

# Health Related Quality of Life among Norwegian children and adolescents with Type 1 diabetes at the Paediatric Department at Oslo University Hospital



Fanni Lundgren

Student thesis at the Faculty of Medicine, University of Oslo, Norway

February 2017

Supervisor

Torild Skrivarhaug, MD PhD, Department of Paediatrics, Oslo University Hospital

## Table of contents

Abstract .....	3
Acknowledgement.....	4
Abbreviations .....	5
List of figures, tables and appendices .....	6
Introduction .....	7
Diabetes Mellitus .....	7
Type 1 diabetes	
Epidemiology .....	8
Aetiology and pathogenesis.....	8
Complications.....	9
Microvascular complications.....	9
Macrovascular complications .....	10
Mortality .....	11
Treatment.....	12
Psychosocial aspects of living with type 1 diabetes .....	13
Health Related Quality of Life .....	14
Aims and objectives .....	15
Subjects and methods .....	15
Design .....	15
Subjects.....	15
Instrument.....	18
Statistical analysis.....	19
Ethical considerations.....	20
Results .....	21
Chronic Generic Module (DCGM-37) .....	23
Diabetes Specific Module (DDM-10) .....	24
Discussion .....	29
Conclusion.....	31
Conflicts of interest .....	32
Reference list.....	32
Appendix .....	38

## **Abstract**

### ***Background***

Living with type 1 diabetes (T1D) is challenging. Not only because of the somatic manifestations, but also because of the psychosocial challenges represented by the disease itself, its management and treatment. In the last decades there has been an increasing focus on the impact health status has on the Quality of Life (QOL). By screening for Health Related Quality of Life (HRQOL) one wishes to identify unmet health requirements and optimize quality of care.

### ***Aims and objectives***

The aim of this study was to assess HRQOL in a selected Norwegian paediatric diabetic population in relation to different clinical and sociodemographic variables and to look at continuity between self- and proxy reports.

### ***Subjects and methods***

All children and adolescents with T1D, age ten years and older ( $n = 148$ ), and all parents of children with T1D, disregarding the age of their children ( $n = 206$ ), at the Paediatric Department of Oslo University Hospital, were invited to complete the DISABKIDS Chronic Generic Module 37 (DCGM-37) and the DISABKIDS diabetes specific module (DDM-10) questionnaires describing HRQOL. HRQOL was subsequently related to different clinical and sociodemographic factors obtained from the Norwegian Childhood Diabetes Registry (NCDR).

### ***Results***

74 (36%) of the parents and 59 (40%) of the children answered. HRQOL was significantly associated with poor metabolic control, but not with gender, episodes of acute complications or age of the patient. Treatment modality (insulin pen) was associated with a lower HRQOL score for one DCGM-37 subscale. Although parents tended to score a lower HRQOL than their children, the only significant difference between the self-and proxy reports was regarding boys in the DCGM-37 subscale social inclusion, where parents reported a lower score.

### ***Conclusion***

HRQOL was related to metabolic control, but not to gender, occurrence of acute complications or age. Furthermore, parents tended to give a quite accurate assessment of their children's HRQOL.

## **Acknowledgement**

This student thesis was carried out between January 2015 and February 2018, while I was a student at Oslo University Hospital (OUS).

I want to thank my supervisor Torild Skrivarhaug for her help and support in writing my thesis. For offering her time and guidance by reading through my drafts and providing me with feedback. Furthermore, I would like to thank statistician Ann Kristin Drivvoll in NCDR for helping me analyse the data necessary for my study.

I would also like to thank the people responsible for developing and validating the questionnaires, providing me with a clinical tool for my thesis.

### Abbreviations

ACR	Albumin/creatinine ratio
AER	Albumin excretion rate
BG	Blood glucose
CGM	Continuous Glucose Monitor
CVD	Cardiovascular disease
DCCT	Diabetes Control and Complications Trial
DCGM-37	DISABKIDS Chronic Generic Module 37
DDM-10	DISABKIDS Diabetes Specific Module 10
DM	Diabetes mellitus
DME	Diabetic macular oedema
DKA	Diabetic ketoacidosis
DR	Diabetic retinopathy
EDIC	Epidemiology of Diabetes Interventions and Complications Study
ESRD	End-stage renal disease
GFR	Glomerular filtration rate
HbA1c	Glycosylated haemoglobin
HLA	Human Leukocyte Antigen
HRQOL	Health Related Quality of Life
HT	Hypertension
ISPAD	International Society of Paediatric and Adolescent Diabetes
MDI	Multiple daily injections
MODY	Maturity onset diabetes of the young
NCDR	Norwegian Childhood Diabetes Registry
NPDR	Non-proliferative diabetic retinopathy
PYR	Person years
PROM	Patient reported outcome measure
QOL	Quality of Life
SMBG	Self-monitoring of blood glucose
SMR	Standardized Mortality Ratio
T1D	Type 1 diabetes
T2D	Type 2 diabetes
WHO	World Health Organization

## **List of figures, tables and appendices**

*Figure 1a.* Flow chart showing the study design for the self-report cohort (p. 16)

*Figure 1b.* Flow chart showing the study design for the proxy report cohort (p. 17)

*Figure 2.* Structure of the questionnaires DCGM-37 and DDM-10 (p. 18)

*Figure 3.* Explanation of domains of DCGM-37 and DDM-10 (p. 20)

*Table 1a.* Clinical characteristics of participants and non-participants, self-reports (p. 22)

*Table 1b.* Clinical characteristics of participants and non-participants, proxy reports (p. 23)

*Table 2.* Comparison between reported HRQOL in self- and proxy reports (p. 25)

*Table 3.* Comparison between genders and reported HRQOL in self- and proxy reports (p. 26)

*Table 4.* Effects of different clinical and sociodemographic variables on self-reported HRQOL (p. 27)

*Appendix 1.* DISABKIDS Chronic Generic Module 37 (DCGM-37), self-report (p. 38)

*Appendix 2.* DISABKIDS Diabetes Specific Module (DDM-10), self-report (p. 39)

*Appendix 3.* DISABKIDS Chronic Generic Module 37 (DCGM-37), proxy report (p. 40)

*Appendix 4.* DISABKIDS Diabetes Specific Module (DDM-10), proxy report (p. 41)

## Introduction

Accepting diabetes can be difficult. Living with knowledge of possible complications, having to regulate everyday life, to carry equipment and to follow the restrictions provided by disease and treatment requires a great deal of self-control and personal strength. Considering the huge psychosocial demands diabetes puts on each individual it is no surprise that psychosocial variables are considered the most important factors affecting its management and care. Monitoring for Health Related Quality of Life (HRQOL) can therefore help identify these psychosocial factors and help steer treatment and management in the right direction.

### *Diabetes Mellitus*

Diabetes mellitus (DM) is not a single disease entity but rather a group of metabolic disorders characterized by hyperglycaemia. The hyperglycaemia results from defects in insulin secretion, insulin action, or most commonly both (1). Classically we divide DM into two main types, type 1 diabetes (T1D) and type 2 diabetes (T2D), based on their pathogenesis. It is important to distinguish the two, as they require different management and treatment regimes. T1D is an autoimmune disease where the hyperglycaemia is due to an absolute insulin deficiency, caused by a selective destruction of the insulin producing  $\beta$ -cells in the pancreas. Most commonly, it becomes clinically evident in childhood and adolescence presenting with symptoms such as polydipsia, polyuria, weight loss and ketonemia (2). T2D is the most common form of diabetes, and may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with or without insulin resistance (3). T2D used to be considered as a disease of middle aged and older generations, however lately there has been seen an increase amongst children and adolescents. Both genetic and lifestyle factors are involved in the pathogenesis. T1D accounts for about 5 to 10% of all diabetic cases in United States, Canada and Europe, and T2D for approximately 90%(4). However, in children under 19 years-of-age T1D makes up two thirds of the affected diabetic cases (2). In Norway, T1D constitutes about 98% of all diabetic cases in children and adolescents under the age of 15 years (5). There are also several other diabetes subtypes associated with monogenic defects of  $\beta$ -cell function, so called monogenic diabetes, formerly referred to as maturity-onset diabetes of the young (MODY). Diabetes mellitus may also occur secondarily

to other conditions, such as cystic fibrosis, pancreatitis and pancreatic cancer (6). Although the major types of diabetes arise by different pathogenic mechanisms, the long-term complications in kidneys, eyes, nerves, and blood vessels are the same, and constitute the principal causes of morbidity and death in all patients with DM (1).

### *Epidemiology*

T1D is a common chronic life-long disease usually presenting in childhood. The incidence varies a lot between countries and continents. In Europe, the risk appears to rise as the geographical latitude (distance from the equator) increases (2, 7), hence, incidence rates are low in the southern, central, and eastern countries and high in northern and north-western countries. There are however some countries that are exceptions to this rule. An example of this are the islands Sardinia and Sicilia, that despite the southern latitude have a high incidences of T1D (8). Norway is a high incidence country. According to the Norwegian Childhood Diabetes Registry (NCDR) annual rapport from 2015, the incidence of T1D is 36.5 cases per 100 000-person years (PYR) in the age group 0-14 years (5). This is an increase from earlier years (6). In addition to geographical variations of incidence, there are also variations between age of onset and gender. T1D may occur at any age, but has a characteristic peak in incidence in early puberty (2, 9, 10) . In Norway there is a larger incidence amongst boys compared with girls, in 2015 presenting with an incidence of 38.8 per 100 000 PYR and 34.1 per 100 000 PYR, respectively (5).

### *Aetiology and pathogenesis*

T1D is a chronic autoimmune disease characterized by a decline in pancreatic  $\beta$ -cell function. The aetiology of the disease, although not completely understood is thought to be a combination of genetically susceptible individuals being exposed to environmental risk factors. In most cases, the serological markers present in the patients' blood can prove the autoimmunity. The genetic predisposition is connected with polymorphism of multiple genes (11-14). The most important genes contributing to the disease has been linked to certain human leukocyte antigens (HLA) types (11, 15). However, of the genetically predisposed only about 10 % develop the disease. This implies that there must be other factors



contributing to the occurrence of the disease in the predisposed individuals. Environmental factors have been implicated in the pathogenesis of T1D, both as triggers and catalysts of  $\beta$ -cell destruction. However, the exact nature of these triggers remains unknown. T1D becomes clinically symptomatic when approximately 10% of pancreatic  $\beta$ -cell insulin production remains (16). This implies that the disease process starts before the clinical manifestation (17). In most cases the disease becomes clinically evident with onset of polydipsia, polyuria, and weight loss with hyperglycemia and ketonemia/ketonuria (2), but suddenly presenting diabetic ketoacidosis (DKA) may be the first clinical symptom, and can lead to coma and death if left untreated.

### *Complications*

There are several complications associated with T1D (18). These complications can be divided into acute and long-term complications. The acute complications can be due to the hyperglycaemia produced by the disease, or the hypoglycaemia caused by the treatment. The lack of insulin, and subsequent hyperglycaemia, can cause DKA and following coma, while hypoglycaemia can lead to states of confusion and unconsciousness. The long-term complications are caused by the chronically maintained hyperglycaemia, which cause damage to small and large vessels, resulting in micro- and macrovascular complications (19-23). Both acute and long-term complications contribute to the increased morbidity and mortality amongst the patients with T1D (18, 24, 25).

### *Microvascular complications*

The microvascular complications primarily affect the eyes, the kidneys and the peripheral and autonomic nervous system, causing diabetic retinopathy, nephropathy and neuropathy (18).

The ocular complications of diabetes include diabetic retinopathy (DR), diabetic macular oedema (DME), cataracts and glaucoma. DR and DME being the most important affecting the diabetic population. DR is today a leading cause of blindness and visual impairment amongst people of working age worldwide (26). It can be divided into non-proliferative retinopathy (NPDR), which can be subdivided into groups after its severity, and proliferative retinopathy (PDR) (18). The vision threatening retinopathies are caused by severe NPDR and PDR.

NPDR, depending on the degree or severity of the disease, is characterized by a combination of microaneurysms, haemorrhage, deposition of exudates and microinfarctions. PDR causes, in addition, neovascularization in the retina and/or posterior vitreous surface (18). While PDR is the most important cause of severe visual loss in patients with DM, the majority of moderate visual loss is caused by DME (26). However, DME is very uncommon in children and adolescents with T1D (18, 27).

Diabetic nephropathy is today a major cause of morbidity and mortality amongst patients with T1D, causing hypertension, a diminishing glomerular filtration rate and ultimately, if left untreated, end stage renal disease (ESRD) (21, 28). The disease usually presents with increased albumin excretion rates (AER), defined as any one of the following: AER between 20-200  $\mu\text{g}/\text{min}$ , AER between 30-300  $\text{mg}/24\text{h}$  in 24 h or timed urine collections, albumin concentration 30-300  $\text{mg}/\text{L}$  or an albumin/creatinine ratio (ACR) of 2,5-25  $\text{mg}/\text{mmol}$  in males and 3,5-25  $\text{mg}/\text{mmol}$  in females, in the first morning urine sample (18, 28). The microalbuminuria can progress to albuminuria  $>300 \text{ mg}/24\text{h}$ , or regress to normo-albuminuria. This can be spontaneous or related to treatment (29-32).

Diabetic neuropathy can affect both the somatic and the autonomic nervous system. Somatic neuropathy can be: focal/multifocal and generalized (19). The first group comprises the mononeuropathies, and the second, the more “classical” generalized polyneuropathies. The neuropathies affect the peripheral motor- and sensory and autonomic nerve fibres (18). The sensorimotor affection can cause loss of sensory and motor function, especially in the feet, resulting in pain, muscle weakness and paraesthesia (18). The autonomic affection can cause disturbances in bowel, bladder, heart and sometimes sexual function. Clinically evident autonomic dysfunction is uncommon in children and adolescents, however subclinical findings of affected heart rate have been reported in these populations (18, 33).

### *Macrovascular complications*

There is an increased mortality and morbidity of cardiovascular disease (CVD) in patients with diabetes (18, 20, 24, 34). Having T1D predisposes the individual to accelerated atherosclerosis, which causes damage to the vessels in the body, making them susceptible to disease entities associated with atherosclerosis (e.g. CVD) (1). The progression of the atherosclerosis is associated with poor glycaemic control (18). CVD is associated with several

risk-factors such as smoking, hypertension, dyslipoproteinemia and high body mass index (BMI) (18). There has been found an abundance of these risk factors in children and adolescents with T1D (35). Furthermore, the risk factors and the diabetes seem to potentiate each other increasing the morbidity and mortality from CVD.

In recent years there has been observed a decline in the prevalence of complications. This has been related to improvements in screening, identification and management of diabetes and diabetes long-term complications. The decline has been especially evident amongst the young, and relating to development of retinopathy and nephropathy (36, 37). However, it should be taken into consideration that this progression has only been observed in the richer parts of the world, where specialized clinics and more optimal treatment regimens are available.

### *Mortality*

Individuals with T1D has a higher mortality rate than the general population, related to both acute and long-term complications of their disease (34, 38-42). Mortality varies considerably between countries, and the relative mortality seems to be lower in the high-incidence countries compared with the low-incidence countries (43-45). In low-income and lower middle-income countries the main cause of death in the diabetic population is lack of insulin (46), while in the developed world the main cause of mortality is due to CVD and renal disease (47). There exists a divide in mortality between those under the age of 30 years, and those over, in the developed world. Amongst the young the main cause of mortality is acute complications, while after the age of 30 years it is the long-term complications (48, 49). Also, in Norway having T1D is associated with an increased mortality rate (34). A nationwide, population-based cohort in Norway following childhood-onset diabetes (diagnosed < 15 years) showed that the mortality in the diabetic population was as 3.6 times higher than in the general population (24, 34). The same study showed that the main cause of diabetes-related deaths in Norway was acute complications (with two-thirds of the cases being attributable to DKA and one third to hypoglycaemia), unlike in the rest of the developed world, where the main cause of mortality is due to long-term complications (24). Differences in mortality was also observed to be related to age and sex. While acute complications were the main reason for death under the age of 30 years, CVD was the leading cause after the age of 30 years (24). Men had an elevated risk for death compared with women in absolute mortality (2.44/1,000

vs 1.22/1,000; rate ratio 2.00; 95% CI 1.52, 2.61;  $p < 0.001$ ). However, looking at a standardized mortality ratio (SMR), mortality was approximately similar for the two sexes (3.5 for men and 3.8 for women), reflecting an increased mortality for men in the general population as well (24). Furthermore, the study observed that, despite the improved treatment regimens we have today, the mortality from the acute complications remain the same (35). This may indicate the need for increased focus on diabetes education and the psychosocial aspects of the disease in order to lower mortality rates.

### *Treatment*

In patients with T1D insulin is required to stay alive and to manage blood glucose (BG). The aim for treatment is a BG as close to normal as possible, avoiding hypoglycaemia, hyperglycaemia and large fluctuations (50). There are several ways of achieving this goal. The most important being self-monitoring of blood glucose (SMBG) and/or using a continuous glucose monitor (CGM). SMBG and/or CGM are the recommended ways to determine immediate and daily level of BG, and to help assess daily basal and bolus requirements of insulin. In addition to daily monitoring, periodic monitoring of overall glycaemia should be performed, this can be achieved by measuring the HbA1c level. The level of HbA1c works as a predictor for both long-term micro- and macrovascular complications (25, 51). Better metabolic control, represented by lower HbA1c is associated with fewer and delayed complications (25, 51-53). HbA1c is a result of glucose irreversibly attaching to the haemoglobin molecule in a process called glycosylation. The level of glycosylation reflects the BG level over the last 4-12 weeks, weighted towards the last 4 weeks, with the exception of the week prior to the testing when the glycosylation is reversible (54). The importance of a near normal HbA1c was largely determined as a result of The Diabetes Control and complications Trial (DCCT), conducted in North America between 1983 and 1993. The DCCT trial randomized people into two groups, one receiving conventional therapy and one receiving more intensive therapy, achieving a significantly lower HbA1c. The results from the DCCT trial showed a significantly lower risk for microvascular complications in the group receiving intensive treatment (25). The Epidemiology of Diabetes Interventions and Complications (EDIC) Study continued to follow these patient groups after the end of the DCCT trial (53). After 4 years the EDIC Study measured no difference in HbA1c level between the two groups. Despite this, significant

benefits of intensive treatment were documented, including reduction in macrovascular complications, suggesting a memory effect of the treatment (55). The results from the DCCT/EDIC Study proved the favourable effects of intensive therapy on diabetes related complications (25, 53). Today the treatment goal for T1D is BG concentrations as close to normal as possible without hypoglycaemia, concretized as an HbA1c level  $< 7, 5\%$  for all patients under 18 years of age (50). In addition to monitoring of BG, regular visits to specialists for assessment of possible complications should be performed (18). Treatment goals entailing medical outcomes alone is however not enough. In fact, management of the psychosocial aspects of the disease have been advocated as the most important measure for achieving optimal treatment and treatment adherence (56). Psychosocial and behavioural interventions are therefore needed to address the psychosocial issues provided by the disease and treatment, and for providing youth and children with the tools necessary to cope with the challenges they face. This can be done on an individual level or group level. Targeting stress management and coping skills have shown to reduce diabetes related stress (57, 58), increase glucose monitoring and metabolic control (59) and improve social interactions (60). The disease does, however, not solely affect the patient, but their relatives as well. In fact, family dynamics have become a pivotal factor in diabetes treatment and care. Worse glycaemic control and regimen adherence has been observed in families with increased conflict, especially if related to treatment (61, 62). Furthermore, parental support and education has shown a positive effect on treatment outcome and adherence (63, 64). All this promoting the application of psycho-educational interventions on both patient and family. In order to cover every aspect of diabetes management, all diabetes teams should, in addition to health-care personnel attending to the disease, include specialists in areas concerning mental and psychosocial health. The contact between the diabetes team and the patient and their family should be uninterrupted, constant and regular, as patients with irregular follow up has been proved to have worse glycaemic control, and increased frequency of both acute and long-term complications (65, 66).

### *Psychosocial aspects of living with type 1 diabetes*

There is widespread consensus around the fact that T1D represents a major challenge in the day-to-day life of both patients and their families. In part, due to the impact of the disease and in part, because of the personal restraint and patience needed for the disease treatment and

management. The psychosocial effects of T1D are diverse and many, affecting amongst others psychosocial wellbeing, intellectual development, family dynamics and HRQOL. In my study, the focus was on how the disease affected the Quality of Life (QOL) of children and adolescents with T1D.

Young people with T1D have an increased occurrence of psychosocial issues and psychiatric disease compared to their healthy peers (56, 67). This includes an increased occurrence of depression, anxiety and eating disorders (67-69). All disorders have been associated with poor metabolic control and lacking treatment adherence (70-72).

Furthermore, children and adolescents with diabetes appear to have an increased risk for learning difficulties (73-75). Having T1D has been associated with reduced ability for acquisition of new knowledge, information processing weakness, and decreased memory and learning capacity (75, 76). This have been connected to early debut of the disease, severe hypoglycaemia and chronic hyperglycaemia (73, 74, 77-79).

The disease does, however, not only affect the children, but their parents and siblings as well. Studies show that parents, like their offspring, can experience psychological distress and anxiety after their child have become diagnosed with T1D (80, 81). Providing support for parents is therefore of great importance. Especially considering the beneficial effects of parental support and co-operation on treatment outcome and adherence (82, 83).

Despite, the somatic and psychosocial complications, patients with T1D tend to report a HRQOL similar to their healthy peers (84). However, there are internal variations within the diabetic population. Boys, in general, report a better HRQOL than girls (85-89), as do people of younger age (90, 91), good metabolic control (85, 92) and better socioeconomic status (93). Parents tend to score lower HRQOL than their kids themselves do (88, 94), and mothers give lower scores than the fathers (85). Achieving a good HRQOL for everyone within the group is a goal in itself (9), but it is also important in order to achieve other treatment goals (10-13).

### *Health Related Quality of Life*

Highlighting psychosocial support of children and adolescents is important in order to reach treatment recommendations, and screening for HRQOL has been promoted as an important complementary outcome to clinical and laboratory markers (56). HRQOL is a concept that refers to the individual perception of the effect health status has on the domains of Quality of

Life (i.e., physical, mental, emotional and social functioning). This multidimensional concept is applicable to any condition affecting health status, including T1D. Furthermore, there has been reported positive correlation between high self-perceived HRQOL and people's ability to manage their treatment and achieve treatment goals (95, 96). The opposite has also been hypothesized, predicting reduced treatment adherence, poor glycaemic control and adverse psychological effects in people reporting low HRQOL score (96). Screening and monitoring of HRQOL should therefore be integrated into clinical practice, for early detection of individuals at risk. There has been developed several HRQOL score sheets to evaluate patients with T1D. Amongst these are the DISABKIDS screening tools used in my study (97).

### **Aims and objectives**

The aim of this study was to assess HRQOL in a selected population-based child and adolescent cohort with T1D and to determine the clinical and sociodemographic influences. Furthermore, to look at consistency between the self- and proxy reports.

### **Subjects and methods**

#### *Design*

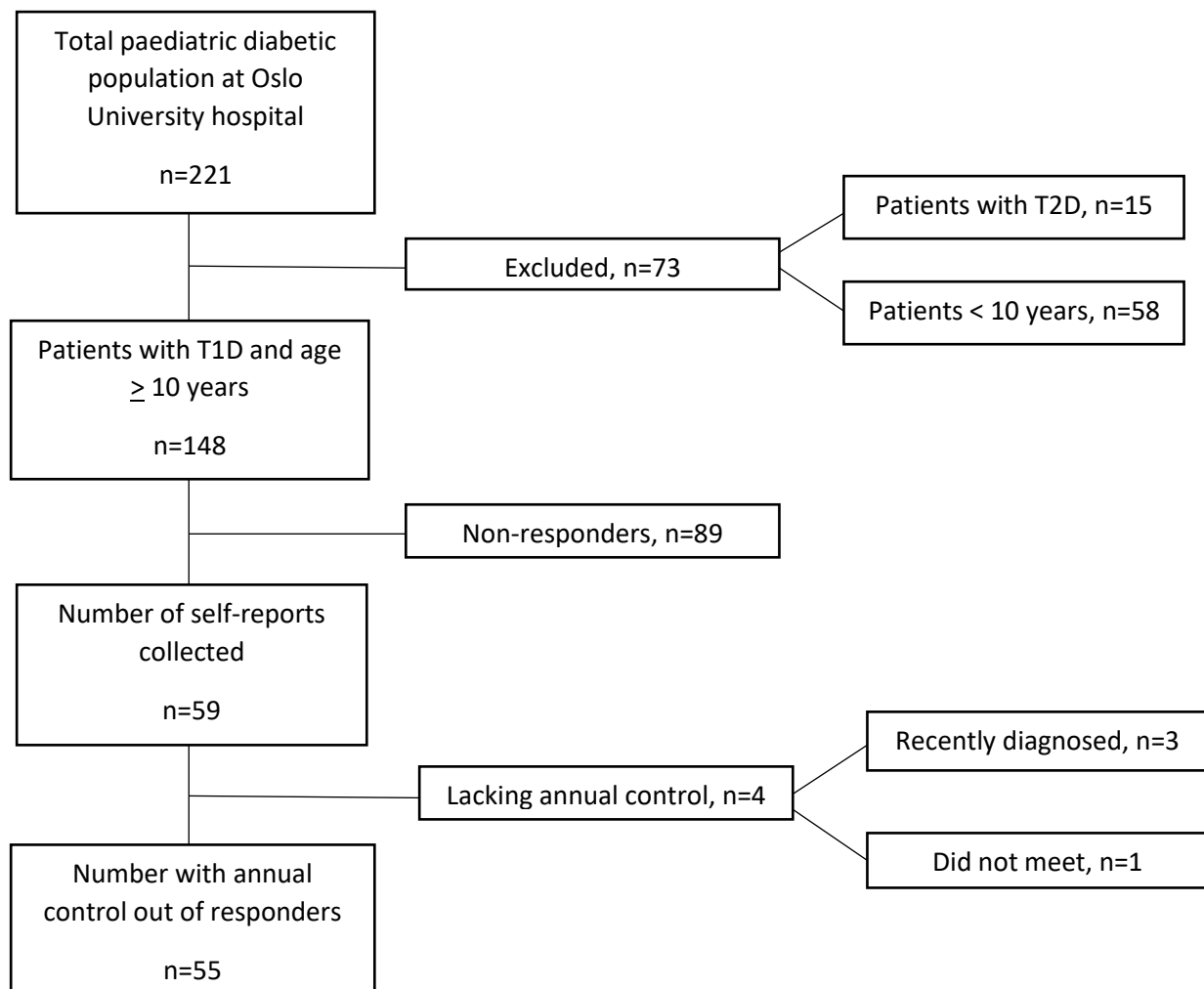
The study was a cross-sectional, descriptive study using self-reports and parent's proxy reports from the Paediatric Department at Oslo University Hospital, Ullevål, Oslo, Norway.

#### *Subjects*

The data was collected from 1<sup>st</sup> January 2015 to 31<sup>st</sup> December 2015. The Paediatric Department at the University Hospital of Oslo, had a total of 221 diabetic patients. Out of these 206 have T1D (98), and 148 had an age of ten years and older (Figure 1a and 1b). All children and adolescents with T1D, aged 10 years and older, and parents of all children (0-18 years) with T1D, visiting the outpatient clinic at OUS, were asked to participate in the

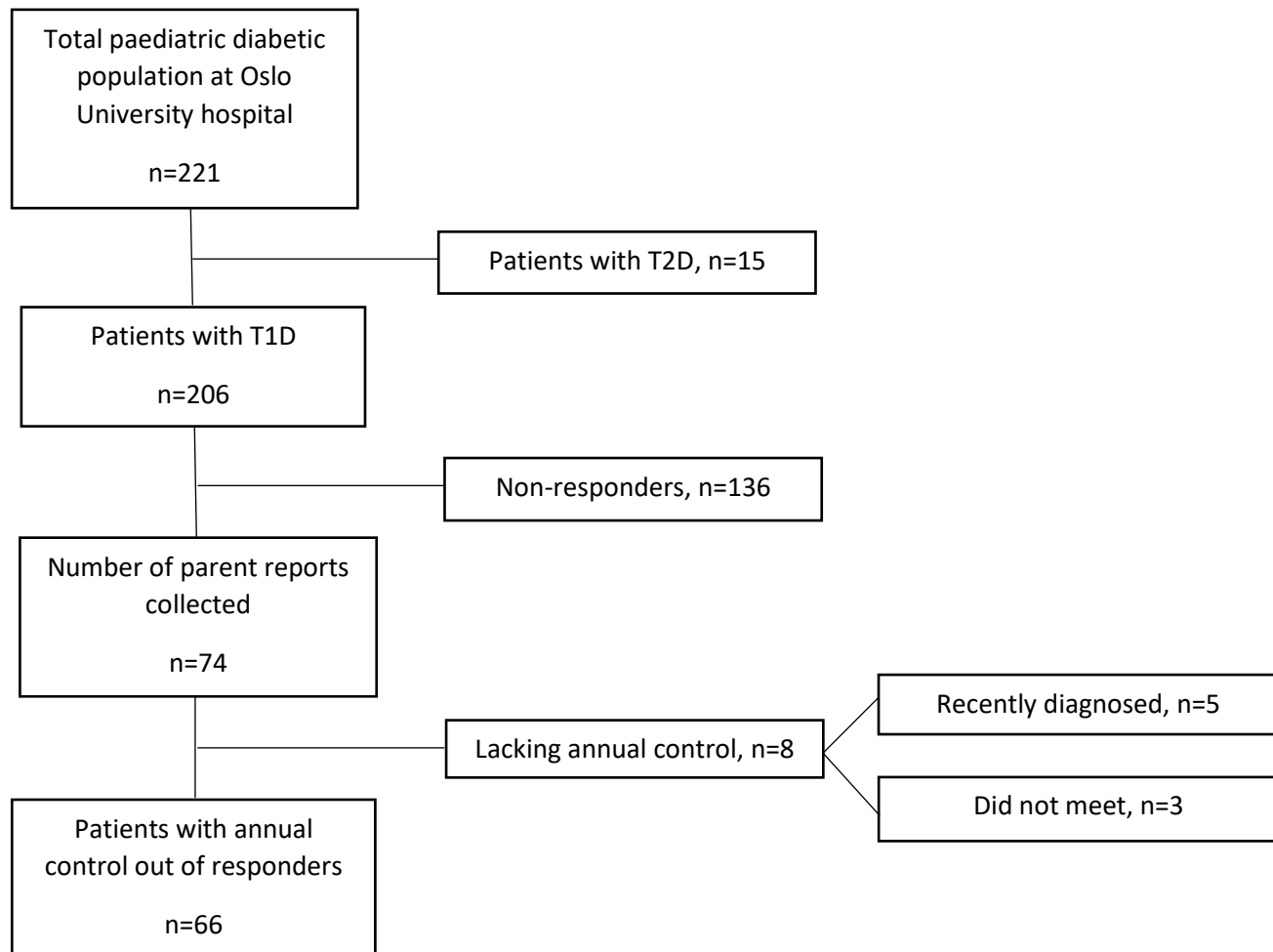
HRQOL study by filling out the DISABKIDS Chronic Generic Module (DCGM-37) and the Diabetes Specific module (DDM-10) forms. Patients who could not read in Norwegian were helped to answer the forms orally at the out-patient clinic. Whether it was the mother or father who completed the proxy reports was left up to the parents to decide.

**Figure 1a.** Flow chart showing the study population out of all patients  $\geq 10$  years with T1D at Oslo University Hospital





**Figure 1b.** Flow chart showing the study cohort out of all patients with T1D at Oslo University Hospital



### *Instrument*

The DISABKIDS DCGM-37 and DDM-10 questionnaires were used in this study. The questionnaires have previously been validated and termed applicable on a Norwegian childhood diabetes population (99). The DISABKIDS questionnaires are clinical tools developed to screen for HRQOL in children and adolescents (97, 100). They were developed in cross-cultural and cross-national study groups, in seven different European countries, funded by the European commission (97). The purpose of developing such tools was coming up with an instrument for systematic monitoring of HRQOL of children with different health conditions using self- and proxy reports (87, 101). DISABKIDS includes a Chronic Generic Module (DCGM-37) which measures general HRQOL and level of distress caused by a chronic disease. It can be supplemented with condition-specific modules for asthma, arthritis, cerebral palsy, cystic fibrosis, dermatitis, epilepsy and diabetes (e.g. DISABKIDS Diabetes Specific Module) (97).

The DCGM-37, which consists of six domains, is used to evaluate general HRQOL (87, 101), while DDM-10, which has two domains, addresses items specifically related to diabetes (97) (Figure 2). Both instruments are based on a four-week recall period except for item 11 on the DDM-10 “about symptoms” which has a one year recall period.

**Figure 2.** The structure of the questionnaire DCGM-37 and DDM-10.

<b>DCGM-37</b>	HRQOL general score	<i>Mental</i>	Independence
			Inner strength
		<i>Social</i>	Inclusion
			Equality
		<i>Physical</i>	Ability
			Treatment
<b>DDM-10</b>	HRQOL disease specific score	Diabetes acceptance	
		Diabetes treatment	

DCGM-37: DISABKIDS Chronic Generic Module; DDM-10: DISABKIDS Diabetes Specific Module

The DCGM-37 consists of six domains, or subscales, made up of 37 items. The subscales fit into three main domains regarding health status, conceptualized by the World Health Organisation (WHO): mental, social and physical (102). The domains of the DCGM-37 are the following: independence, inner strength (mental emotion), social inclusion, social equality (social exclusion), physical ability (physical limitation) and physical treatment (Figure 3). The domains in parenthesis are the old ones that due to previous confusion of mixed positive and negative domains were altered into positive statements (86, 103). For example, high score in a positive domain (e.g. independence) was good, but a high score in a negative domain (e.g. physical ability) was bad. The DDM-10 consists of an impact and a treatment scale, including 10 items and an additional item 11 “about symptoms” (100) (Figure 3). The diabetes-impact scale was later renamed to diabetes acceptance, in accordance with the positive reconceptualization of the domains (85).

Each of the items in the DISABKIDS questionnaires can be rated on a 5 point Likert-scale indicating frequency of feelings or behaviours, 1 = never, 2 = seldom, 3 = quite often, 4 = very often, 5 = always. This score can subsequently be transformed into a HRQOL score ranging from 0-100 for each subscale, a higher score indicating a higher HRQOL.

### *Statistical analysis*

In accordance with the DISABKIDS manual all data were transformed and summarized into HRQOL scores ranging from 0-100 (104). Results are presented as means with one standard deviation (SD) or as rates (percentages). Floor and ceiling effects are reported by number of patients with a HRQOL score of 0 (floor) and 100 (ceiling). To assess whether the studied cohort was representative for the Norwegian paediatric childhood population, clinical parameters were compared with non-participants based on data from the NCDR. The comparison between the participants to non-participants, was done using independent sample t-test for continuous variables and chi square tests for dichotomous variables. Using multiple linear regression analysis, the HRQOL reported in the subscales and in total was related to multiple background variables (e.g. age, gender, HbA1c). Paired sample t-test were used to assess continuity between HRQOL scores obtained from the children and their parents. Values of  $p < 0.05$  were considered significant. SPSS version 21.0 (SPSS IBM, NY, USA) was used for analyses.

**Figure 3.** Domains of DCGM-37 and DDM-10 with re-conceptualizations into positive statements, question numbers, and examples of questions. DCGM-37: DISABKIDS Chronic Generic Module; DDM-10: DISABKIDS Diabetes Specific Module

<b>Chronic generic module</b>	
Independence (1-6)	Confidence about the future and living an autonomous life without impairments caused by the disease, "Are you able to do everything you want despite your disease?"
Physical Ability (7-12)	Not experiencing somatic limitations due to the condition, "Are you able to run and move as you wish?"
Inner Strength (13-19)	Emotional reactions, e.g. worry, anger or concerns caused by the condition, "Do you worry because of your disease?"
Social Equality (20-25)	Feelings of being left out and stigmatized, "Do you feel lonely due to your disease?"
Social Inclusion (26-31)	Positive social relationships, and the understanding of others, "Does other children/adolescents understand your disease?"
Treatment (32-37)	Acceptance of receiving treatment and taking medication, "Does it bother you to take medication?"
DCGM-37 total score	Total Health Related Quality of Life score for the chronic generic module
<b>Diabetes module</b>	
Diabetes acceptance (d1-d6)	Emotional reactions to the everyday influence of the disease and disease management, "Do you worry about your blood sugar?"
Diabetes Treatment (d7-d10)	Emotional reactions to planning treatment and carrying equipment, "Does it bother you to take insulin?"

### *Ethical considerations*

All children and adolescents participating in the study are registered in the NCDR. To be included in the NCDR all patients (over the age of 12) and/or their parents must sign an informed consent (105). Established consent allows for the NCDR to retrieve patient reported outcome measures (PROM) and clinical data in accordance with Norwegian ethical requirements.

## Results

Eligibility requirements for this study included a) having T1D, b) age 10 years and older in the self-reports, but not in the proxy reports and c) being registered in the NCDR. An additional requirement d) of having undergone an annual control was necessary for comparison of clinical characteristics between the cohort and non-participants. Out of 148 eligible children and adolescents 59 filled out the self-reports (40%). For the proxy reports 206 children and adolescents were found to meet the requirements and 74 parents responded (36%). Whether the children in the cohort were representative for the Norwegian child and adolescent diabetic population was assessed comparing clinical characteristics of the cohort population with data from the NCDR, a population based, nationwide registry covering all paediatric departments in Norway. In 2015 the registry included 97% of all children and adolescents under diabetes treatment in paediatric departments in Norway (5). For this purpose, four of the self-reports and eight of the proxy reports were excluded due to not complying with eligibility requirement d (Figure 1a and 1b).

The clinical characteristics of the participants and non-participants are presented in table 1a for self-reports and table 1b for proxy reports. In the self-report group the cohort population was made up of 55 individuals. The number of non-participants was 1,987 (Table 1a). There were no significant differences between the cohort and non-participants regarding gender distribution (55% versus 53%), HbA1c value ( $8.2 \pm 1.2$  versus  $8.3 \pm 1.3$  (mean $\pm$ SD)), age ( $14.5 \pm 2.4$  versus  $14.7 \pm 2.4$  (mean $\pm$ SD)), duration of the disease ( $6.8 \pm 3.8$  versus  $6.1 \pm 3.8$  (mean $\pm$ SD)), age at diagnosis ( $7.7 \pm 4.1$  versus  $8.6 \pm 3.8$  (mean $\pm$ SD)) and occurrence of acute complications (DKA (4% versus 3%) or severe hypoglycaemic event (9% versus 4%)). The only significant difference between the two groups was regarding the treatment, p-value = 0.027. A substantially higher percentage of the study cohort used the insulin pump as their treatment modality, the respective percentages being 84% and 69%. This difference can be attributed to the high utilization of the insulin pump in Oslo (Oslo being 6<sup>th</sup> in the country), which in itself is above the national standard, combined with a big patient population, making this department the second in the country regarding the number of patients using the pump (98).

**Table 1a.** Clinical characteristics of the participants (study cohort) and non-participants based on data from the annual standardized examination 2015 in the Norwegian Childhood Diabetes Registry. Selected for patients ten years or older. Study cohort (n=55), non-participants (n=1987)

<i>Continuous variables</i>	Study cohort	Non-participants	Statistical difference <sup>1</sup> p Value
HbA1c - mean (SD)	8.2 (1.2)	8.3 (1.3)	0.610
Age (yrs) – mean (SD)	14.5 (2.4)	14.7 (2.4)	0.408
Diabetes duration (yrs) – mean (SD)	6.8 (3.8)	6.1 (3.8)	0.189
Age at diagnosis – mean (SD)	7.7 (4.1)	8.6 (3.8)	0.066
<i>Categorical variables</i>			
Boys – n (%)	30 (55)	1043 (53)	0.764
Diabetic ketoacidosis - n(%)	2 (4)	59 (3)	0.762
Severe hypoglycemic event – n (%)	5 (9)	87 (4)	0.083
Insulin pump – n (%)	46 (84)	1379 (69)	0.027

<sup>1</sup> T-test for continuous variables and chi-square test for categorical variables

Using the proxy reports our cohort expanded to include the children under the age of ten, giving a total of 79 children and adolescents in our cohort and 2,581 children and adolescents in the non-participating group (Table 1b). No significant difference was found between the cohort and the non-participants in the distribution of sexes (59% versus 53%), duration of the disease ( $5.6 \pm 3.7$  versus  $5.4 \pm 3.7$  (mean $\pm$ SD)), HbA1c value ( $7.9 \pm 1.1$  versus  $8.1 \pm 1.2$  (mean $\pm$ SD)) or the occurrence of severe hypoglycaemic events (8% versus 4%) or DKA (3% versus 3%). However, there were significant differences between the two populations regarding age ( $p = 0.009$ ), mean age being  $11.8 \pm 3.8$  (mean $\pm$ SD) in the cohort versus  $13.0 \pm 3.9$  (mean $\pm$ SD) in the non-participating population. Furthermore, there was a significant difference in age at diabetes onset ( $p = 0.004$ ) which was over a year younger in the cohort population ( $6.2 \pm 4.0$  versus  $7.6 \pm 3.9$  (mean $\pm$ SD)). Also, in this cohort there was observed a significant difference ( $p = 0.002$ ) in the usage of the insulin pump, 89% in the study cohort versus 72% amongst the non-participants.

**Table 1b.** Clinical characteristics of the participants (study cohort) and non-participants based on data from the annual standardized examination 2015 in the Norwegian Childhood Diabetes Registry. Study cohort (n=66), non-participants (n=2581)

<i>Continuous variables</i>	Study cohort	Non-participants	Statistical difference <sup>1</sup> p Value
HbA1c-mean (SD)	7.9 (1.1)	8.1 (1.2)	0.187
Age (yrs) – mean (SD)	11.8 (3.8)	13.0 (3.9)	0.009
Diabetes duration (yrs) – mean (SD)	5.6 (3.7)	5.4 (3.7)	0.720
Age at diagnosis	6.2 (4.0)	7.6 (3.9)	0.004
<i>Categorical variables</i>			
Boys – n (%)	39 (59)	1366 (53)	0.322
Diabetic ketoacidosis – n(%)	2 (3)	76 (3)	0.959
Severe hypoglycemic event – n (%)	5 (8)	112 (4)	0.189
Insulin pump – n (%)	59 (89)	1838 (72)	0.002

<sup>1</sup> T-test for continuous variables and chi-square test for categorical variables

### *Chronic Generic Module (DCGM-37)*

The mean self-reported scores for the DCGM-37 were in the range 73-83, and the mean general HRQOL score was 78 (Table 2). The parents scores in the different subscales varied between 70 and 79, with a total mean of 73. Parents scored lower than their children in all of the subscales. However, significant difference was only established for the subscale social inclusion (p=0.001). There was a big difference between the self-reported and parental reported mean general HRQOL score, however most likely due to the small cohort size the difference was not significant (p=0.061).

The mean general HRQOL score was 77 for girls and 78 for boys in the self-reports (Table 3). The boys reported higher mean HRQOL for all subscales, except for physical ability, social equality and treatment. There were no significant differences between the genders for any of the subscales in the self-reports. In the proxy reports the mean general HRQOL score was 72 for girls and 73 for boys. The parents reported higher mean HRQOL for boys in the subscales physical ability, treatment and general HRQOL. The scores were equal for the subscales social equality and social inclusion. There were found no significant differences comparing

girls between the self- and proxy reports. Comparing boys between the self- and proxy reports showed a significant difference for the subscale social inclusion, parents reporting a lower HRQOL than the boys did themselves.

Low DCGM-37 total and subscale scores were significantly associated with high HbA1c, and with treatment modality (insulin pen) for one subscale (Table 4). There were found no association between HRQOL score and gender, occurrence of DKA or severe hypoglycaemic event, age or duration of the disease. However, the incidence of both DKA and hypoglycaemia was very low, making it hard to get an actual relation.

#### *Diabetes Specific Module (DDM-10)*

In the DDM-10 subscales the parents gave higher mean scores than their children. The mean scores in the self-reports were 66 for impact and 62 for treatment, while the parents had a mean score of 67 in both subscales (Table 2).

There were no significant differences between the genders in the DDM-10 subscales in the self-reports. The boys did however report higher mean HRQOL scores for both subscales. The boys reported a mean score of 68 for diabetes acceptance and a mean score of 67 for diabetes treatment, while the girls had mean scores of 65 and 56 respectively. Equal scores (67 versus 67), between the genders were measured in the proxy reports for the subscale diabetes acceptance, but boys reported a higher HRQOL regarding treatment (68 versus 66). There were found no significant differences between the self-and proxy reports regarding genders (Table 3).

In the multiple linear regression analysis low scores on the DDM-10 subscales were associated with having a high HbA1c value, but not with any of the other sociodemographic factors. There were no association between mode of insulin delivery and diabetes acceptance or treatment scales (Table 4).



**Table 2.** Comparison between self- and proxy reports. Higher score signifies higher HRQOL.

DCGM-37 + DDM-10	Self-report			Proxy report			p Value
	n	Mean	SD ( $\pm$ )	n	Mean	SD ( $\pm$ )	
Independence	59	76	18	74	72	17	0.307
Physical ability	58	74	17	74	72	15	0.430
Inner strength	57	78	19	74	73	17	0.252
Equality	56	83	15	71	79	15	0.200
Social inclusion	55	80	14	71	70	18	0.001
Treatment	55	73	23	72	70	17	0.310
General HRQOL score	56	78	14	72	73	14	0.061
Diabetes acceptance	54	66	22	74	67	17	0.543
Diabetes treatment	53	62	25	72	67	21	0.189

DCGM-37: DISABKIDS Chronic Generic Measure; DDM-10: DSABKIDS diabetes module; HRQOL: Health Related Quality of Life

**Table 3.** Shows the difference in Quality of Life (QOL) between the genders in the separate reports. In the third column, self- and proxy reports, the comparison is between girls/girls and boys/boys.

DCGM-37 + DDM-10	<u>Self-report</u>					<u>Proxy report</u>					<u>Self- and proxy report</u>	
	Girls		Boys		p Value	Girls		Boys		p Value	Girls/ girls	Boys/ boys
	n	Mean/ SD	n	Mean/ SD		n	Mean/ SD	n	Mean/ SD		p Value	p Value
Independence	25	74±18	34	78±18	0.301	32	73±17	42	72±17	0.870	0.841	0.109
Physical ability	24	75±19	34	74±16	0.890	32	70±17	42	74±14	0.302	0.398	0.784
Inner strength	23	76±23	34	79±16	0.610	32	74±17	42	73±18	0.703	0.980	0.097
Equality	24	84±16	32	83±14	0.661	30	79±14	41	79±15	0.826	0.441	0.300
Social inclusion	23	79±17	32	81±12	0.648	30	70±17	41	70±19	0.935	0.077	0.006
Treatment	23	74±25	32	73±22	0.976	30	68±16	42	71±18	0.412	0.411	0.515
General HRQOL score	24	77±16	32	78±14	0.690	30	72±14	42	73±14	0.637	0.313	0.099
Diabetes acceptance	22	65±22	32	68±22	0.630	32	67±16	42	67±18	0.934	0.292	0.871
Diabetes treatment	21	56±30	32	67±21	0.123	32	66±20	40	68±21	0.766	0.096	0.867

DCGM-37: DISABKIDS Chronic Generic Measure; DDM-10: DSABKIDS diabetes module; HRQOL: Health Related Quality of Life

**Table 4.** Effects of gender, HbA1c, an episode of diabetic ketoacidosis, a severe hypoglycaemic event, treatment modality and age on self-reported total and sum scores in DISABKIDS.

Subscale	Gender girl/boy*				HbA1c**				Ketoacidosis***				Severe hypoglycaemic events****				Treatment modality: insulin pen*****				Age*****			
DCGM-37	Una dj. effe ct	p	Adj. effe ct <sup>a</sup>	p	Una dj. effe ct	p	Adj. effe ct <sup>a</sup>	p	Una dj. effe ct	p	Adj. effe ct <sup>a</sup>	p	Una dj. effe ct	p	Adj. effe ct <sup>a</sup>	p	Una dj. effe ct	p	Adj. effe ct <sup>a</sup>	p	Una dj. effe ct	p	Adj. effe ct <sup>a</sup>	p
Total HRQOL score	0.45	0.991	-0.004	0.999	-4.16	0.010	-5.82	0.002	-0.04	0.997	-0.26	0.981	-5.69	0.404	-5.56	0.423	-5.95	0.280	-6.11	0.277	0.29	0.714	0.31	0.702
Independence	-1.16	0.802	-1.88	0.687	-1.26	0.504	-2.97	0.187	1.87	0.880	0.53	0.966	-9.62	0.231	-9.18	0.247	-3.30	0.596	-3.59	0.564	1.37	0.138	1.31	0.170
Inner strength	-0.55	0.916	-1.01	0.853	-3.74	0.078	-6.24	0.015	-6.73	0.629	-8.94	0.541	-11.30	0.258	-11.76	0.248	-7.52	0.281	-7.52	0.289	0.36	0.738	0.26	0.818
Social inclusion	0.70	0.856	0.77	0.844	-2.05	0.206	-3.03	0.112	1.00	0.920	-0.73	0.945	-4.87	0.459	-4.98	0.454	-5.96	0.262	-5.77	0.285	-0.65	0.395	-0.71	0.366
Social equality	2.57	0.538	2.01	0.635	-2.34	0.161	-4.44	0.023	6.64	0.545	4.98	0.659	-2.43	0.736	-2.06	0.774	-11.08	0.054	-11.73	0.042	0.95	0.249	0.86	0.314
Physical ability	0.23	0.962	0.85	0.861	-5.12	0.007	-6.29	0.006	9.17	0.470	11.31	0.394	5.42	0.516	5.27	0.534	-7.96	0.210	-7.94	0.217	-0.62	0.512	-0.49	0.616
Physical treatment	2.67	0.678	2.61	0.690	-8.34	0.002	-10.87	0.000	-11.28	0.497	-11.91	0.496	-11.25	0.303	-11.02	0.320	-2.33	0.793	-2.61	0.773	0.71	0.576	0.78	0.550
<b>DDM-10</b>																								
Acceptance	-0.30	0.962	0.001	1.000	-6.57	0.004	-9.79	0.001	-17.66	0.267	-18.48	0.271	-19.41	0.092	-19.32	0.102	-4.99	0.560	-5.32	0.543	0.26	0.839	0.36	0.792

Treatment	-	0.3	-	0.3	-	0.0	-	0.0	-	0.5	-	0.6	-	0.3	-	0.2	-	0.9	-	0.9	-	0.4	-	0.5
	7.3	12	6.6	70	9.2	01	11.	00	10.	54	8.3	64	13.	21	14.	92	0.5	54	0.5	55	1.0	86	0.8	82
	2		3		5		75		71		0		07		12		6		5		3		3	

DCGM-37: DISABKIDS Chronic Generic Measure; DDM-10: DSABKIDS diabetes module; HRQOL: Health Related Quality of Life

\*Effect of being a girl, \*\*Effect per % increment of HbA1c, \*\*\*Effect of having had a ketoacidosis, \*\*\*\*Effect of having had a severe hypoglycaemic event, \*\*\*\*\*Effect of using insulin pen compared with insulin pump, \*\*\*\*\*Effect per year increased age

<sup>a</sup>Adjusted for age and duration of diabetes

All subscales are scored from 0 to 100 with higher scores indicating a higher self-perceived HRQOL

## Discussion

Lower HRQOL was significantly associated with poor metabolic control, represented by an increase in HbA1c. There was also found a significant negative correlation between use of insulin pen and the DCGM-37 subscale social equality, but not for any of the other subscales. Lower HRQOL was not associated with gender, having experienced DKA, a severe hypoglycaemic event or with patient age. Parents tended to report a lower HRQOL than the children and adolescents did themselves, however this difference was not significant.

In the multiple regression analysis, poor metabolic control had a significant negative effect on HRQOL. This negative effect was observed for all subscales of the DCGM-37, except for independence and social inclusion, and for both subscales of the DDM-10. Several previous studies have reported the same negative correlation between poor metabolic control and low self-perceived HRQOL (88-90, 92, 106). Furthermore, a beneficial effect has been observed between better HbA1c values, high self-perceived HRQOL and the patients ability to cope with their disease (95).

The only significant difference regarding treatment modality was for the DCGM-37 subscale social equality, where using the insulin pen was associated with a lower HRQOL. Children and adolescents with T1D, treated at the Paediatric Department at OUS, are offered the possibility to choose the treatment modality they want, insulin pen or insulin pump, as full reimbursement is offered by the Norwegian social security system. This presumably leads to greater satisfaction and fewer differences in HRQOL regarding equipment use. The difference observed in the subscale social equality, could be explained by the physical presence of the insulin pen measuring BG, leaving the patient feeling more stigmatized.

In the self-reports, boys reported higher self-perceived HRQOL than the girls in three out of six domains in addition to reporting a higher mean general HRQOL score. They also scored higher for both subscales of the DDM-10. However, none of the differences were significant. For the proxy reports boys were reported to have a lower HRQOL than the girls for all DCGM-37 subscales, except physical ability and treatment, though the mean total HRQOL score was higher for boys than for girls. In previous studies boys have generally had higher HRQOL scores than girls (85-89). This could be due to that boys to a lesser extent incorporate their disease into their social identities. Leaving them less susceptible to the impact of

diabetes. The lack of difference between the genders in my study was unlike in previous studies. This could be due to a small cohort size. It could also be related to having a quite homogenous patient population at OUS. They receive the same treatment disregarding gender, social status and economy. This could contribute to a more equal view and more equal expectations to disease and disease management, hence less difference between the measured scores.

There were found no associations between DKA and severe hypoglycaemic events and HRQOL in the study. Possibly due to the low occurrence of these events (two episodes of DKA and five episodes of severe hypoglycaemic events in the last year in both cohort populations). No differences were found for the variable age. This is in contrast to earlier studies that showed a correlation between younger age and better HRQOL (90, 91, 107).

The parents reported in general lower mean HRQOL scores than their children. The mean general HRQOL score, though not significantly different between the self- and proxy reports, did show a discrepancy between the parental and self-reports. The only significant difference, however, was for the DCGM-37 subscale social inclusion. In previous studies parents tended to score their kids HRQOL lower than the kids themselves did (88, 94). This could imply that parents find it hard to assess their child's health status accurately. The reasons could be limited insight into the child's experiences and feelings or different views on health and wellbeing. The lack of significant differences in my study could suggest that the parents in this cohort in fact are quite good at understanding their off-springs perception. There was, however, a significant difference between the self- and the proxy reports for the domain social inclusion. This may be due to parents lacking first-hand experience concerning their kids social interactions with peers (108). In contrast to the general notion of lower scores in the proxy reports, parents scored higher on both the DDM-10 subscales. This may suggest that parents consider diabetes management and treatment less burdensome than their children, who carry the equipment and are prone to the different kinds of restrictions.

Personal evaluation with respect to HRQOL is crucial. One of the strength of this study was that such evaluation was made possible thanks to the DISABKIDS questionnaires. These questionnaires were internationally created and tested in cross-national study groups providing great confidence in the instruments. Furthermore, the way in which they were developed allows for comparison in a standardized fashion between a large range of children and adolescents, both on a national and international scale (108). Another strength is the fact

that parents and children could assess HRQOL using the same questionnaires, making comparison between the two groups possible. The questionnaires used consists of a generic module and a disease specific module allowing for good coverage of HRQOL. Being able to complement the score with medical variables and clinical data from the NCDR allowed for an even more precise assessment of the HRQOL. The study was performed at the Oslo University Hospital, which offers the same standardized modern intensified treatment to everyone disregarding socioeconomic status. This made it possible to look for other sociodemographic and clinical variables affecting HRQOL.

Weakness of my study was the small cohort size and a relatively low response rate making it harder to discover any significant differences, and evaluating the value of the discoveries. This was in part compensated by the ability to compare my cohort to a larger nationwide population based diabetes population through the NCDR. The statistical differences between the cohort populations and the total diabetic population registered in the NCDR were small, rendering the cohorts reasonably representative of the Norwegian diabetic childhood population.

## **Conclusion**

Decreased HRQOL was associated with poor metabolic control (represented by a high HbA1c), and with treatment modality (insulin pen) for one subscale of the DCGM-37. It was not associated with gender, episodes of acute complications or age. There was consistency between the child- and parent reports, suggesting good parental insight into the feelings and beliefs of their kids.

It is important to monitor for HRQOL on a regular basis, in order to identify the factors with positive effect and the factors with negative effect on self-perceived QOL. Such screening can help identify patients in need for help and steer treatment in the right direction. Furthermore, using both self- and proxy reports, and evaluating the results with the families present, could help patients and parents achieve insights into each other's perception, improve communication between the generations, and consequently help improve care.

## Conflicts of interest

There were no conflicts of interest in this study.

## Reference list:

1. Kumar V, Abbas A, Aster J. Robbins Basics Pathology. Elsevier Inc. 1971 (ninth edition 2013 ). Chapter 19.
2. Lynne L Levitsky M, Madhusmita Misra, MD, MPH. Epidemiology, presentation, and diagnosis of type 1 diabetes mellitus in children and adolescents. UpToDate. 2016.
3. Organization WH. WHO: Definition, diagnosis and classification of diabetes mellitus: Report of the expert committee on the diagnosis and classification of diabetes mellitus. . 1999.
4. David K McCulloch M. Classification of diabetes mellitus and genetic diabetic syndromes. UpToDate. 2016.
5. Skrivarhaug T, Kummernes S, Drivvoll A. Annual report 2015 Norwegian Childhood Diabetes Registry. 01.10.2016;Oslo University Hospital
6. Skrivarhaug T. The prognosis of children with Type 1 diabetes in Norway, A 24-year follow-up study 2007.
7. Rosenbauer J, Herzig P, von Kries R, Neu A, Giani G. Temporal, seasonal, and geographical incidence patterns of type I diabetes mellitus in children under 5 years of age in Germany. Diabetologia. 1999;42(9):1055-9.
8. Incidence and trends of childhood Type 1 diabetes worldwide 1990-1999. Diabet Med. 2006;23(8):857-66.
9. Skrivarhaug T, Stene LC, Drivvoll AK, Strom H, Joner G. Incidence of type 1 diabetes in Norway among children aged 0-14 years between 1989 and 2012: has the incidence stopped rising? Results from the Norwegian Childhood Diabetes Registry. Diabetologia. 2014;57(1):57-62.
10. Joner G, Sovik O. Increasing incidence of diabetes mellitus in Norwegian children 0-14 years of age 1973-1982. Diabetologia. 1989;32(2):79-83.
11. Concannon P, Rich SS, Nepom GT. Genetics of Type 1A Diabetes. N Engl J Med. 2009;360(16):1646-54.
12. Concannon P, Onengut-Gumuscu S, Todd JA, Smyth DJ, Pociot F, Bergholdt R, et al. A human type 1 diabetes susceptibility locus maps to chromosome 21q22.3. Diabetes. 2008;57(10):2858-61.
13. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature. 2007;447(7145):661-78.
14. Lowe CE, Cooper JD, Brusko T, Walker NM, Smyth DJ, Bailey R, et al. Large-scale genetic fine mapping and genotype-phenotype associations implicate polymorphism in the IL2RA region in type 1 diabetes. Nat Genet. 2007;39(9):1074-82.
15. Davies JL, Kawaguchi Y, Bennett ST, Copeman JB, Cordell HJ, Pritchard LE, et al. A genome-wide search for human type 1 diabetes susceptibility genes. Nature. 1994;371(6493):130-6.
16. Gepts W. Pathologic anatomy of the pancreas in juvenile diabetes mellitus. Diabetes. 1965;14(10):619-33.
17. Rodriguez-Calvo T, Zapardiel-Gonzalo J, Amirian N, Castillo E, Lajevardi Y, Krogvold L, et al. Increase in Pancreatic Proinsulin and Preservation of beta-Cell Mass in Autoantibody-Positive Donors Prior to Type 1 Diabetes Onset. Diabetes. 2017;66(5):1334-45.
18. Donaghue KC, Wadwa RP, Dimeglio LA, Wong TY, Chiarelli F, Marcovecchio ML, et al. ISPAD Clinical Practice Consensus Guidelines 2014. Microvascular and macrovascular complications in children and adolescents. Pediatr Diabetes. 2014;15 Suppl 20:257-69.



19. Dyck PJ, Albers JW, Andersen H, Arezzo JC, Biessels GJ, Bril V, et al. Diabetic polyneuropathies: update on research definition, diagnostic criteria and estimation of severity. *Diabetes Metab Res Rev.* 2011;27(7):620-8.
20. Laing SP, Swerdlow AJ, Slater SD, Burden AC, Morris A, Waugh NR, et al. Mortality from heart disease in a cohort of 23,000 patients with insulin-treated diabetes. *Diabetologia.* 2003;46(6):760-5.
21. Schultz CJ, Konopelska-Bahu T, Dalton RN, Carroll TA, Stratton I, Gale EA, et al. Microalbuminuria prevalence varies with age, sex, and puberty in children with type 1 diabetes followed from diagnosis in a longitudinal study. Oxford Regional Prospective Study Group. *Diabetes Care.* 1999;22(3):495-502.
22. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol.* 1984;102(4):520-6.
23. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmol.* 1984;102(4):527-32.
24. Gagnum V, Stene LC, Jenssen TG, Berteussen LM, Sandvik L, Joner G, et al. Causes of death in childhood-onset Type 1 diabetes: long-term follow-up. *Diabet Med.* 2017;34(1):56-63.
25. Group DR. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. *N Engl J Med.* 1993;329(14):977-86.
26. Aiello LP, Cahill MT, Wong JS. Systemic considerations in the management of diabetic retinopathy. *Am J Ophthalmol.* 2001;132(5):760-76.
27. Hietala K, Forsblom C, Summanen P, Groop PH. Higher age at onset of type 1 diabetes increases risk of macular oedema. *Acta Ophthalmol.* 2013;91(8):709-15.
28. Mogensen CE, Keane WF, Bennett PH, Jerums G, Parving HH, Passa P, et al. Prevention of diabetic renal disease with special reference to microalbuminuria. *Lancet.* 1995;346(8982):1080-4.
29. Stone ML, Craig ME, Chan AK, Lee JW, Verge CF, Donaghue KC. Natural history and risk factors for microalbuminuria in adolescents with type 1 diabetes: a longitudinal study. *Diabetes Care.* 2006;29(9):2072-7.
30. Couper JJ, Clarke CF, Byrne GC, Jones TW, Donaghue KC, Nairn J, et al. Progression of borderline increases in albuminuria in adolescents with insulin-dependent diabetes mellitus. *Diabet Med.* 1997;14(9):766-71.
31. Perkins BA, Ficociello LH, Silva KH, Finkelstein DM, Warram JH, Krolewski AS. Regression of microalbuminuria in type 1 diabetes. *N Engl J Med.* 2003;348(23):2285-93.
32. Ficociello LH, Perkins BA, Silva KH, Finkelstein DM, Ignatowska-Switalska H, Gaciong Z, et al. Determinants of progression from microalbuminuria to proteinuria in patients who have type 1 diabetes and are treated with angiotensin-converting enzyme inhibitors. *Clin J Am Soc Nephrol.* 2007;2(3):461-9.
33. Jaiswal M, Urbina EM, Wadwa RP, Talton JW, D'Agostino RB, Jr., Hamman RF, et al. Reduced heart rate variability among youth with type 1 diabetes: the SEARCH CVD study. *Diabetes Care.* 2013;36(1):157-62.
34. Gagnum V, Stene LC, Sandvik L, Fagerland MW, Njolstad PR, Joner G, et al. All-cause mortality in a nationwide cohort of childhood-onset diabetes in Norway 1973-2013. *Diabetologia.* 2015;58(8):1779-86.
35. Margeirsdottir HD, Larsen JR, Brunborg C, Overby NC, Dahl-Jorgensen K. High prevalence of cardiovascular risk factors in children and adolescents with type 1 diabetes: a population-based study. *Diabetologia.* 2008;51(4):554-61.
36. Bojestig M, Arnqvist HJ, Hermansson G, Karlberg BE, Ludvigsson J. Declining incidence of nephropathy in insulin-dependent diabetes mellitus. *N Engl J Med.* 1994;330(1):15-8.
37. Downie E, Craig ME, Hing S, Cusumano J, Chan AK, Donaghue KC. Continued reduction in the prevalence of retinopathy in adolescents with type 1 diabetes: role of insulin therapy and glycemic control. *Diabetes Care.* 2011;34(11):2368-73.

38. Lind M, Svensson AM, Kosiborod M, Gudbjornsdottir S, Pivodic A, Wedel H, et al. Glycemic control and excess mortality in type 1 diabetes. *N Engl J Med.* 2014;371(21):1972-82.
39. Harjutsalo V, Forsblom C, Groop PH. Time trends in mortality in patients with type 1 diabetes: nationwide population based cohort study. *BMJ.* 2011;343:d5364.
40. Skrivarhaug T, Bangstad HJ, Stene LC, Sandvik L, Hanssen KF, Joner G. Long-term mortality in a nationwide cohort of childhood-onset type 1 diabetic patients in Norway. *Diabetologia.* 2006;49(2):298-305.
41. Patterson CC, Dahlquist G, Harjutsalo V, Joner G, Feltbower RG, Svensson J, et al. Early mortality in EURODIAB population-based cohorts of type 1 diabetes diagnosed in childhood since 1989. *Diabetologia.* 2007;50(12):2439-42.
42. Morgan E, Cardwell CR, Black CJ, McCance DR, Patterson CC. Excess mortality in Type 1 diabetes diagnosed in childhood and adolescence: a systematic review of population-based cohorts. *Acta Diabetol.* 2015;52(4):801-7.
43. Asao K, Sarti C, Forsen T, Hyttinen V, Nishimura R, Matsushima M, et al. Long-term mortality in nationwide cohorts of childhood-onset type 1 diabetes in Japan and Finland. *Diabetes Care.* 2003;26(7):2037-42.
44. Matsushima M, LaPorte RE, Maruyama M, Shimizu K, Nishimura R, Tajima N. Geographic variation in mortality among individuals with youth-onset diabetes mellitus across the world. *DERI Mortality Study Group. Diabetes Epidemiology Research International. Diabetologia.* 1997;40(2):212-6.
45. Podar T, Solntsev A, Reunanen A, Urbonaite B, Zalinkevicius R, Karvonen M, et al. Mortality in patients with childhood-onset type 1 diabetes in Finland, Estonia, and Lithuania: follow-up of nationwide cohorts. *Diabetes Care.* 2000;23(3):290-4.
46. Organization WH. Global report on diabetes. World Health Organization. 2016 (<http://www.who.int>).
47. Nam Han Cho (chair) JK, Jean Claude, Mbanya KO, Leonor Guariguata,, Wolfgang Rathmann GR, Nita Forouhi,, Rana Dajani AE, Edward Boyko, Ian, Hambleton OldMN, Pablo, Aschner Montoya SJ, Juliana Chan,, et al. IDF Diabetes Atlas. International Diabetes Foundation. 2017;8th edition
48. Laing SP, Swerdlow AJ, Slater SD, Botha JL, Burden AC, Waugh NR, et al. The British Diabetic Association Cohort Study, II: cause-specific mortality in patients with insulin-treated diabetes mellitus. *Diabet Med.* 1999;16(6):466-71.
49. Secrest AM, Becker DJ, Kelsey SF, Laporte RE, Orchard TJ. Cause-specific mortality trends in a large population-based cohort with long-standing childhood-onset type 1 diabetes. *Diabetes.* 2010;59(12):3216-22.
50. Rewers MJ, Pillay K, de Beaufort C, Craig ME, Hanas R, Acerini CL, et al. ISPAD Clinical Practice Consensus Guidelines 2014. Assessment and monitoring of glycemic control in children and adolescents with diabetes. *Pediatr Diabetes.* 2014;15 Suppl 20:102-14.
51. Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group. *J Pediatr.* 1994;125(2):177-88.
52. Nathan DM, Genuth S, Lachin J, Cleary P, Crofford O, Davis M, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med.* 1993;329(14):977-86.
53. White NH, Cleary PA, Dahms W, Goldstein D, Malone J, Tamborlane WV. Beneficial effects of intensive therapy of diabetes during adolescence: outcomes after the conclusion of the Diabetes Control and Complications Trial (DCCT). *J Pediatr.* 2001;139(6):804-12.
54. Tahara Y, Shima K. Kinetics of HbA1c, glycated albumin, and fructosamine and analysis of their weight functions against preceding plasma glucose level. *Diabetes Care.* 1995;18(4):440-7.
55. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med.* 2005;353(25):2643-53.

56. Delamater AM, de Wit M, McDarby V, Malik J, Acerini CL. ISPAD Clinical Practice Consensus Guidelines 2014. Psychological care of children and adolescents with type 1 diabetes. *Pediatr Diabetes*. 2014;15 Suppl 20:232-44.
57. Boardway RH, Delamater AM, Tomakowsky J, Gutai JP. Stress management training for adolescents with diabetes. *J Pediatr Psychol*. 1993;18(1):29-45.
58. Hains AA, Davies WH, Parton E, Totka J, Amoroso-Camarata J. A stress management intervention for adolescents with type 1 diabetes. *Diabetes Educ*. 2000;26(3):417-24.
59. Cook S, Herold K, Edidin DV, Briars R. Increasing problem solving in adolescents with type 1 diabetes: the choices diabetes program. *Diabetes Educ*. 2002;28(1):115-24.
60. Mendez FJ, Belendez M. Effects of a behavioral intervention on treatment adherence and stress management in adolescents with IDDM. *Diabetes Care*. 1997;20(9):1370-5.
61. Tsiouli E, Alexopoulos EC, Stefanaki C, Darviri C, Chrousos GP. Effects of diabetes-related family stress on glycemic control in young patients with type 1 diabetes: Systematic review. *Can Fam Physician*. 2013;59(2):143-9.
62. Miller-Johnson S, Emery RE, Marvin RS, Clarke W, Lovinger R, Martin M. Parent-child relationships and the management of insulin-dependent diabetes mellitus. *J Consult Clin Psychol*. 1994;62(3):603-10.
63. Idalski Carcone A, Ellis DA, Weisz A, Naar-King S. Social support for diabetes illness management: supporting adolescents and caregivers. *J Dev Behav Pediatr*. 2011;32(8):581-90.
64. Grey M, Jaser SS, Whittemore R, Jeon S, Lindemann E. Coping skills training for parents of children with type 1 diabetes: 12-month outcomes. *Nurs Res*. 2011;60(3):173-81.
65. Jacobson AM, Hauser ST, Willett J, Wolfsdorf JL, Herman L. Consequences of irregular versus continuous medical follow-up in children and adolescents with insulin-dependent diabetes mellitus. *J Pediatr*. 1997;131(5):727-33.
66. Kaufman FR, Halvorson M, Carpenter S. Association between diabetes control and visits to a multidisciplinary pediatric diabetes clinic. *Pediatrics*. 1999;103(5 Pt 1):948-51.
67. Reynolds KA, Helgeson VS. Children with diabetes compared to peers: depressed? Distressed? A meta-analytic review. *Ann Behav Med*. 2011;42(1):29-41.
68. Young V, Eiser C, Johnson B, Brierley S, Epton T, Elliott J, et al. Eating problems in adolescents with Type 1 diabetes: a systematic review with meta-analysis. *Diabet Med*. 2013;30(2):189-98.
69. Lawrence JM, Standiford DA, Loots B, Klingensmith GJ, Williams DE, Ruggiero A, et al. Prevalence and correlates of depressed mood among youth with diabetes: the SEARCH for Diabetes in Youth study. *Pediatrics*. 2006;117(4):1348-58.
70. Herzer M, Hood KK. Anxiety symptoms in adolescents with type 1 diabetes: association with blood glucose monitoring and glycemic control. *J Pediatr Psychol*. 2010;35(4):415-25.
71. Hood KK, Huestis S, Maher A, Butler D, Volkening L, Laffel LM. Depressive symptoms in children and adolescents with type 1 diabetes: association with diabetes-specific characteristics. *Diabetes Care*. 2006;29(6):1389-91.
72. Hilliard ME, Wu YP, Rausch J, Dolan LM, Hood KK. Predictors of deteriorations in diabetes management and control in adolescents with type 1 diabetes. *J Adolesc Health*. 2013;52(1):28-34.
73. Holmes CS, Richman LC. Cognitive profiles of children with insulin-dependent diabetes. *J Dev Behav Pediatr*. 1985;6(6):323-6.
74. Ryan CM, van Duinkerken E, Rosano C. Neurocognitive consequences of diabetes. *Am Psychol*. 2016;71(7):563-76.
75. Northam EA, Anderson PJ, Werther GA, Warne GL, Adler RG, Andrewes D. Neuropsychological complications of IDDM in children 2 years after disease onset. *Diabetes Care*. 1998;21(3):379-84.
76. Northam EA, Anderson PJ, Werther GA, Warne GL, Andrewes D. Predictors of change in the neuropsychological profiles of children with type 1 diabetes 2 years after disease onset. *Diabetes Care*. 1999;22(9):1438-44.
77. Rovet JF, Ehrlich RM, Hoppe M. Specific intellectual deficits in children with early onset diabetes mellitus. *Child Dev*. 1988;59(1):226-34.


78. Asvold BO, Sand T, Hestad K, Bjorgaas MR. Cognitive function in type 1 diabetic adults with early exposure to severe hypoglycemia: a 16-year follow-up study. *Diabetes Care*. 2010;33(9):1945-7.
79. Perantie DC, Lim A, Wu J, Weaver P, Warren SL, Sadler M, et al. Effects of prior hypoglycemia and hyperglycemia on cognition in children with type 1 diabetes mellitus. *Pediatr Diabetes*. 2008;9(2):87-95.
80. Whittemore R, Jaser S, Chao A, Jang M, Grey M. Psychological experience of parents of children with type 1 diabetes: a systematic mixed-studies review. *Diabetes Educ*. 2012;38(4):562-79.
81. Streisand R, Mackey ER, Herge W. Associations of parent coping, stress, and well-being in mothers of children with diabetes: examination of data from a national sample. *Maternal and child health journal*. 2010;14(4):612-7.
82. Ellis DA, Podolski CL, Frey M, Naar-King S, Wang B, Moltz K. The role of parental monitoring in adolescent health outcomes: impact on regimen adherence in youth with type 1 diabetes. *J Pediatr Psychol*. 2007;32(8):907-17.
83. La Greca AM, Auslander WF, Greco P, Spetter D, Fisher EB, Jr., Santiago JV. I get by with a little help from my family and friends: adolescents' support for diabetes care. *J Pediatr Psychol*. 1995;20(4):449-76.
84. Nieuwesteeg A, Pouwer F, van der Kamp R, van Bakel H, Aanstoot HJ, Hartman E. Quality of life of children with type 1 diabetes: a systematic review. *Curr Diabetes Rev*. 2012;8(6):434-43.
85. Froisland DH, Graue M, Markestad T, Skriverhaug T, Wentzel-Larsen T, Dahl-Jorgensen K. Health-related quality of life among Norwegian children and adolescents with type 1 diabetes on intensive insulin treatment: a population-based study. *Acta Paediatr*. 2013;102(9):889-95.
86. Chaplin JE, Hanas R, Lind A, Tollig H, Wramner N, Lindblad B. Assessment of childhood diabetes-related quality-of-life in West Sweden. *Acta Paediatr*. 2009;98(2):361-6.
87. Petersen C, Schmidt S, Power M, Bullinger M. Development and pilot-testing of a health-related quality of life chronic generic module for children and adolescents with chronic health conditions: a European perspective. *Qual Life Res*. 2005;14(4):1065-77.
88. Hanberger L, Ludvigsson J, Nordfeldt S. Health-related quality of life in intensively treated young patients with type 1 diabetes. *Pediatr Diabetes*. 2009;10(6):374-81.
89. Kalyva E, Malakonaki E, Eiser C, Mamoulakis D. Health-related quality of life (HRQoL) of children with type 1 diabetes mellitus (T1DM): self and parental perceptions. *Pediatr Diabetes*. 2011;12(1):34-40.
90. Wagner VM, Muller-Godeffroy E, von Sengbusch S, Hager S, Thyen U. Age, metabolic control and type of insulin regime influences health-related quality of life in children and adolescents with type 1 diabetes mellitus. *Eur J Pediatr*. 2005;164(8):491-6.
91. Sand P, Kljajic M, Schaller J, Forsander G. The reliability of the Health Related Quality Of Life questionnaire PedsQL 3.0 Diabetes Module for Swedish children with type 1 diabetes. *Acta Paediatr*. 2012;101(8):e344-9.
92. Hoey H, Aanstoot HJ, Chiarelli F, Daneman D, Danne T, Dorchy H, et al. Good metabolic control is associated with better quality of life in 2,101 adolescents with type 1 diabetes. *Diabetes Care*. 2001;24(11):1923-8.
93. Delamater AM, Shaw KH, Applegate EB, Pratt IA, Eidson M, Lancelotta GX, et al. Risk for metabolic control problems in minority youth with diabetes. *Diabetes Care*. 1999;22(5):700-5.
94. Petersson C, Huus K, Samuelsson U, Hanberger L, Akesson K. Use of the national quality registry to monitor health-related quality of life of children with type 1 diabetes: a pilot study. *Journal of child health care : for professionals working with children in the hospital and community*. 2015;19(1):30-42.
95. Grey M, Davidson M, Boland EA, Tamborlane WV. Clinical and psychosocial factors associated with achievement of treatment goals in adolescents with diabetes mellitus. *J Adolesc Health*. 2001;28(5):377-85.
96. Cameron FJ, Smidts D, Hesketh K, Wake M, Northam EA. Early detection of emotional and behavioural problems in children with diabetes: the validity of the Child Health Questionnaire as a screening instrument. *Diabet Med*. 2003;20(8):646-50.

97. Bullinger M, Schmidt S, Petersen C. Assessing quality of life of children with chronic health conditions and disabilities: a European approach. *Int J Rehabil Res.* 2002;25(3):197-206.
98. Torild Skrivarhaug SJK, Ann Kristin Drivvoll NCDR: Annual Report 2015 2015.
99. Froisland DH, Markestad T, Wentzel-Larsen T, Skrivarhaug T, Dahl-Jorgensen K, Graue M. Reliability and validity of the Norwegian child and parent versions of the DISABKIDS Chronic Generic Module (DCGM-37) and Diabetes-Specific Module (DSM-10). *Health and quality of life outcomes.* 2012;10:19.
100. Ravens-Sieberer U, Schmidt S, Gosch A, Erhart M, Petersen C, Bullinger M. Measuring subjective health in children and adolescents: results of the European KIDSCREEN/DISABKIDS Project. *Psychosoc Med.* 2007;4:Doc08.
101. Simeoni MC, Schmidt S, Muehlan H, Debensason D, Bullinger M. Field testing of a European quality of life instrument for children and adolescents with chronic conditions: the 37-item DISABKIDS Chronic Generic Module. *Qual Life Res.* 2007;16(5):881-93.
102. WHO. Constitution of the World Health Organization. 1948.
103. Osoba D, Bezjak A, Brundage M, Zee B, Tu D, Pater J. Analysis and interpretation of health-related quality-of-life data from clinical trials: basic approach of The National Cancer Institute of Canada Clinical Trials Group. *Eur J Cancer.* 2005;41(2):280-7.
104. Europe TDG. The DISABKIDS Questionnaires Quality of Life Questionnaires for Children with Chronic Conditions Langericht, Germany: Pabst Science Publischers. 2006.
105. Skrivarhaug T. Norwegian Childhood Diabetes Registry: Childhood onset diabetes in Norway 1973-2012. *Norsk Epidemiologi.* 2013.
106. Guttmann-Bauman I, Flaherty BP, Strugger M, McEvoy RC. Metabolic control and quality-of-life self-assessment in adolescents with IDDM. *Diabetes Care.* 1998;21(6):915-8.
107. Hilliard ME, Lawrence JM, Modi AC, Anderson A, Crume T, Dolan LM, et al. Identification of minimal clinically important difference scores of the PedsQL in children, adolescents, and young adults with type 1 and type 2 diabetes. *Diabetes Care.* 2013;36(7):1891-7.
108. Ravens-Sieberer U, Erhart M, Wille N, Wetzel R, Nickel J, Bullinger M. Generic health-related quality-of-life assessment in children and adolescents: methodological considerations. *Pharmacoeconomics.* 2006;24(12):1199-220.

## Appendix

Dato for registrering:     
Dag Måned År

NAVNELAPP



*disabkids*

### Spørreskjema for barn og unge med kroniske sykdommer

Hei

Vi vil gjerne at du svarer på noen spørsmål om hvordan du har hatt det i løpet av de siste fire ukene.

Vi ber deg om å svare på alle spørsmålene hvis det er mulig for deg. Hvis det er et spørsmål du ikke forstår eller ikke ønsker å svare på, så hopp over det og gå til det neste.

→ Tenk tilbake på de siste fire ukene når du svarer på spørsmålene  
→ Velg det svaret som du synes passer best og kryss av i ruten som hører til.

Hvis du er sammen med vennene dine "svært ofte" krysser du av i ruten som vist i dette eksemplet.

	Aldri	Sjelden	Ganske ofte	Svært ofte	Alltid
Hvor ofte er du med vennene dine?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Det er ingen riktige eller gale svar. Det som er viktig er hva **du** mener.

Dato  
for registrering:

Dag
Måned
År

NAVNELAPP


disabkids

Spørreskjema for barn og unge med diabetes

Hei  

Vi vil gjerne at du svarer på noen spørsmål om hvordan du har hatt det i løpet av de siste fire ukene.

Vi ber deg om å svare på alle spørsmålene hvis det er mulig for deg. Hvis det er et spørsmål du ikke forstår eller ikke ønsker å svare på, så hopp over det og gå til det neste.

→ Tenk tilbake på **de siste fire ukene** når du svarer på spørsmålene

→ Velg det svaret som du synes passer best og kryss av i ruten som hører til.

Hvis du er sammen med vennene dine "svært ofte" krysser du av i ruten som vist i dette eksemplet.

	Aldri	Sjelden	Ganske ofte	Svært ofte	Alltid
Hvor ofte er du med vennene dine?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Det er ingen riktige eller gale svar. Det som er viktig er hva **du** mener.

Dato  
for registrering:

Dag
Måned
År

NAVNELAPP


*disabkids*

**Spørreskjema for foresatte til barn og unge med kroniske sykdommer**

**Kjære foresatte**

Takk for at du tar deg tid til å fylle ut dette spørreskjemaet om ditt barns velvære og helse relaterte livskvalitet.

Vi vil gjerne at du svarer på dette spørreskjemaet på vegne av barnet ditt, men vennligst besvar spørsmålene uten å be barnet ditt om hjelp. Alle svarene du gir vil bli behandlet strengt konfidensielt.

Med mindre du blir bedt om noe annet ber vi deg tenke over hvordan barnet ditt har hatt det i løpet av de siste fire ukene når du svarer på spørsmålene.

**EKSEMPEL:**

	Aldri	Sjelden	Ganske ofte	Svært ofte	Alltid
Hvor ofte er barnet ditt sammen med vennene sine?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>



Dato  
for registrering:

Dag
Måned
År

NAVNELAPP



**Spørreskjema for foresatte til barn og unge med diabetes**

**Kjære foresatte**

Takk for at du tar deg tid til å fylle ut dette spørreskjemaet om ditt barns velvære og helse relatert livskvalitet.

Vi vil gjerne at du svarer på dette spørreskjemaet på vegne av barnet ditt, men vennligst besvar spørsmålene uten å be barnet ditt om hjelp. Alle svarene du gir vil bli behandlet strengt konfidensielt.

Med mindre du blir bedt om noe annet ber vi deg tenke over hvordan barnet ditt har hatt det i løpet av de siste fire ukene når du svarer på spørsmålene.

**EKSEMPEL:**

	Aldri	Sjelden	Ganske ofte	Svært ofte	Alltid
Hvor ofte er barnet ditt sammen med vennene sine?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>