick leave and were slightly more education. Finally, a recent study by Lovén (2017) found that the onset of type 1 diabetes at ages 6–15 results in negative consequences for both the affected individual and his or her siblings, at least for the brothers.

The papers included in this thesis contribute to this line of literature by using large-scale, longitudinal register data to explore the effect of type 1 diabetes on socioeconomic outcomes in adolescence, young adulthood, and midlife, and by exploring potential pathways in which the effect may operate.

Aims and objectives

General aim

The overall purpose of the thesis was to explore the socioeconomic consequences of childhood onset type 1 diabetes and through this investigate how an early life health shock can affect adult socioeconomic status. The included papers aim to capture the overall effect of type 1 diabetes on socioeconomic outcomes, in adolescence, young adulthood, and midlife, and to explore potential pathways through which the disease may ultimately lead to detrimental labor market outcomes.

Specific aims

Four specific aims were identified in the development of the thesis:

1. To study the effect of childhood onset of type 1 diabetes on school performance in compulsory and upper secondary school and to identify groups of children that suffer a greater disadvantage from the disease (Paper I).
2. Study the effect of childhood onset type 1 diabetes on employment and earnings, respectively, in young adulthood, and to study whether the effect differs by gender, age, and disease duration (Paper II).
3. To study whether the effect of type 1 diabetes on school performance has changed over time (Paper III).
4. To study potential mechanisms behind the effect of childhood onset type 1 diabetes on labor market outcomes. In particular, to examine the role of adult health, education, occupation, and family formation (Paper IV).

Methods and materials

Context

Setting

The analyses in this thesis were performed in Sweden, a country that offers several advantages for conducting observational research (Ludvigsson et al., 2016, Ludvigsson et al., 2011). Sweden has several national, population-based registers including information about socioeconomic and demographic factors as well as use of health care services. There are also a number of disease-specific registers covering information about incidence, health care, and clinical outcomes for different disease groups, e.g., diabetes, cancer, skin diseases, and infectious diseases (Swedish National Quality Registries, 2017, Emilsson et al., 2015). Additionally, the unique Swedish personal identity numbers, given to all permanently registered individuals, allow for linkage between the different registers for research purposes after ethical approval.

The Swedish health care system is primarily tax-funded and largely decentralized. All citizens are covered by the social insurance system and the county councils and local authorities are responsible for the management and prioritizing of their own health care resources. The out of pocket costs to the patients are low (Anell et al., 2012) and patients pay about SEK100–400 (EUR11–42, EUR1 = SEK9.470 in 2016) per health care visit. Over a 12-month period, the maximum out of pocket cost for a patient for publicly financed care is SEK1,100 (EUR116) and SEK2,200 (EUR226) for outpatient pharmaceuticals (Vårdguiden, 2016).

For patients with diabetes, the entire cost of insulin is subsidized by the social insurance, as are the costs for the equipment for administering insulin (e.g., pens and pumps) and for self-monitoring (blood glucose tests), if prescribed by a doctor or diabetes nurse (Diabetesförbundet, 2016c).

Type 1 diabetes

Diabetes is a set of diseases that differ in several ways, e.g., in terms of etiology and treatment, but have a common consequence: inability to control the glucose level in the blood. Type 1 diabetes accounts for about 5–10% of all cases of diabetes (Daneman, 2006b) and is one of the most common chronic diseases in childhood (Simmons and Michels, 2015). Worldwide, approximately 480,000 children have been estimated to have type 1 diabetes, with around 76,000 new cases each year (Shulman and Daneman, 2010). Over the last decades, the incidence of the disease has increased dramatically in Western countries. After Finland, Sweden has the highest incidence rate of type 1 diabetes in the world. In children aged 0–14, the yearly incidence in Sweden has been estimated at 44/100,000 in 2005–2007 (Berhan et al., 2011); around 700 children experience the onset each year (Patterson et al., 2009).

Onset and complications

The onset of type 1 diabetes is often sudden and symptoms such as weight loss, dehydration, and polyuria develop rapidly over a short period of time. The disease destroys the insulin-producing beta cells in the pancreas. Insulin is necessary to regulate the level of glucose in the blood and to keep the glucose levels within a target range, type 1 diabetes requires a lifelong, daily insulin treatment (Daneman, 2006b, Shulman and Daneman, 2010). If the blood glucose levels are not controlled, the disease is associated with both short- and long-term diabetic complications (The Diabetes Control Complications Trial/Epidemiology of Diabetes Interventions Complications Study Research Group, 2005). Short-term hypoglycemia (low blood glucose) may cause dizziness, lack of self-control, and, in severe cases, unconsciousness. On the other hand, episodes of hyperglycemia (high blood glucose) with ketoacidosis may lead to slow cerebration, thirst, dehydration, and, ultimately, death. In a longer perspective, type 1 diabetes is associated with cardiovascular complications, such as heart disease and stroke, as well as microvascular complications, including nerve, kidney, and eye diseases (Daneman, 2006b, Shulman and Daneman, 2010). The long-term complications develop gradually over time. According to the Swedish National Diabetes Register covering close to all type 1 diabetes patients over 18 years of age in Sweden, the prevalence of diabetic retinopathy (damage to the retina of the eyes) and albuminuria (limitations in kidney function) among 32-year-old individuals was 62% and 14%, respectively, in 2010. In the same year, the corresponding prevalence among 52-year-olds was 73% and 27%, respectively (The Swedish National Diabetes Register, 2017). Due to the risk of several severe complications, type 1 diabetes is also associated with an increased mortality risk (Lind et al., 2014, Rawshani et al., 2015).

Treatment

The treatment and management of type 1 diabetes includes constant monitoring of blood glucose levels and several daily injections of insulin, as well as strict routines regarding food and exercise. This everyday management of the disease can be time-consuming and requires responsibility of the affected children and their families (Wennick et al., 2009, Sparud-Lundin et al., 2013).

Over the last 50 years, the management and treatment of type 1 diabetes has changed in several respects and enhanced treatment technology has been developed to facilitate the complex management of the disease. During the late 1970s, new tools for self-monitoring of blood glucose were developed, enabling better scheduling of food, activities, and medication. In 1984, treatment with multiple daily injections of insulin was introduced in Sweden and in 1985, the first insulin pens were available, enabling a freer lifestyle with more flexible mealtime routines. Long-acting insulin agents were introduced in Sweden in the early 2000s (Hanås, 2014), enabling a more stable level of insulin during the day and at night. Additionally, the access to and technology of insulin pumps has increased, including continuous glucose monitoring systems. In 1997, insulin pump therapy was included in the Swedish reimbursement system (Diabetesförbundet, 2016b) and in 2015, more than 50% of children with type 1 diabetes had insulin pump-based treatment, compared to 39% in 2008 (SWEDIABKIDS, 2015, Sarnblad et al., 2016). In adults, the use of insulin pumps is less frequent; in 2014, it was estimated to be slightly above 20% (The Swedish National Diabetes Register, 2014).

Etiology

Despite extensive research, the exact cause of type 1 diabetes is still unclear. Current evidence, however, suggests that the onset is related to a complex combination of genetic and environmental factors that the individual needs to be exposed to in a certain sequence and during a vulnerable time period to trigger the onset (Maahs et al., 2010, Åkerblom et al., 2002, Dahlquist et al., 1999, Dahlquist et al., 1989, Gan et al., 2012). Heredity has been identified as one component; however, more than 90% of diagnosed individuals in Sweden have no affected first-degree relative (i.e., parent or sibling) (Dahlquist et al., 1989). Disease onset has also been associated with the presence of certain genotypes and ongoing research is exploring the possibility to screen for type 1 diabetes using these genotypes in the future (The TEDDY Study Group, 2007). There are also a number of environmental factors that could be of importance although, to date, no specific environmental factor has been shown to clearly and definitely trigger the onset of type 1 diabetes (Gan et al., 2012). The incidence of type 1 diabetes is known to vary between countries, and over time within countries. Some viruses have also been associated with disease onset (Patterson et al., 2009, Soltesz et al., 2007). Additionally, a few perinatal factors have been associated with risk of type 1 diabetes in early childhood. For instance,

older maternal age may increase the risk, whereas low birth weight and short birth length may decrease the risk (Dahlquist et al., 1999). Later in life, a rapid increase in height may possibly accelerate the risk in puberty (Dahlquist, 2006). Serious life events, such as death and illness in the family, and some dietary factors related to early exposure to cow's milk and gluten have also been indicated to potentially play a role in the onset (Nygren et al., 2015, Åkerblom et al., 2002).

While these factors together may contribute to an increased risk of developing type 1 diabetes, the majority of them are evidently beyond control for the individuals and their families, with little chance to influence or anticipate the onset beforehand. Additionally, there is no firm evidence that T1DM is related to lifestyle factors, such as smoking and exercise, which could also be related to socioeconomic factors (Daneman, 2006a).

Conceptual framework

In the economic literature, sudden reductions in health are often referred to as "health shocks" that shifts the initial health of the individual to a lower level (Lundborg et al., 2011, Currie and Stabile, 2003, Currie and Hyson, 1999). An early life health shock may impact socioeconomic outcomes in several ways. Childhood is often, in the human capital literature, referred to as a formative period with long-lasting consequences of the choices made (Cunha and Heckman, 2008). The choice of education and time invested in studies may, for example, be decisive for labor market choices later in life. Consequently, decreased health during childhood may impact adult socioeconomic outcomes through its impact on educational choices.

The health of a child and his or her family is commonly analyzed within the human capital framework (Bolin et al., 2002, Jacobson, 2000) using Grossman's demand for health model (Grossman, 1972). This theoretical framework considers health and education as two important stocks of human capital. Individuals use time and other goods to invest in health and education. The individual will gain welfare both from the stock itself, as it is good to be healthy and knowledgeable, and from the returns to the investments, as, e.g., increased health means more healthy time available for work or leisure (Grossman, 1972).

Following Grossman's model, we expect that a health shock in childhood may impact on school performance as a consequence of the shock, implying a shift in the level of health that indicates less healthy time available for leisure and educational investments. In the case of type 1 diabetes, self-monitoring of blood glucose, self-care education programs, health care visits, and strict daily routines are all factors that can take time and focus from school participation and studying. The self-management may also introduce psychological distress (Forsander et al., 2016). Furthermore, the direct complications associated with type 1 diabetes, such as

episodes of hyperglycemia and ketoacidosis, may also affect mental alertness and learning capacity and may therefore increase the time investment needed to accumulate human capital. Knowledge about the risks associated with the long-term diabetes-related complications may reduce incentives to invest in education as a consequence of uncertainty about future labor market productivity and life expectancy. The management of type 1 diabetes may also put a strain on the whole family (Wennick et al., 2009, Sparud-Lundin et al., 2013, Marshall et al., 2009), with reduced financial resources and less available time for the parents to compensate for school-related difficulties of their child.

In a longer perspective, a childhood health shock may reduce adult health. Labor market outcomes may be directly impacted by reduced adult health as a consequence of high sickness absence, reduced productivity, and early retirement. Furthermore, the health of individuals having experienced a health shock in childhood may decline more rapidly over the life course. In the case of type 1 diabetes, the risk of diabetes-related complications increases with age, further diminishing the health of the affected individuals.

The time-consuming daily treatment may also impact on productivity and flexibility (Sparud-Lundin et al., 2013). This could influence the choice of occupation as less demanding jobs or jobs with regular working hours may facilitate the daily disease management. Additionally, labor market opportunities are restricted for people with type 1 diabetes as the risk of hypoglycemia may mean limited access to some types of jobs due to safety issues, e.g., jobs in professional vehicular traffic and in the police force (Diabetesförbundet, 2016d).

Furthermore, reduced fertility associated with the disease and an increased risk of pregnancy complications (Vargas et al., 2010, Jonasson et al., 2007, Sjöberg et al., 2013) may affect the choice regarding, and opportunity of, having children. Having a more complicated pregnancy could increase the need for sick leave, which could further increase labor market consequences; on the other hand, not having children at all would reduce the need for parental leave and perhaps counteract differences in labor market outcomes.

Data sources

The Swedish Childhood Diabetes Register

This thesis is based on national register data from several registers and databases which have been linked at the individual level to the Swedish Childhood Diabetes Register (SCDR). The SCDR is an incidence register in which incident cases of type 1 diabetes in Sweden, in individuals younger than 15 years, are registered to enable studies on incidence trends over time (Dahlquist et al., 1982). Newly diagnosed cases of type 1 diabetes have been reported to the SCDR by the pediatric clinics, after informed consent from the parents, since July 1st, 1977. Since 2010, cases have been identified using information from the Swedish National Drug Register; cases have been enrolled after collecting prescribed insulin at least twice.

The SCDR currently includes more than 18,000 individuals with childhood onset type 1 diabetes and has been estimated to have a high level of coverage. In 1985, the coverage was estimated to be 99% after comparison to the Swedish Diabetes Association's register (Nyström et al., 1990); in 1990, the coverage was estimated to be 96% after comparison to the Swedish Military Services register (Dahlquist and Mustonen, 1994).

Linked national administrative registers

To study the long-term consequences of type 1 diabetes, a comparison group has been created for the SCDR using a matched case-control design with four individuals from the Swedish general population matched to each person in the register. Statistics Sweden has performed the matching of these controls based on year of birth and municipality of residence at the time of the type 1 diabetes diagnosis. Through the Multi-Generation Register (Statistics Sweden, 2010), linkage of information on the parents of type 1 diabetes cases and controls has also been performed. Furthermore, using the Swedish personal identity number, Statistics Sweden has linked the SCDR data to other national population registers, including the Longitudinal Integration Database for Health Insurance and Labor Market Studies (LISA) (Statistics Sweden, 2011), the Swedish Register of Education (Statistics Sweden, 2006), the National Patient Register for in- and outpatient care (The National Board of Health and Welfare (Socialstyrelsen), 2014a), and the Swedish Medical Birth Register (The National Board of Health and Welfare (Socialstyrelsen), 2014b). Figure 1 illustrates the linkage between the SCDR, the controls, the parents, and the national registers and databases.

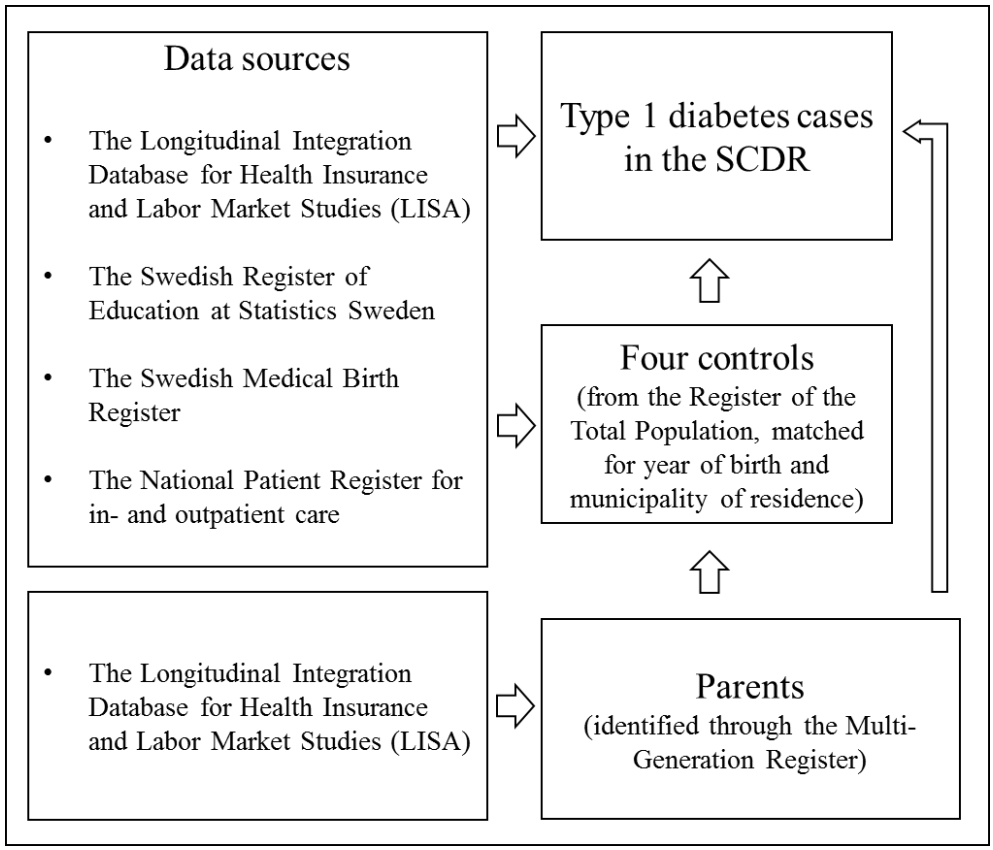

Figure 1: The linkage between the Swedish Childhood Diabetes Register (SCDR), the controls, the parents, and the national registers and databases.

Table 1 presents the data sources used for the analysis in each specific paper. The four papers are based on data from different cohorts registered in the SCDR and their matched population controls. Additionally, the analyses in all four papers include data from the LISA database. The LISA database integrates existing annual information from national administrative registers of education, income, employment, sick leave, etc with several national population registers (Statistics Sweden, 2011). Since 1990, all individuals aged 16 years and older, who are registered in Sweden as of December 31st each year, have been included. For the cases and controls, LISA data was used as outcome variable of different socioeconomic factors. Regarding the parents, LISA data was used as control variables for socioeconomic background. Papers I and III used additional data from the Swedish Register of Education on educational aspects (school grades from compulsory and upper secondary school) not included in the LISA database. Papers II and III complement the control variables for socioeconomic background by also

using some perinatal control variables from the Swedish Medical Birth Register which include information on pregnancies, births, and newborns reported in the maternity and neonatal care sector. The Swedish Medical Birth register has been active since 1973 and the number of included variables has been extended gradually over the years. Finally, the analysis in Paper IV includes data also from the National Patient Register for inpatient and outpatient specialist care.

Table 1: Data sources used in Papers I–IV

	Paper I	Paper II	Paper III	Paper IV
The Swedish Childhood Diabetes Register (SCRD)	x	x	x	x
The Longitudinal Integration Database for Health Insurance and Labor Market Studies (LISA)	x	x	x	x
The Swedish Register of Education	x		x	
The Swedish Medical Birth Register		x	x	
The National Patient Register for inpatient care				x
The National Patient Register for outpatient specialist care				x

Study populations

Table 2 presents the study populations analyzed in the four studies. Papers I and II explored the same cohort of individuals, born in 1972–1978, but focused on outcomes at different periods in life, as illustrated in Figure 2. This cohort was selected because individuals born during these years in Sweden have been exposed to the same educational grading system which was one of the main outcomes in Paper I. This cohort consisted of 2,485 individuals from the SCDR and 9,940 controls. Children with type 1 diabetes were diagnosed between 1977 and 1993 at the average age of 9.45 years. Paper I was a cross-sectional study, analyzing school performance at age 16, when pupils in Sweden finish compulsory school, and in upper secondary school at age 19. Paper II focused on outcomes in early adulthood, after finishing upper secondary school, and used a longitudinal design to explore labor market outcomes at ages 19–38. Similar as in Paper I, the analysis in Paper III focused on school performance when pupils were completing their compulsory and upper secondary schooling, but was based on a later cohort of children born in 1982–1993 for the analysis of compulsory school and in 1979–1990 for the analysis of upper secondary school. In this paper, the type 1 diabetes group had been diagnosed between 1982 and 2008 at the average age of 9.01 years. In the final paper, Paper IV, we wanted to allow for the longest possible follow-up time and therefore included also the earliest cohorts in the register. Consequently, 4,281 cases with diabetes were selected, as well as 17,120 matched controls, born in 1962–1979, and studied at the ages of 30–50.

Table 2: Outline of the study populations and their characteristics in Papers I–IV

	Paper I	Paper II	Paper III	Paper IV
Birth cohort	1972–1978	1972–1978	1982–1993*	1962–1979
Type 1 diabetes cases (n)	2,485	2,485	6,269	4,281
Controls (n)	9,940	9,940	25,076	17,120
Year of diagnosis, mean (range)	1985 (1977–1993)	1985 (1977–1993)	1997 (1982–2008)	1984 (1977–1994)
Age at diagnosis, yrs, mean (min–max)	9.45 (0–15)	9.45 (0–15)	9.01 (0–15)	10.23 (0–15)
Women (%)	50%	50%	48%	49%
Age (yrs)	16 and 19	19–38	16 and 19	30–50

*In the compulsory school analyses.

Figure 2: Socioeconomic outcomes studied over the life course in Papers I–IV.

Ethics

The studies included in this thesis, and the linkage of data form various registers to the SCDR, have been approved by the Regional Research Ethics Board at Umeå University (REPN Umeå 8/1, 2008 Dnr 07-169M). Statistics Sweden performed the linkage and coded data only were delivered to the researchers.

The continuous registering of incident type 1 diabetes cases in the SCDR was initially approved by the Swedish Data Inspection Board and the regional research ethics committees; Karolinska Institute in Stockholm and Umeå University. Parents and/or children gave informed consent to be registered and the children/parents had the opportunity to opt out at any time. Fewer than 1% denied being registered.

Empirical strategy

This section presents and discusses some of the key aspects of the statistical methods used for the data analysis, first in general and thereafter separately for each paper.

Dealing with confounding

Form a methodological point of view, the ideal strategy for identifying the effect of type 1 diabetes on socioeconomic factors would be to randomly assign type 1 diabetes to individuals and follow them over the life cycle and compare the outcomes of interest between them and a general population group. Such a study design would, for ethical reasons, not be possible. Thus, inferences have to be drawn from observational data where the independent variable is not under the control of the researcher which normally complicates the identification issue. However, in the case of diabetes type 1 the specific etiology, as explained earlier, implies that the sudden onset of the disease may be similar to a randomized assignment with respect to socioeconomic outcomes. This is based on two main assumptions. Firstly, individuals and their families do not by themselves, through actions or through choices, influence the type 1 diabetes onset. Secondly, individuals and their families have no reason to anticipate the onset before it happens. Consequently, the systematic differences concerning socioeconomic and other background characteristics between the diabetic case and his or her controls are expected to be small, if present at all. This is favorable from a methodological point of view as it implies less concern about confounding. However, endogeneity can never be completely ruled out in any observational study and therefore the four papers explore the robustness of the estimated effect of type 1 diabetes by controlling for a wide range of parental demographic and socioeconomic factors, as well as perinatal factors. Additionally, propensity score matching (PSM) was used as an alternative approach to handle potential bias due to model misspecification and to restrict the analysis to individuals within the region of common support. It is, however, important to keep in mind that both the regression and the PSM approach assume that the bias introduced by potential confounding factors can be controlled for through the observed variables. Neither method is able to account for unobservable factors that we are not able to control for in our data.

What other methods could we potentially use to further account for unobserved confounders if they exist? In a panel data settings, the fixed effects method is commonly used to avoid bias due to factors that are constant over time. The idea of using the fixed effects approach is that if subjects serve as their own controls, omitted variables that are constant or "fixed" over time will not bias the result. This, however, makes it impossible to estimate the effect of variables that do not vary

over time (Angrist and Pischke, 2009). Consequently, this strategy was not appropriate for answering the questions posed in this thesis as the explanatory variable of interest (type 1 diabetes) is time-invariant due to the fact that all individuals in the study population were, or were not, diagnosed before the analysis period. However, if interest lies in estimating age-specific effects of diabetes, it is possible to construct a fixed effects model for the diabetes effect in specific age groups that is allowed to vary over time. This method was applied by Lovén (2017) along with a simpler ordinary least squares (OLS) specification of the age-specific effects. The author found that the results were fairly stable when controls for the individual fixed effects were added.

Another version of the fixed effects approach is to use siblings or twins as controls to deal with omitted variable bias at the family and genetic level. While this approach would have been possible for the studies in this thesis, as the SCDR also holds data for siblings, it is natural to argue that this method is not appropriate in the case of type 1 diabetes if the aim is to estimate the total effect of the disease. Qualitative studies show that a child's sudden development of type 1 diabetes impacts the daily life of the whole family (Wennick and Hallström, 2007, Wennick et al., 2009) as the everyday management of the disease may constrain both time and financial resources. The risk of hypoglycemia and other diabetes-related complications may also impose long-term stress on the parents. For siblings, the illness brings changes to their everyday life including worry about their sick sibling and the need to help around the house (Wennick and Huus, 2012). Lovén (2017) even reports that future earnings of brothers of children with T1DM are negatively affected by the disease. Consequently, these studies indicate that using siblings as a control group would likely underestimate the total effect of type 1 diabetes as the controls are impacted by the disease themselves. Moreover, the sibling fixed effects approach is not ideal as it controls only partially for genetic and family environmental factors. Nevertheless, if we had had data on monozygotic twins, with and without type 1 diabetes, then we could have estimated a conservative approximation of the effect without worrying about confounding due to genetic and family level factors. The low incidence of type 1 diabetes would, however, likely not permit such a strategy as the sample size would be substantially limited if including only monozygotic twins with one twin diagnosed with type 1 diabetes during childhood.

Another approach to statistically adjust for omitted variable bias is the instrumental variable method. The basic idea of this method is to estimate the causal effect of some variable, X, on another variable, Y, using a third variable, Z, which affects Y only through its effect on X (Angrist and Pischke, 2009). A valid instrument for the studies in this thesis is a variable that is strongly associated with type 1 diabetes and related to the socioeconomic outcomes only through its effect on type 1 diabetes. This approach has been applied by, for example, Brown et al. (2005) and Minor (2011) to estimate the effect of type 2 diabetes on labor market

outcomes using family history of diabetes or mother's diabetes status as an instrument for diabetes. However, this strategy may introduce bias in itself if, e.g., the mother's history of diabetes has an effect on her labor market outcomes which also impacts future labor market prospects for her children. Furthermore, when considering type 2 diabetes, which is known to be caused by several lifestyle-related factors linked to socioeconomic status, such as overweight, low physical activity, smoking, etc (Hu et al., 2001), correlation between the diabetes status of the mother and the child's socioeconomic outcomes may be driven by the correlation between the mother's diabetes status and her own socioeconomic status. For the studies in this thesis, we have searched the data for possible instrument variables suitable for analyzing the effect of type 1 diabetes on education and labor market outcomes, but have found no reliable instrument that meets the necessary criteria. For example, one potential instrument variable could have been ethnicity, which is known to be related to risk of type 1 diabetes as the incidence is higher in Nordic countries. However, ethnicity would not have been a valid instrument for the analyses in this thesis as ethnicity is likely to have a direct effect on labor market outcomes (Constant et al., 2009), which is not channeled only through its effect on the risk of type 1 diabetes.

To sum up, none of the other econometric strategies proposed in the literature appear to be appropriate for answering the research questions posed in this thesis. In other situations, the potential problems associated with other available methods may be small in relation the confounding bias that they reduce. However, in this data, where the endogeneity problem is likely to be very small, if present at all, this may not be the case.

Paper I

The effect of type 1 diabetes on school performance and educational attainment

The main focus of Paper I was to estimate the effect of type 1 diabetes on educational attainment in a cohort of children born in 1972–1978. This cohort was selected because individuals born during these years had the same numerical grading system in compulsory school. This grading system was based on a 5-point scale and was intended to be relative and normally distributed at the national level.

The study analyzed three measures of educational attainment: (1) the probability of completing compulsory and upper secondary school, respectively; (2) the mean final school grades from compulsory and upper secondary school; and (3) the school grades in the three core/compulsory subjects Swedish, English, and Mathematics, as well as in Athletics. Additionally, the study provided an indication of the long-term consequences of the disease by estimating the probability of gainful employment 10 years after the end of upper secondary school. An individual was defined as "gainfully employed" if his or her monthly earnings were at least equal

to the 10th percentile of earnings in the Swedish population. At this level of earnings, individuals were expected to be able to support themselves on their income.

The effect of type 1 diabetes on the outcomes was assessed using parametric and non-parametric regression methods and different model specifications to explore different aspects of the disease onset. Logistic regression was used to estimate the odds ratio (OR) of receiving a final grade from compulsory and upper secondary school at the age of 16 and 19 years, respectively, and of being gainfully employed at the age of 29 years. Linear repression was used to estimate the effect of the disease on mean final grades from the two named levels of education. To explore whether the impact of diabetes differed between groups of individuals, quantile regression was used to estimate the effect in the 10th, 25th, 50th, 75th, and 90th quantiles of the conditional distribution of mean final grades. Furthermore, ordered logistic regression was used to analyze the impact of type 1 diabetes on the grade in the three core subjects and in Athletics.

Throughout the analyses, we controlled for gender, year of issuance of the grade, socioeconomic background (the educational level and permanent earnings, i.e., average earnings in 1990–2007, of the parents), and country of birth of the parents (Nordic/non-Nordic).

Paper II

The effect of type 1 diabetes on labor market outcomes

In the analysis of Paper II, the cohort of individuals selected for the analysis in Paper I was followed beyond upper secondary school to explore how the childhood onset of type 1 diabetes impacts on labor market outcomes in young adulthood, at 19–38 years of age.

This study had a longitudinal design and the analyses were performed in a panel data setting including observations over a 20-year period (1991–2010). Logistic and linear random effects models were used to estimate the effect on the two main outcomes in the study: employment status and the log of annual earnings conditional on employment. Different model specifications were used to test the robustness of the results when controlling for demographic and socioeconomic background (a measure of permanent earnings (average earnings) in 1990–2010 and educational level of the mother and father, and whether the parents were born in a Nordic or non-Nordic country) together with perinatal factors (mother's diabetes status and age at delivery, birth weight and length, length of pregnancy, twin birth, and Cesarean section or natural birth) and time trends (year-specific dummy variables). The paper also investigated the effect of type 1 diabetes duration (after <15 years, after 15–25 years, and after >25 years) and on different age groups (19–26, 27–32, and 33–38 years old).

Finally, to provide some understanding of the mechanisms behind the estimated effect of type 1 diabetes and to further support the argument of a causal effect, the paper explores three choice-related mechanisms: highest achieved educational level, occupational status, and having children. The effect of type 1 diabetes was analyzed separately for each of these factors. In a final step, we included the factors in the regression of earnings to investigate how this changed the magnitude of the estimated diabetes effect.

Paper III

The effect of type 1 diabetes on school performance in later cohorts, and changes over time

Over time, several factors may change the conditions in school for children with type 1 diabetes. Firstly, new health care technologies and improved diabetes education may diminish the influence of type 1 diabetes as they may improve health and facilitate the situation for the affected children through easier diabetes self-management and improved disease control and health. Secondly, school setting-related changes may influence the conditions for children with poor health to achieve well in school. In 1997, the educational grading system in Sweden switched from a relative grading system to an absolute and goal-oriented grading system. This structural change may have increased or decreased the effect of type 1 diabetes depending on potential parallel mechanisms, such as changes in criteria for grading of students, or additional requirements for children with special needs in school, implemented along with the reform (Sarnblad et al., 2016). Together, these changes raise the question of how type 1 diabetes affects school performance in more recent birth cohorts of children.

To address this question, Paper III examined if the effect of type 1 diabetes on school performance is still present in a later cohort of children, born in the 1980s and early 1990s. As a first step in this study, a similar regression approach as in Paper I was used to estimate the conditional effect of type 1 diabetes on final grades in compulsory and upper secondary school. A potential limitation of traditional regression is that even if all relevant confounders are controlled for, the model may still yield biased estimates if the relationship between these factors and the outcome measure is not appropriately modelled (Fortson et al., 2015). To address this issue, the analysis was extended using PSM to estimate the average treatment effect of the treated (ATT) (Abadie and Imbens, 2006). Logistic regression was used to estimate the probability of having type 1 diabetes, given a large set of background variables, and this estimated probability (the propensity score) was then used to identify and match similar controls to each type 1 diabetes case (Rosenbaum and Rubin, 1983). The PSM method differs from regression analysis in that it requires no model assumption for the outcome, e.g., linearity. Moreover, by matching, it is possible to

restrict the analysis to individuals within the region of common support (i.e., in order to only include cases and controls with similar background characteristics, expressed through overlapping propensity scores) (Fortson et al., 2015).

The matched case control design of the data implies that type 1 diabetes is overrepresented in the sample compared to the general population, and a concern with using PSM in this setting is that additional knowledge may be needed to account for this sampling design (Persson et al., 2017). More specifically, information is needed about the prevalence of type 1 diabetes in the population, as well as prevalence at the levels of year of birth and municipality (the initial matching variables), to correctly estimate the propensity score. To account for this sampling design, weighted maximum likelihood was used to estimate the propensity score (Persson et al., 2017). The weights were approximated using information about the prevalence of type 1 diabetes in the population as well as year of birth.

In a final step, the standardized effect size of the type 1 diabetes effect (Cohen's d) was calculated and compared to the size of the effect reported in Paper I among children born in 1972–1978. Cohen's d is the mean difference between the cases and the control group, divided by the average of their standard deviations (Cohen J, 1988). This is a common effect measure used to compare various educational and cognitive measurements that are not directly comparable due to different scales (Gaudieri et al., 2008, Bangert-Drowns et al., 2004).

Paper IV

The mediating factors explaining the effect of type 1 diabetes on labor market outcomes

The main purpose of Paper IV was to investigate the mechanisms behind the effect of childhood onset type 1 diabetes on labor market outcomes using a formal mediation approach. The paper explored the relative importance of four potential mediating factors: education, occupation, family formation, and health.

For the health mediator, three indicators were constructed based on social insurance sickness benefit data (accessible from the national social insurance system after ≥14 days of sick leave) from the LISA dataset and in- and outpatient hospital care data from the National Patient Register: (1) sickness benefits received during the year; (2) inpatient care received during in the year; and (3) two or more outpatient care visits in the year.

The first step of the analysis explored the effect of type 1 diabetes on the potential mediators separately at the ages of 30 and 40 years. The second step used mediation analysis to investigate to what extent the relationship between type 1 diabetes and employment and earnings was channelled through each mediator.

Traditional mediation analysis is often carried out by adjusting for the mediators in standard regression models and comparing the coefficients to a model

without the mediators (Baron and Kenny, 1986). Over the last decades, new statistical methods have been developed to account for several limitations associated with the traditional approach to improve the validity of mediation analysis (Richiardi et al., 2013, Shrout and Bolger, 2002). Following the approach used by, e.g., Tubeuf et al. (2012), Yang and Park (2015), Damman et al. (2011), McDonough et al. (2015), Monnat and Rigg (2016), the KHB method developed by Karlson, Holme, and Breen (Breen et al., 2013, Kohler et al., 2011, Karlson and Holm, 2011) was used for the mediation analysis in this paper. This method allowed us to formally decompose the total effect of type 1 diabetes into direct and indirect (mediating) effects and enabled us to disentangle how much each of the mediators contributes to the indirect effect. Using the KHB method, we were also able to simultaneously investigate multiple mediators. This is necessary when assessing mediators that are not independent of each other, which was likely the case here, to avoid double counting of the contributions of each mediator (VanderWeele and Vansteelandt, 2014). This method also adjusts for scaling issues that may arise in cross-model comparison of non-linear models. The basic idea of the KHB method is to compare the full model (including mediators) to a reduced model that substitutes the mediator variables with the residuals of the mediators estimated in regressions of the mediators on the treatment variable (type 1 diabetes).

The mediation analysis was performed in a panel data setting with annual data of ages 30 to 50 years. Logit and OLS regression with clustered standard errors (SEs) was used, controlling for demographic and socioeconomic background and calendar year. The 95% confidence intervals (CIs) around the estimate effects were calculated using bootstrapping with 500 replicates (Tubeuf et al., 2012, Shrout and Bolger, 2002). The third, and final, step, investigated whether the effect of type 1 diabetes differed across individuals with different parental socioeconomic status, by estimating interaction effects between type 1 diabetes and parents' educational level and permanent earnings (using 1990–2013 averages).

General statistical comments

The analyses included in this thesis were performed using Stata software version 12 (StataCorp, 2012) in Paper I and version 14 (StataCorp, 2014) in Papers II–IV. The PSM in Paper III was performed using the statistical software R (R, 2017). All analyses of the effect of type 1 diabetes on labor market outcomes were performed separately for women and men, which is in line with the labor economic literature and the epidemiological literature. Robust SEs were used in all regression analyses to correct for potential heteroscedasticity.

Results

This section briefly presents the main results of the four papers included in this thesis. For a full presentation of the results, the reader is referred to the separate papers.

Paper I

The effect of type 1 diabetes on school performance and educational attainment

The analysis of school performance in compulsory and upper secondary school among children born in 1972–1978 (Table 3) showed that type 1 diabetes is associated with a negative effect on school grades at both levels of schooling. On the 5-point grading scale, individuals with type 1 diabetes on average had −0.07 points lower grades ($p<0.001$) when completing compulsory schooling at the age of 16 years, controlling for demographic and socioeconomic characteristics (Model 1). The greatest difference in grades between the diabetes group and the control group was found in Athletics (3.09 vs. 3.31, $p<0.001$). The largest effect of type 1 diabetes, compared to the control group, was found among children diagnosed at a very young age, of 0–4 years (−0.15, $p=0.001$, Model 2). Additionally, quantile regression detected differential effects of diabetes on the conditional distribution in mean final grades. In compulsory school, the strongest negative effect was found in the lowest decile (−0.13, $p<0.001$) and no significant effect was seen in the top decile, suggesting that diabetes may be a greater challenge for children with weaker overall school performance.

A smaller proportion of individuals with type 1 diabetes completed upper secondary school (diabetics 79% vs. controls 81%; OR 0.81; 95% CI 0.71–0.92). Among those who completed upper secondary school, a negative effect of type 1 diabetes was seen also at this level of schooling, but the effect was statistically significant only in the grades from theoretical programs (−0.07, $p=0.001$, Model 1). The effect of type 1 diabetes in upper secondary school was estimated, controlling for the mean final grade from compulsory school. Thus, the estimated diabetes effect was the impact of type 1 diabetes on top of effects already manifested in compulsory school, indicating an accumulative negative effect. Furthermore, the results indicated a lower probability of gainful employment at 29 years of age among the individuals with type 1 diabetes.

Table 3: Linear regression of the effect of type 1 diabetes on the mean final grades from compulsory and upper secondary school

Diabetes effect	β ± SE	95% CI	p
Compulsory school (n=11,236)			
Model 1: Diabetes effect[a]	-0.07 ± 0.02	-0.10, -0.04	<0.001
Model 2: Effect of age at diagnosis[a]			
- Controls (reference group)			
- Onset of diabetes at 0–4 years	-0.15 ± 0.05	-0.24, -0.06	0.001
- Onset of diabetes at 5–9 years	-0.07 ± 0.02	-0.12, -0.03	0.001
- Onset of diabetes at 10–15 years	-0.06 ± 0.02	-0.10, -0.02	0.003
Upper secondary school – theoretical programs (n=3,840)			
Model 1: Diabetes effect[b]	-0.07 ± 0.02	-0.11, -0.03	0.001
Model 2: Effect of age at diagnosis[b]			
- Controls (reference group)			
- Onset of diabetes at 0–4 years	-0.11 ± 0.05	-0.20, -0.01	0.025
- Onset of diabetes at 5–9 years	-0.11 ± 0.03	-0.17, -0.05	<0.001
- Onset of diabetes at 10–15 years	-0.03 ± 0.03	-0.08, 0.02	0.236
Upper secondary school – vocational programs (n=4,098)			
Model 1: Diabetes effect[b]	-0.02 ± 0.02	-0.06, 0.01	0.181
Model 2: Effect of age at diagnosis[b]			
- Controls (reference group)			
- Onset of diabetes at 0–4 years	-0.03 ± 0.06	-0.14, 0.08	0.644
- Onset of diabetes at 5–9 years	0.01 ± 0.02	-0.04, 0.05	0.833
- Onset of diabetes at 10–15 years	-0.04 ± 0.02	-0.09, 0.00	0.066

[a]Controlling for gender, year of grade, socioeconomic background, and country of birth (Nordic/non-Nordic) of the parents. [b]Controlling for gender, year of grade, socioeconomic background, country of birth (Nordic/non-Nordic) of the parents, and mean final grade from compulsory school. 95% CI = 95% confidence interval; SE = standard error.

Paper II

The effect of type 1 diabetes on labor market outcomes

In Paper II, we extended the analysis of the cohort born in 1972–1978, studied in Paper I, to explore the long-term labor market consequences of childhood onset of type 1 diabetes.

The results show that type 1 diabetes has a significant impact on labor market outcomes in early adulthood. Figure 3 illustrates the annual earnings (using first, second (median), and third quartiles) from 19 to 38 years of age in the type 1 diabetes group and the control group separately. Before the age of 27, men with type 1 diabetes had similar, or slightly higher, earnings, but thereafter they started lagging behind the control group, as observed in all quartiles. Women with type 1 diabetes had lower earnings throughout the period, at least in the first and second quartiles, with a larger gap after the age of 25 in the first quartile.

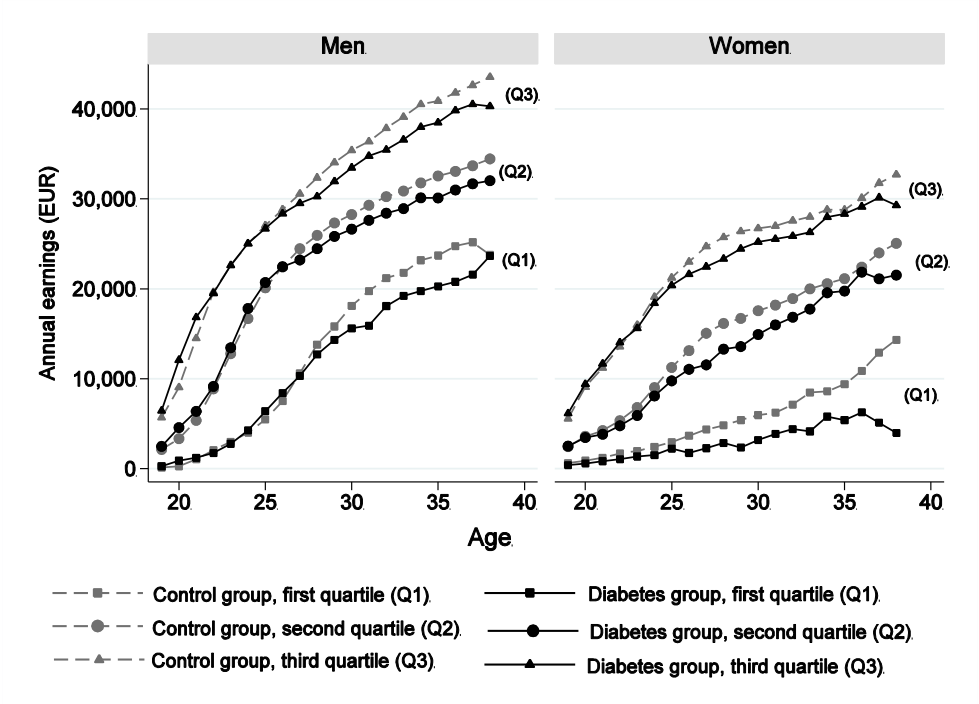

Figure 3: Annual earnings for the type 1 diabetes group and control group, from 19 to 38 years of age, deflated into 2010 prices.

Table 4 shows the effect of type 1 diabetes on employment and (log of) earnings between the ages of 19 and 38 years. The results show that women with type 1 diabetes were less likely to be employed (OR 0.830; 95% CI 0.738–0.934)

and those employed on average had 6% (p=0.001) lower earnings compared to the comparison group (Model 1). The second model specification (Model 2) shows that the effect on employment and log of earnings was not significant until after 15 years of disease duration.

In contrast to women, the effect of type 1 diabetes on employment for men was observed only after 15 years' disease duration (Model 2). However, an average effect of about 5% (p=0.001) lower earnings was observed throughout the study period among employed men and this effect tended to increase with disease duration (Models 1–2). The negative effect on earnings was significant after 15–25 years since onset (5.8% lower, p<0.001) and increased to 12.4% (p<0.001) lower earnings after more than 25 years.

When splitting the period into early, mid-, and older young adulthood (19–26, 27–32, and 33–38 years, respectively), no effect was observed in the first period (19–26 years) among women. For men, this period was even associated with a slightly positive effect on employment and earnings. Later in young adulthood, the effect increased considerably, particularly at the ages of 27–32 years (for women: OR for employment 0.564; 95% CI 0.451–0.706; and 9.1% lower earnings (p<0.001); for men: OR for employment 0.623; 95% CI 0.483–0.803; and 9.6% lower earnings (p<0.001)).

Although type 1 diabetes had a negative effect on achieved education, defined both as years of schooling and as level of highest education, the effect on earnings changed negligible after controlling for own educational level. Furthermore, the effect of type 1 diabetes remained stable when controlling for having children, whereas controlling for expected income in the occupational field reduces the effect on earnings (from 6.0% to 3.3% lower earnings among women and from 4.7% to 3.2% among men.

Table 4: Effect of type 1 diabetes on employment and earnings for women and men between the ages of 19 and 38

	Women				Men			
	Logistic random effect Employment		Linear random effect Ln (earnings) if employed		Logistic random effect Employment		Linear random effect Ln (earnings) if employed	
	OR	95% CI	β	p	OR	95% CI	β	p
Model 1: Diabetes effect, adjusted for socioeconomic and perinatal factors[a]	0.779	0.678–0.900	-0.060	0.001	0.894	0.765–1.045	-0.047	0.001
Model 2: Duration effect, adjusted for socioeconomic and perinatal factors[a] and age								
- Controls (reference group)								
- Years since diagnosis: <15 years	0.880	0.762–1.018	-0.025	0.254	1.077	0.919–1.262	0.018	0.301
- Years since diagnosis: 15–25 years	0.712	0.621–0.817	-0.072	<0.001	0.807	0.689–0.944	-0.058	<0.001
- Years since diagnosis: >25 years	0.723	0.574–0.910	-0.073	0.059	0.419	0.329–0.533	-0.124	<0.001
Individuals (observations)	4,876 (77,884)		4,690 (53,481)		4,866 (78,164)		4,713 (57,376)	

[a]Adjusted for parents' education and income; having a parent born in a non-Nordic country; mother's diabetes status; mother's age at delivery; birth weight (low); birth length (short); length of pregnancy (premature birth); twin birth; Cesarean section; and calendar year. CI = confidence interval; OR = odds ratio; SE = standard error.

Paper III

The effect of type 1 diabetes on school performance in later cohorts, and changes over time

The analysis performed in Paper III shows that childhood onset of type 1 diabetes tent to have a negative effect on school performance, measured as final grades from both compulsory school and theoretical upper secondary school, also in later cohorts of children born in 1979–1993 and receiving their final grades during 1998–2010. The compulsory school results showed a negative effect of type 1 diabetes on grades based on the goal-oriented grading system, of -7.246 ($p<0.001$) and -7.784 ($p<0.001$) points on a 320-point scale, using the regression and the PSM approach, respectively. The effect of type 1 diabetes was significant also in the final grades from upper secondary school using both approaches: -0.280 ($p<0.001$) and -0.319 ($p<0.001$) points on a 20-point scale.

Similar effects were found for boys and girls in both levels of schooling, with overlapping CIs. The effect, however, appeared to be larger among children diagnosed at ages 0–4 or 10–15 years compared to children diagnosed at 5–9 years. This indicates a particular vulnerability among children with a very early onset age, when hypo- and hyperglycemic episodes may result in more permanent damage (Dekelbab and Sperling, 2006, Flykanaka-Gantenbein, 2004), as well as among children diagnosed during the last years of compulsory school, who are close to receiving final grades.

The standardized comparison of results obtained in children born in the 1970s (Paper I) indicates that the negative effect of type 1 diabetes was still present and only marginally smaller among children born in the 1980s and early 1990s (Table 5). Subgroup analysis indicated a more reduced effect among women, particularly in upper secondary school grades. Among men, however, no reduction was seen.

The finding that the effect of type 1 diabetes has only marginally decreased in later birth cohorts, and that for some groups it has not decreased at all, may be interpreted in several ways. Firstly, the persistent effect on a group level, despite improved treatment, may suggest that the new, goal-oriented grading system is less beneficial for students with chronic diseases compared to students in general. Another possible interpretation is that the negative effect of type 1 diabetes on school performance may be driven by some characteristics of the disease that have little relation to the changes in treatment seen over the last decades. The benefits of enhanced treatment may generate improvements in other aspects of the children's life or benefits that appear later in life, such as delayed diabetic complications that may not develop before 10–15 years of diabetes duration, or later. Nevertheless, the results from this study clearly show that the effect of type 1 diabetes on school grades is still present among individuals who have recently completed school.

Table 5: Effect size comparisons of final grades from compulsory and upper secondary school between children born in 1979–1993 and children born in 1972–1978

	Individuals born in 1979–1993 (Paper III)	Individuals born in 1972–1978 (Paper I)
	d (95% CI)	*d* (95% CI)
Compulsory education		
Total	-0.109 (-0.137, -0.080)	-0.124 (-0.169, -0.079)
Males	-0.114 (-0.153, -0.074)	-0.108 (-0.170, -0.046)
Females	-0.096 (-0.137, -0.054)	-0.113 (-0.178, -0.048)
Onset of diabetes at age 0–4 years	-0.139 (-0.203, -0.074)	-0.181 (-0.277, -0.084)
Onset of diabetes at age 5–9 years	-0.070 (-0.116, -0.025)	-0.111 (-0.169, -0.052)
Onset of diabetes at age 10–15 years	-0.127 (-0.165, -0.088)	-0.102 (-0.152, -0.052)
Upper secondary school		
Total	-0.070 (-0.105, -0.034)	-0.113 (-0.167, -0.060)
Theoretical program	-0.058 (-0.107, -0.010)	-0.091 (-0.172, -0.010)
Vocational program	-0.045 (-0.097, 0.007)	-0.079 (-0.151, -0.007)
Males	-0.063 (-0.112, -0.013)	-0.067 (-0.141, -0.008)
Females	-0.065 (-0.116, -0.015)	-0.141 (-0.219, -0.064)
Onset of diabetes at age 0–4 years	-0.119 (-0.199, -0.038)	-0.144 (-0.311, 0.022)
Onset of diabetes at age 5–9 years	-0.019 (-0.076, 0.037)	-0.099 (-0.173, -0.026)
Onset of diabetes at age 10–15 years	-0.090 (-0.138, -0.042)	-0.122 (-0.176, -0.068)

CI = confidence interval.

Paper IV

Mediating factors that explain the effect of type 1 diabetes on labor market outcomes

Several potential mediating factors of the relationship between childhood onset type 1 diabetes and labor market outcomes were explored in the analyses of Paper IV. More specifically, the role of education, occupation, family formation, and adult health was evaluated to gain further understanding of the relationship between type 1 diabetes and employment and earnings.

The results show that the onset of type 1 diabetes has a significant negative effect on all the mediators evaluated. At the age of 30, women and men with type 1diabetes on average had 0.23 and 0.18 ($p<0.001$) fewer years of education, respectively, which, for women, was equivalent to about 1 year less education for one out of four individuals in the diabetes group. Furthermore, individuals with type 1 diabetes worked in occupational areas with lower average expected earnings, quantified in the regressions by average monthly earnings of peers in the chosen occupational field (-2%, $p<0.001/=0.001$, at the age of 30, and -3%, $p<0.001/0.004$, at the age of 40, for women and men, respectively). Type 1 diabetes was also associated with a lower likelihood of having children, which was particularly notable at the age of 40 (OR 0.65; 95% CI 0.53–0.79, and OR 0.69; 95% CI 0.59–0.80, for women and men, respectively). Additionally, type 1 diabetes had a significant effect on three indicators of adult health. Compared to controls, results showed increased likelihood of having sickness benefits (OR 1.88; 95% CI 1.69–2.11, and 1.89; 95% CI 1.59–2.19, for women and men, respectively) as well as increased likelihood of receiving in- and outpatient care, particularly for having two or more outpatient care visits (OR 7.74; 95% CI 6.62–9.05, and 8.77; 95% CI 7.62–10.08, respectively).

The average total effect of childhood onset type 1 diabetes on employment through ages 30–50 was estimated at OR 0.68 (95% CI 0.61–0.76) and OR 0.76 (95% CI 0.67–0.86) for women and men, respectively, and the effect on earning among those employed was -6% ($p<0.001$) and -8% (<0.001). Figure 4 graphically illustrates the earnings penalty from type 1 diabetes on annual earnings at the ages of 30–50 years.

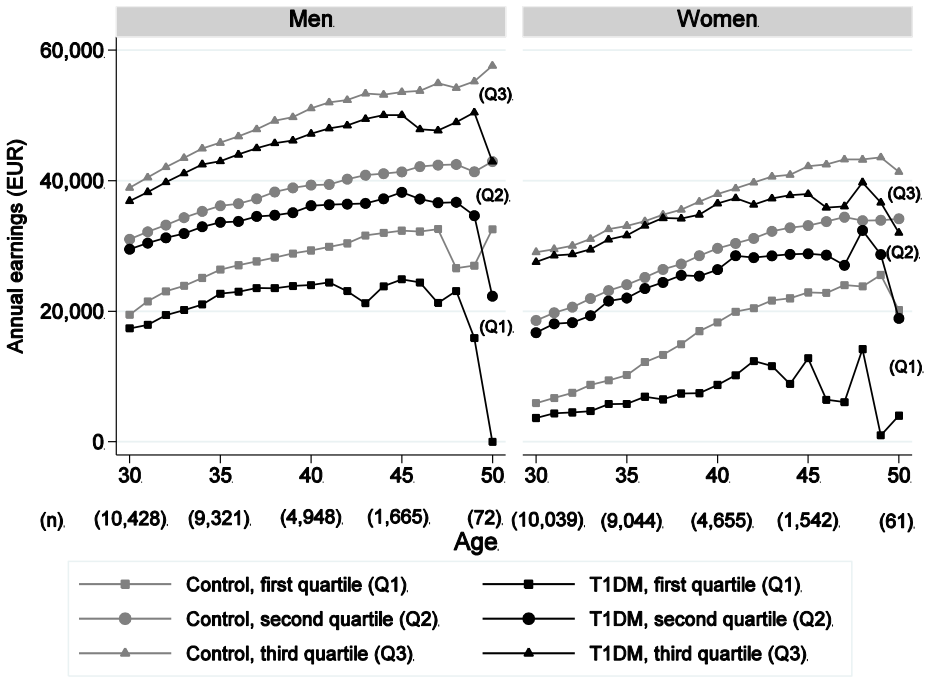

Figure 4: Annual earnings for the type 1 diabetes mellitus (T1DM) group and comparison group (using first, second (median), and third quartiles), from 30 to 50 years of age, deflated into 2013 prices.

Each of the mediators studied contributed to part of the total effect on employment and earnings. The different health indicators together accounted for a large effect on employment and earnings, indicating that a large part of the effect is driven by increased absenteeism, reduced work capacity, and health-related early retirement. Area of occupation was also an important mediator, indicating that part of the effect may be related to choice, as individuals with type 1 diabetes may choose different types of jobs. Yet some of the effect could not be attributed to any of the mediators studied, particularly among men, for whom about 23% of the effect on employment and 40% of the effect on earnings was not explained, and was therefore likely related to other characteristics of the disease that hamper career opportunities.

Discussion

Main findings

This thesis consists of four papers contributing to the medical and economic literature on how the onset of type 1 diabetes before the age of 15, a possible indicator of how a childhood health shock may impact socioeconomic outcomes later in life.

The results show that childhood onset type 1 diabetes impacts several educational aspects, including school grades in compulsory school, at age 16, and upper secondary school, at age 19, as well as the probability of attaining a university education and the total number of years of schooling. The disease also impacts on later labor market outcomes, such as employment and earnings. The size of the effect differs between groups depending on individual characteristics, such as gender and age at diagnosis, but also on duration of the disease and age when investigating the effect.

The analysis of school performance showed similar effects for boys and girls, but a larger effect among children with a very early disease onset (i.e., at 0–4 years old) (Paper I). This is consistent with direct medical effects, such as hypo- and hyperglycemic episodes, which are known to be more harmful and result in permanent damage in early childhood (Dekelbab and Sperling, 2006, Flykanaka-Gantenbein, 2004). Furthermore, children with an early diagnosis have already lived longer with the disease and have had a longer time to accumulate potential disadvantages. The difference in the effect of type 1 diabetes across the grade distribution also suggests that having diabetes may be a greater challenge for children with weaker overall school performance. Despite changes, over the last decades, in the management and treatment of the disease as well as in the educational system, the negative effect of type 1 diabetes on compulsory and upper secondary school grades appears fairly persistent (Paper III). This indicates that continued efforts are needed to improve the situation in school for children with type 1 diabetes.

Men and women were analyzed separately throughout the analysis of labor market outcomes, in line with the standard labor market approach. For women with type 1 diabetes, employment rates and levels of earnings seemed consistently reduced at longer diabetes duration (>15 years). For men, the diabetes effect

appeared somewhat later, but increased more rapidly with disease duration, with a marked decline in both employment and earnings after 25 years of diabetes duration, compared to controls (Paper II). One speculation is that the differences between men and women may be explained by it being more common for women to do part-time work at those ages and also by more compressed wage structures in female-dominated occupations. In 2010, the wage dispersion, measured as the ratio of the 90th percentile to the 10th percentile, was 1.83 for women and 2.23 for men, according to Statistics Sweden (2015). In other words, it may be more difficult to keep pace with, the male comparison group with a higher wage dispersion and a higher percentage of persons in well-paid career positions. The finding that the effect of type 1 diabetes appears in younger ages among women is in line with previous research indicating that female adolescents may be particularly vulnerable and challenged by the psychological distress related to the disease (Forsander et al., 2016).

To be able to reduce the adverse impact of type 1 diabetes on labor market outcomes in the future, an understanding of the mechanisms at play is needed. As the positive relationship between education and labor market status is well known and well documented in the human capital literature (see, e.g., Card (1999), Goldberg and Smith (2007)), it seems natural to assume that the labor market effect of type 1 diabetes may be driven by the negative effect of the disease on education. Nevertheless, the results from mediation analysis show that, although education accounted for part of the effect, other aspects, such as adult health and occupation, appeared to be more profound for the total effect on employment and earnings (Paper IV). Furthermore, conditioning on level of education in the empirical model for earnings increases the goodness of fit measure, but only marginally decreases the estimated effect of type 1 diabetes (Paper II). This further indicates that the greatest part of the effect is related to other characteristics of the disease.

Neither did the type 1 diabetes effect appear to be driven by individual choices or possibilities concerning family formation. Regarding the earnings of women, the lower likelihood of women with diabetes having children rather appeared to reduce part of the negative diabetes effect, probably because not having children may result in more available time for focusing on working and career opportunities. This tendency was not observed in men, for whom family formation accounted for a small part of the negative diabetes effect on employment and earnings, perhaps because men are not physically impacted by pregnancy and child birth to the same extent as women.

The strongest mediator appeared to be adult health, which was indicated by sickness compensation and in- and outpatient care. Health accounted for more than half of the indirect effect of type 1 diabetes on earnings, indicating that a large part of the effect is driven by increased absenteeism and reduced work capacity. However, it may also be related to the need for longer sick leave periods due to non-

diabetes-related illnesses, such as infections and surgery that can affect metabolic control.

Occupation was another strong mediator, which was quantified in the analysis by average monthly earnings of peers in the same occupational area. This finding indicates that the diabetes effect may be related to choice, as individuals with type 1 diabetes appear to choose somewhat different types of jobs from non-diabetics. It could also be related to career constraints, as the risk of hypoglycemia may restrict access to some types of jobs due to safety issues (Diabetesförbundet, 2016d).

Part of the effect of type 1 diabetes could not be attributed to any of the mediators examined. This implies that there are other characteristics of the disease that hamper productivity and stand in the way of career opportunities, which could not to be extracted from our data. A life with type 1 diabetes involves a number of less obvious burdens of self-care not requiring in- or outpatient specialist care or resulting in sick leave longer than 14 days, such as less severe episodes of hypoglycemia or depression (Hassan et al., 2006). Results from the qualitative literature suggest that daily disease management may play an important role as it can be time-consuming and decrease flexibility in daily activities (Sparud-Lundin et al., 2013). Moreover, a recent study suggests that young adults with type 1 diabetes experience difficulties with diabetes management in the workplace because of work-related time pressures and common non-routine work (Balfe et al., 2014). Another study estimates that the average time spent on diabetes-related self-care is close to an hour per day (Safford et al., 2005), with daily care including time spent on self-monitoring of blood glucose and taking insulin as well as on foot care, exercise, and shopping for/preparing food in accordance with diabetes guidelines. Additionally, some studies discuss discrimination against people with diabetes as one potential reason behind the negative labor market effect (Matsushima et al., 1993, Songer et al., 1989), which is another factor that may not be picked up by any of the examined mediators.

Finally, it should be noted that the studies in this thesis contribute to the literature on the effects of health and socioeconomic outcomes by exploring a less studied health indicator of childhood health, with interesting properties from a methodological and empirical perspective. In this broader perspective, the results show an effect running from childhood health to adult labor market outcomes. The magnitude of the effect is, of course, only directly generalizable to illnesses with similar attributes concerning daily management regimens and long-term complications.

Is the effect large enough to be important?

When considering the results of the papers included in this thesis, an obvious question is: How important, in a broader sense, is the negative effect of the disease on educational and labor market outcomes, both for the affected individuals and for society?

We know that the final grade from both compulsory and upper secondary school is important when applying to higher levels of education, and therefore a good final grade is a prerequisite to the ability to choose the preferred upper secondary or university program. Even though the estimated effect of type 1 diabetes may appear small in magnitude, it could still mean the qualitative difference between being admitted to a program of choice in upper secondary school and at university and not being admitted. The strong positive relationship between education and labor market outcomes (Goldberg and Smith, 2007, Card, 1999) also indicates that the educational effect of type 1 diabetes will translate into long-term consequences, involving fewer career opportunities, greater probability of unemployment, and lower earnings. There is also evidence suggesting that more education has a positive impact on diabetic health investments, such as diet, blood glucose control, and smoking (Kahn, 1998). In the long run, this may imply that the negative impact of type 1 diabetes on educational performance could generate negative effects also on adult health. Nevertheless, as mentioned above, other characteristics of type 1 diabetes appear to account for the largest part of the effect on employment and earnings, as indicated in Paper IV.

To understand the broader societal impact of the estimated effect of the disease on earnings, we can use a simple illustrative calculation to approximate the lifetime earnings penalty. If we assume that the impact of type 1 diabetes remains constant as people age (an estimated 6% and 8% lower for women and men, respectively, see Paper IV) and if we further assume average earnings of EUR42,000 and EUR54,500 per year for employed women and men (including social services and taxes of 42.8%, Statistics Sweden (2015)) over a 40-year working life, we can estimate a total working life impact of around EUR101,000 for women and EUR174,000 men. In a societal perspective, this translates to nearly EUR7 billion (EUR4.04 billion if discounting by 3%) assuming that the number of affected persons with type 1 diabetes in Sweden remains around 50,000 individuals (Diabetesförbundet, 2016a). This impact would be even larger if we also included earnings lost due to unemployment.

Main findings in relation to other research

The findings reported in this thesis are generally in line with findings from previous research suggesting that type 1 diabetes is associated with negative consequences

on education and labor market outcomes (Dahlquist and Källén, 2007, Milton et al., 2006, Steen Carlsson et al., 2010, Lovén, 2017, Parent et al., 2009, Wennick et al., 2011). Nonetheless, there are a few studies reporting contrary findings. For example, the results in Paper III are not in line with the results reported by Cooper and colleagues, who investigated school performance in children with type 1 diabetes born 1994–2003 in Australia (Cooper et al., 2014). When studying test scores in compulsory school, they found no impact of type 1 diabetes, except among children with poor glycemic control. They concluded that their results provide reassuring evidence to clinicians and families, that a type 1 diabetes diagnosis during childhood should not be expected to lower school performance (Cooper et al., 2014).

There may be several reasons for this conflicting result. Firstly, the studies were performed in different school and health care settings (in Sweden and Australia). Secondly, the studies used different measures of school performance (final grade from compulsory and upper secondary school vs. test scores from a standardized school achievement test administered in years 3, 5, 7, and 9 of school). Thirdly, the studies assessed school performance among children of different ages (children aged 16 and 19 years completing compulsory and upper secondary school, vs. children aged 7–14 years when the standardized test was administered). Therefore, the children in the Australian study were still young, had had shorter disease duration on average, and had had less time to accumulate effects of the disease.

Furthermore, results from the resent Danish study by Nielsen et al. (2016) shows that, while individuals with type 1 diabetes are more frequently unemployed and have more sick leave, they are slightly better educated compared to the general public. This is a result that is not supported by any of the analysis within this thesis.

Finally, the results in Papers II and IV are not entirely in line with the results of Minor (2011) and Minor (2013). In these studies, no statistically significant effect of type 1 diabetes on labor market outcomes was found and the author concluded that the effect of diabetes appears to be driven by type 2 rather than by type 1 diabetes. This conflicting result could be due to limitations in sample size. Although these studies in total are based on a fairly large survey dataset, the analyses of type 1 diabetes specifically are based on relatively small samples of individuals (about 60 and 355 individuals with type 1 diabetes, respectively, in the two studies). These individuals were defined as having type 1 diabetes if they had reported onset of diabetes before the age of 20 years. Thus, there may also be concerns about measurement errors in the separate analysis of type 1 diabetes, due to the fact that the onset of type 1 diabetes can occur also in adulthood (Dahlquist et al., 2011) and type 2 diabetes may occur also among children and adolescents (Wilmot and Idris, 2014).

Methodological considerations

Strengths and limitations

A major strength of this thesis is the use of diabetes registry data covering nearly all cases of type 1 diabetes in Sweden, together with national population registers from Statistics Sweden. To be enrolled in the SCDR during the years that these studies focus on (1977–1994), type 1 diabetes must be physician-diagnosed. This should reduce the risk of mix up with other types of diabetes, which is a common concern in many other diabetes studies. Furthermore, the socioeconomic data in the Swedish national registers is reported by employers and educational institutions, which should decrease the risk of measurement error and selection bias compared to self-reported survey data. Together, these data sources should therefore ensure a high level of representativeness within the Swedish setting.

The linkage of data from several other registers also allowed the analysis to account for a large set of demographic and socioeconomic background factors, as well as perinatal events factors, to rule out confounding bias due to them. However, throughout the analyses in this thesis, the effects of type 1 diabetes on the different outcomes studied remained robust to changes in model specification and also to sample size. This supports the idea of considering the onset of type 1 diabetes to be related to an exogenous source of variation in childhood health. The use of alternative estimation strategies, linear regression, and PSM in Paper III also enabled us to assess the robustness of the diabetes effect on educational performance. The two methods generated similar results and the magnitude of the effects differed only marginally, further indicating that the potential confounding factors are unlikely to strongly influence the estimated effect of type 1 diabetes on socioeconomic factors. Furthermore, the longitudinal nature of the data allowed us to follow the study sample during a large period of their life, with the earliest outcomes measured at the age of 16 and the latest at the age of 50. To the best of our knowledge, this is the longest perspective of socioeconomic consequences of type 1 diabetes in the literature to date.

Some general limitations should, however, be noted. First, since 1977, the SCDR has registered individuals diagnosed with type 1 diabetes before the age of 15. Consequently, data on individuals born before 1977 did include individuals diagnosed at the youngest ages. For example, data on individuals born in 1970 incudes those diagnosed at the age of 7 to <15 years. This limits the representativeness of the analysis of the earliest cohorts as they did not include the total type 1 diabetes population.

Another concern is that there could be bias due to attrition in the studied panels. However, examining the number of observations each year in the data suggests that the representation of individuals with diabetes and controls is fairly similar

throughout the time periods studied. It is also important to note that, although the quality of the registers used for these analyses is generally considered to be high (Cnattingius et al., 1990, Ludvigsson et al., 2016, Ludvigsson et al., 2009), there is always a concern about measurement errors and missing data.

Generalizability

An important aspect to discuss is the generalizability of the findings in this thesis and the external validity, i.e., the extent to which the results can be generalized to other situations and study populations. All studies in this thesis are based on observational register data, covering nearly all individuals with type 1 diabetes in Sweden diagnosed since 1977, which should ensure a high level of generalizability within the Swedish setting. The findings are, however, likely contextual and it is not clear to what extent the results may be applied to other countries. Firstly, the results of the thesis may not be generalizable outside the Swedish health care system. Health care in Sweden is mainly government-funded and highly decentralized, with a low level of direct costs to the patients. For people with diabetes, the total cost of insulin has been government-funded since 1955 (Diabetesförbundet, 2014). Consequently, the financial burden of the disease to the patients may be larger in countries that do not reimburse treatment costs to the same extent as Sweden. In a recent systematic review of the costs of type 2 diabetes, Seuring, Archangelidi et al., 2015 found that diabetes generates a large economic burden that most directly affects patients in low and middle income countries. Based on this finding, the socioeconomic consequences of type 1 diabetes may be larger in countries where a greater part of the health care costs fall on the patient. Furthermore, Sweden is a country with free access to higher education, a factor that may further limit the generalizability of the results to countries with different educational systems. Nonetheless, the generalizability to other Nordic countries should be reasonably high, as their health care and educational financial systems are fairly similar to the one in Sweden. All Nordic countries have a tax-funded public health service which covers all citizens with access to health care, and includes partial or complete reimbursement of pharmaceuticals (Furu et al., 2010).

In a broader perspective, it is interesting to consider how generalizable the findings of this thesis are to other diseases and in comparison to other health indicators. In this thesis, it is argued that the onset of type 1 diabetes in childhood serves as a well-documented health indicator that provides a clearly identified shift in health. This health shock is associated with well-described risks, acute and long-term health complications, and need for daily disease management that can be time-consuming and restrictive (Sparud-Lundin et al., 2013). Although the magnitude of the effect is, for obvious reasons, directly generalizable only to illnesses with similar attributes, the results from these analyses still provide evidence suggesting that

causality in the often observed correlation between health and socioeconomic status is explained, at least in part, by an effect running from health to earnings.

Policy implications

A number of policy implications can be drawn from the findings of this thesis. Firstly, the findings support further collaborations between families, clinicians, and teachers to identify and assist particularly vulnerable children and teenagers. Secondly, the results suggest that further improving the treatment of diabetes to prevent or delay diabetes-related complications may benefit not only the affected individuals and their families, but also the entire society in terms of decreased productivity loss in the labor market. Thirdly, the results clearly reveal a causal link from childhood health to adult labor market outcomes, which indicates that health-improving interventions for children can result in long-lasting socioeconomic benefits.

Further research

This thesis provides evidence of how the onset of type 1 diabetes during childhood impacts on socioeconomic factors later in life. During work on the included studies (Papers I–IV), a few knowledge gaps were identified. One interesting research question would be to explore the effect of type 1 diabetes on labor market outcomes in an even longer perspective, including the entire labor market period to the age of 65. Such a long-term perspective would further reveal the effect of long-term complications and factors impacting the decision of when to retire from work. Additionally, much work remains to be done on the impact of type 1 diabetes in other settings and using large study populations.

Further research should also explore how poor metabolic control impacts socioeconomic status, as it may be that individuals with poor metabolic control drive the findings in this thesis. For example, Cooper et al. (2014) found no effect of type 1 diabetes on test scores in compulsory school except among children with poor metabolic control. The causal relationship between metabolic control and socioeconomic status is likely very complex as both these factors may impact each other. There is a large literature examining the impact of socioeconomic status on metabolic control, as well as the on short- and long-term diabetes related complications (see e.g. Tao et al. (2016), Gallegos-Macias et al. (2003), Chaturvedi et al. (1996), Secrest et al. (2011)), but less research focus on how poor metabolic control may impact socioeconomic status.

As the analyses included in this thesis are based on incidence register data, no records on metabolic factors, e.g., glycated hemoglobin (HbA1c) level, or specific treatment strategies were available. In further research, information from the Swedish national quality registers for diabetes, such as the Swedish National Diabetes Register (The Swedish National Diabetes Register, 2017) initiated in 1996 or SWEDIABKIDS for childhood diabetes (SWEDIABKIDS, 2013) initiated in 2000, could be used to investigate the role of clinical factors and perhaps also specific treatment strategies for the long-term socioeconomic consequences of type 1 diabetes.

Conclusions

The findings from this thesis show how the onset of type 1 diabetes before the age of 15 impacts on socioeconomic outcomes later in life. In a broader perspective, the results provide insights into how a distinct and definable shift in child health, with well-described risks of medical complications and the need for daily disease management, may translate into working life consequences. The main conclusions from this thesis are:

- The onset of type 1 diabetes in childhood negatively affects educational achievements, in both compulsory schooling and upper secondary school, as well as the final level of education.

- While access to new treatment technologies and improved diabetes management strategies may have reduced the burden of diabetes in daily life, continued efforts are still needed to improve the situation in school for children with type 1 diabetes.

- In a longer perspective, the onset of type 1 diabetes during childhood negatively affects employment and earnings for both women and men. The magnitude of the effect, however, depends on individual characteristics, such as gender, age at diagnosis, and disease duration.

- A large part of the labor market effect of type 1 diabetes is attributed to adult health, but there are also other important mediating factors, such as choice of occupation, and education, that need to be considered to reduce this negative effect in the future.

- Causality in the often observed correlation between health and socioeconomic status can, at least in part, be explained by an effect running from health to earnings.

Acknowledgement

I would like to express my warmest gratitude to all the people around me that in different ways have helped, encouraged and inspired me throughout my work with this thesis. Because of you, I look back on my PhD years as a positive and exciting experience.

First, I would like to thank Ulf-G Gerdtham, my main supervisor, for your guidance through this research process and for sharing your deep knowledge and ideas with me. Thank you for your positive and encouraging attitude at all stages.

I would also like to thank Katarina Steen Carlsson, my co-supervisor, for inspiring and guiding me throughout this work. Especially, I would like to thank you for believing in me and encouraging me to start this PhD project. I am grateful for all your support and positive attitude and thank you for sharing your great knowledge in health economics and diabetes with me.

Many thanks also to Gisela Dahlquist, my co-supervisor, for all your valuable advice and feedback from the medical perspective that have greatly benefitted this work.

Many thanks to the Swedish Childhood Diabetes Study Group for valuable feedback and discussions at the semiannual workshops. Particularly, I would like to thank Emma Persson, co-author of my third Paper, for a great collaboration when writing this paper and many nice discussions over Skype.

I would also like to thank my friends and colleagues at Lund University; Aliasghar Ahmad Kiadaliri, Sanjib Saha, Gawain Heckley, Johan Jarl, Sixten Borg, Ida Lovén, Ye Zhang. Thank you all for making my PhD years a great part of my life and for filling it with so much more than just research.

Many thanks to my colleagues at the Swedish Institute for Health Economics (IHE) for being a positive and inspiring source of support.

To my friends and family, thank you for all your love and support. I am especially grateful to my parents, my father Ulf Persson for encouraging and inspiring me to follow in his footsteps into the field of health economics, and my mother Sylvie Munther for endless love and for always believing in me.

Finally, I like to thank Ralle, my love and best friend, for being there for me every day, no matter what, and to Cornelia, my daughter, for making every day full of joy and for putting all of this into perspective.

Lund, April 2017

Sofie Persson

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Printed by Media-Tryck, Lund 2017 NORDIC ECOLABEL, 3041 0903

LUND UNIVERSITY
Faculty of Medicine

Health Economic Unit

Lund University, Faculty of Medicine
Doctoral Dissertation Series 2017:95
ISBN 978-91-7619-475-1
ISSN 1652-8220