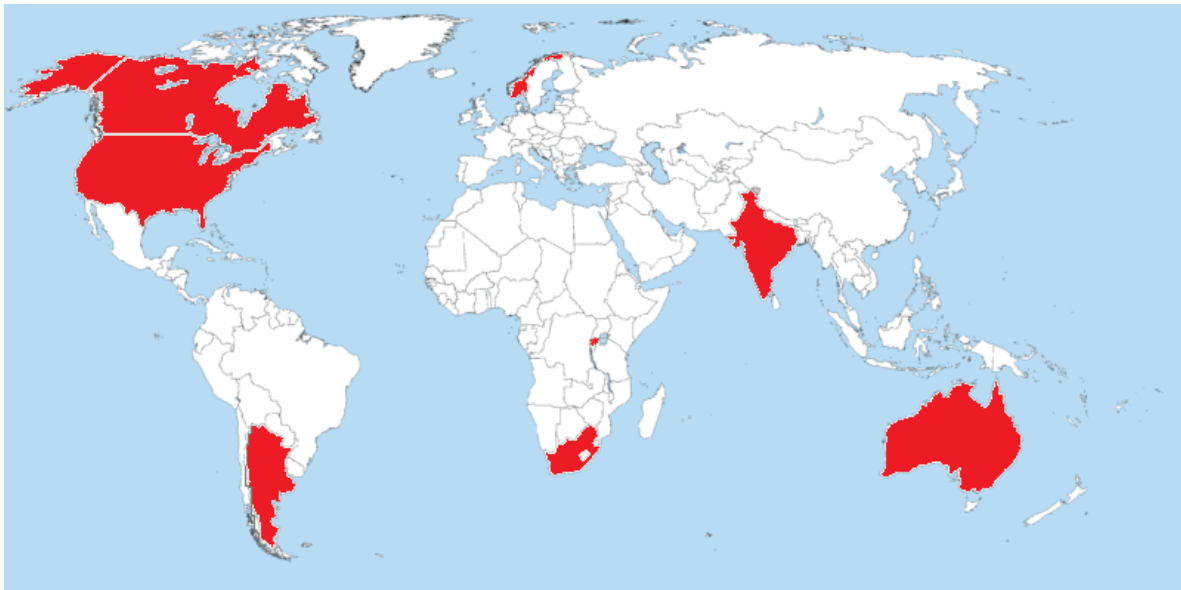


# Diabetes in children; a global comparative study



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

January 2014

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## **Abstract**

### **Aims**

The aim of this study was to explore if international guidelines concerning diabetes care for children are followed, and if they are not, why, and how practice is different from the international recommendations.

### **Methods**

As part of their compulsory student thesis, medical students from the University of Oslo, Norway, made a standardized questionnaire based upon the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines from 2009. A total of 16 hospitals in eight countries, six continents, were visited. Diabetes care in children was observed, and personnel at the hospitals were interviewed semi structured, based on the questionnaire.

### **Results**

Out of 16 hospitals visited, all but the hospital in Rwanda reported that they used guidelines in their care for children with diabetes. Some used national guidelines, but these were quite similar to the ISPAD guidelines. Lack of medical equipment would make it hard to follow guidelines in Rwanda even if tried. The proportion of children with diabetic ketoacidosis at diagnosis varied from six to 100%. All hospitals but the one in Rwanda used treatment goals measured in glycosylated hemoglobin. The amount of patients reaching the treatment goal varied from 9-65%. Countries without registries for incidence and complications generally reported a higher rate of success in diabetes care. At the same time some reported treating children with late diabetes complications.

### **Conclusions**

How the ISPAD guidelines are adhered to varies among different hospitals in different parts of the world. Guidelines give however, objective criteria for registering which again can, via benchmarking and increased awareness, improve diabetes care for children internationally.

## Acknowledgements

This student thesis was carried out between 2012 and 2014, while we were medical students at the Faculty of Medicine, University of Oslo, Norway.

First of all we want to thank our supervisors; Senior Consultant Torild Skrivarhaug MD PhD and Professor Borghild Roald MD PhD at Oslo University Hospital (OUS). They have read through our thesis several times and given us constructive feedback. They have helped us in finding literature and data, and guided us in evaluating references. They have also encouraged and supported us through motivational and educational guidance.

We thank the medical students who made the questionnaire that was used to interview the staff at the different hospitals visited; Lene Sleire, Martine Aurora Munkvold, Eirin Eilertsen, Natalie Lie Berntsen, Lise Haldorsen Willumsen and Idun Stenhammer Aanerød. Together with the medical students; Anja Kwetzinsky, Heidi Lehmann, Celine Urdal, Vigdis Skinnemoen Ottersen and Sigrid Børte, we also want to thank them for the work they did while visiting the different hospitals and accomplishing their student theses which our thesis is built on.

### Title of and links to student theses:

- Childhood diabetes in Argentina and Norway : A comparative study of guideline implementation and follow up: <https://www.duo.uio.no/handle/10852/34078>
- Diabetes: A Neglected Disease In Sub-Saharan Africa : a comparative study between Rwanda and Norway: <https://www.duo.uio.no/handle/10852/35666>
- The importance of a psychosocial focus in the treatment and management of type 1 diabetes in children : A comparison between Norway and Australia: <https://www.duo.uio.no/handle/10852/28834>
- The choice of insulin regimen and target of glycemic control in children with type 1 diabetes mellitus : - A comparative study of Canada and Norway: <https://www.duo.uio.no/handle/10852/29162>
- The Implementation of guidelines in clinical practice : Benefits and challenges exemplified by international guidelines in Diabetes Mellitus in children: <https://www.duo.uio.no/handle/10852/28831>
- Tygerberg Hospital in South Africa; A model for diabetes care in sub-Saharan Africa: <https://www.duo.uio.no/handle/10852/35657>
- Stigmatization of children with chronic diseases, exemplified by type 1 diabetes mellitus. : Differences between India and Norway: <https://www.duo.uio.no/handle/10852/29163>

We thank the informants and the contact persons at all of the hospitals visited.

## Abbreviations

### Hospital abbreviations

Abbreviation	Hospital	State/Province	Country	Region
KEM	King Edward Memorial Hospital	Pune	INDIA	ASIA
UTHB	University Teaching Hospital of Butare	Huye district	RWANDA	AFRICA
TH	Tygerberg Hospital	Western Cape	SOUTH AFRICA	
Hospital N. Lopez	Hospital Narciso Lopez	Buenos Aires	ARGENTINA	SOUTH AMERICA
Hospital de Niños	Hospital de Niños			
RCH	The Royal Children's Hospital in Melbourne	Victoria	AUSTRALIA	OCEANIA
ASH	Alice Springs Hospital	Northern Territory		
JHH	John Hunter Hospital	Newcastle, New South Wales		
BCCH	The British Columbia Children's Hospital	Vancouver, British Columbia	CANADA	NORTH AMERICA
SickKids	The Hospital for Sick Children	Toronto, Ontario		
CHOC	Children's Hospital of Orange County	California	UNITED STATES	
U of M	University of Minnesota Amplatz Children's Hospital	Minneapolis, Minnesota		
UUH (OUH)	Ullevål University Hospital (Oslo University Hospital)	Oslo	NORWAY	EUROPE
BCH	Buskerud Central Hospital	Drammen, Buskerud		
SUH	Stavanger University Hospital	Stavanger, Rogaland		
Elverum Hospital	Innlandet Hospital Elverum	Elverum, Hedmark		

## Medical abbreviations

ADA	American Diabetes Association
APEG	Australian Pediatric Endocrine Group
BG	Blood glucose
CDA	Canadian Diabetes Association
CSII	Continuous subcutaneous insulin infusion
DCCT	The Diabetes Control and Complications Trial
DIAMOND	The Diabetes Mondiale study
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
DR	Diabetes retinopathy
EURODIAB	The Europe and Diabetes study
GDP	Gross domestic product
HbA1c	Glycosylated hemoglobin
HLA	Human leukocyte antigen
IDF	International Diabetes Federation
IGT	Impaired glucose tolerance
ISPAD	The International Society for Pediatric and Adolescent Diabetes
MDI	Multiple daily injections
MIT	Multiple injection therapy
MODY	Maturity onset diabetes of the young
NCDR	Norwegian Childhood Diabetes Registry
OGTT	Oral glucose tolerance test
PDR	Proliferative diabetes retinopathy
SBGM	Self blood glucose monitoring
T1D	Type 1 diabetes
T2D	Type 2 diabetes
USA	The United States of America
WHO	World Health Organization

## Introduction

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (1). DM is classified into different types. Type 1 diabetes (T1D) is characterized by  $\beta$ -cell destruction, usually leading to absolute insulin deficiency. Type 2 diabetes (T2D) is a result of insulin resistance in peripheral tissue. It ranges from relative insulin deficiency because of predominantly insulin resistance to a predominantly defect of insulin secretion with or without insulin resistance. Maturity Onset Diabetes of the Young (MODY) and secondary diabetes, are examples of other less common forms of DM in children. Patient with T1D will die without insulin treatment (2, 3). In contrast, patients with T2D can remain undiagnosed for many years (4). Poorly managed diabetes might lead to serious complications affecting the heart and blood vessels, eyes, kidneys and nerves (2) and early death. Normalized blood glucose (BG) levels, blood pressure and cholesterol can help delay or prevent diabetes complications. Regular controls and monitoring for complications and risk factors are needed (5, 6).

DM is one of the most common non-communicable diseases globally. In 2011 there were 366 million adults between 20-79 years who had diabetes according to the International Diabetes Federation (IDF) (7). IDF also estimated DM to be the cause of as many as 4,6 million deaths in 2011 (8). Among children, T1D has the highest incidence of the different types of DM, with Finland and Sardinia reported to have the highest incidence and China and Venezuela the lowest (9). The increase is highest among the youngest children, especially in the European population. The number of children developing this form of diabetes every year has increased rapidly all over the world, except in Central America and West Indies where the trend is decreasing (9, 10). However, latest research regarding incidence of T1D for children in Finland highlighted two significant changes in the trends between 1980 and 2011. The research showed an annually increase until 2005, followed by a plateau until the end of 2011 (11). Also Sweden has reported a similar plateau in incidence from 2005-2007 (12) and Norway from 2004-2012 (13).



Despite the fact that insulin treatment is lifesaving, even today, almost a century after the discovery of insulin, the most common cause of death in a child with diabetes, in a global perspective, is lack of access to insulin. Many children also die before their diabetes is diagnosed (14, 15). The lack of access to insulin in parts of the world is not only due to insulin availability and cost. Also the availability of supplies to administer insulin play a role (16). Proper diabetes care; trained personnel, diagnostic and monitoring facilities are necessary to improve prognosis. This care is not sufficient in all countries (17).

Over the world, several organizations such as the World Health Organization (WHO), the American Diabetes Association (ADA), the Canadian Diabetes Association (CDA) and others have developed guidelines to ensure optimized diabetes management. In 1995, the International Society for Pediatric and Adolescent Diabetes (ISPAD) developed the first set of international guidelines for management of T1D among children and adolescent. The current guidelines (2011) have been developed by ISPAD and the IDF. While there is extensive evidence on the optimal management of T1D, unfortunately such care is not reaching all people who could benefit. Guidelines are one part of a process which seeks to address those problems (18).

## **Aims**

The aim of this study was to explore if international guidelines describing diabetes care for children are followed in various parts of the world. If they are not followed, we wanted to find out why and how practice is different from the international recommendations. Hopefully this study can contribute to exchange of knowledge about diabetes care and increase awareness about diabetes in children.

## Material and methods

During the spring of 2009 medical students from the University of Oslo, together with Professor Borghild Roald MD PhD and Senior Consultant Torild Skrivarhaug MD PhD, made a questionnaire based on the 2009 ISPAD guidelines. The questionnaire was designed to collect information about T1D in children less than 15 years of age. The questionnaire was composed of two parts. Part one was designed to map the conditions within a country concerning incidence, prevalence, mortality, national health, patient diabetes organizations and diabetes registers. Part two focused on specific hospitals concerning diabetes care in children; hospitalization, diagnostics, treatment and follow up, treatment goals, quality of life and mental health. As part of their compulsory student thesis, students visited 16 different hospitals in eight countries between 2009 and 2011. At the different hospitals diabetes care in children was observed. The daily routines and work was taken part in, and personnel working with children with diabetes were interviewed semi-structurally using the questionnaire. The questionnaire was translated to English before departure and again translated to Spanish with the help of Dr. Adriana Rousaus, specialist in diabetes and nutrition, at Hospital de Niños in Buenos Aires, Argentina. The questionnaire was sent to the interview subject via e-mail prior to the meeting. The interviews were tape recorded and transcribed shortly after the conversations had taken place. Part two of the questionnaire was answered by the interviews. Part one was answered mainly through search in literature and on the internet. The information gathered from the interviews contained no sensitive patient data. When the work with comparing data from the different countries started, an e-mail was also sent to the contact person at KEM (India) to collect missing data for the comparative study to be as complete as possible.

Oslo University Hospital (OUH) consists of what used to be four different hospitals in the city of Oslo. OUH includes Ullevål University Hospital (UUH), which was a single unit before the merge in 2009.

The medical students Anja Kwetzinsky and Heidi Lehmann visited Hospital de Niños in Buenos Aires and Hospital Narciso Lopes south of Buenos Aires in Argentina in January 2011. They also visited Buskerud Central Hospital (BCH) in Drammen, Norway, in December 2010.

Lene Sleire visited University Teaching Hospital of Butare (UTHB), Rwanda, in 2011 and UUH, Norway, in 2009.

Martine Aurora Munkvold visited OUH in 2009 prior to her departure to Australia. There she visited The Royal Children's Hospital (RCH) in Melbourne, Victoria, and Alice Springs Hospital (ASH) in Alice Springs, Northern Territory, in the autumn 2009. She visited John Hunter Hospital (JHH) in Newcastle, New South Wales, in 2010.

Eirin Eilertsen and Natalie Lie Berntsen visited The British Columbia Children's Hospital (BCCH), Vancouver, British Columbia, and The Hospital for Sick Children (SickKids), Toronto, Ontario in Canada during the summer of 2010. They also visited OUH in 2010.

Lise Haldorsen Willumsen and Idun Stenhammer Aanerød visited Children's Hospital of Orange County (CHOC), California, and University of Minnesota Amplatz Children's Hospital (U of M), Minnesota, both in the United States of America in 2009. In addition they visited UUH, also in 2009.

Celine Urdal visited Tygerberg Hospital (TH), Western Cape, South Africa in January 2010 and Stavanger University Hospital (SUH), Norway, in December 2011.

Vigdis Skinnemoen Ottersen and Sigrid Børte visited King Edward Memorial Hospital (KEM) in Pune, Maharashtra, India in 2010 and Elverum Hospital, Norway.

Our literature review derives from a non-systematic search in PubMed and from the ISPAD guidelines' references.

**Table 1:** Hospital addresses and number of subjects in out trial

Hospital name	Address	Number of children followed up
India, King Edward Memorial Hospital	489 Rasta Peth, Sardar Moodliar Road, Pune -411011	275
Norway, OUS/UUH	Kirkeveien 166, 0450 Oslo	303
Norway, SUH	Gerd-Ragna Bloch Thorsens gate 8, 4011 Stavanger	170
NOR, Buskerud Central Hospital	Dronninggata 28, 3004 Drammen	130
Norway, Elverum	Furnesvegen 26, 2380 Brumunddal	113
USA, Children's Hospital of Orange County	1201 W La Veta Ave, Orange, CA	1100
USA, University of Minnesota Amplatz Children's Hospital	2450 Riverside Ave, Minneapolis, MN 55454	250
Canada, British Columbia Children's Hospital	4480 Oak Street, Vancouver BC V6H 3N1	1023
Canada, Hospital for Sick Children	555 University Avenue, Toronto, Ontario	1000
Argentina, Hospital Narciso Lopez	O'Higgins - 1333, Buenos Aires	26
Argentina, Hospital de Niños	Granada 4175 San Justo, 1754, Buenos Aires	600
Rwanda, University teaching hospital of Butare	Huye District, Butare Town	Data not available
South Africa, Tygerberg Hospital	Francie van Zijl Avenue, Tygerberg, 7505	137
Australia, The Royal Children's Hospital in Melbourne	50 Flemington Road, Parkville Victoria 3052	1700
Australia, Alice Springs Hospital	Gap Rd, Alice Springs NT 0870	8
Australia, John Hunter Hospital, Newcastle	2 Lookout Rd, New Lambton Heights NSW 2305	363
Total:		7198

At KEM (India), 829 children with T1D were registered, but 250-300 children were reported to attend regular follow-ups.

Our data could not be collected without the help from our informants at the visited hospitals.

**Table 2:** Informants at the hospitals visited

Hospital	Informants and contact persons
King Edward Memorial Hospital	Professor Chittaranjan Yajnik MD Sonali (unknown profession)
University Teaching Hospital of Butare	Professor J.W.O. Iraka
Tygerberg Hospital	MD Ekkekard Zöllner Diabetes nurse Fiona Liebeuberg, RN
Hospital Narciso Lopez	MD Lidia Caracotche
Hospital de Niños	MD Adriana Rousaus MD Liliana Trifone
The Royal Children's Hospital in Melbourne	Professor George Werther MD Professor Fergus Cameron MD Diabetes educator nurse Andrew Boucher, RN
Alice Springs Hospital	MD Rose Fahy Diabetes educator Glynis Dent
John Hunter Hospital	Professor Patricia Crook
The British Columbia Children's Hospital	MD Daniel Metzger
The Hospital for Sick Children	MD Denis Daneman Different members of the diabetes team
Children's Hospital of Orange County	MD Mark Daniels
University of Minnesota Amplatz Children's Hospital	Professor Antoinette Moran MD Diabetes educator nurse Shannon Beasley, RN Diabetes educator Anne E Jackson
Ullevål University Hospital (Oslo University Hospital)	Diabetes nurse Siv Janne Kummernes, RN MD Torild Skriverhaug, PhD
Buskerud Central Hospital	Diabetes nurse Åse Løkkeberg Figenschau, RN Diabetes nurse Helene Wang, RN
Stavanger University Hospital	Diabetes nurse Liv Haram, RN
Innlandet Hospital Elverum	Head of the pediatric department Jon Grøtta, MD Diabetes nurse Tove Berg, RN

Data from Norwegian hospitals have also been provided by the Norwegian Childhood Diabetes Registry (NCDR). NCDR was established in 2006. Registration is voluntary. Children and/or parents have to give their written consent at diagnosis. When the patient turns 18 years old, he or she must give their consent again. Since 2008, all hospitals in Norway have participated in the registration. In 2011, 2568 children were in the register. That equals 95% of children with diabetes treated in pediatric departments in Norway. One of NDCR's main tasks is to analyze and report back results to the hospitals participating in the register. All the pediatric departments are benchmarked on results and screening procedures. The aim is to promote quality of the care for children and adolescent with T1D in Norway.

## **Part 1: Literature review on diabetes mellitus in children and adolescents**

### **Type 1 Diabetes**

#### **Epidemiology for type 1 diabetes**

T1D is one of the most common endocrine and metabolic conditions in childhood. The total child population of the world (0-14 years) was in 2010 1,9 billion. Approximately 480 000 children have T1D, which equates to 0.02%. 76 000 new cases are diagnosed every year. This reflects an annual incidence of 3% (10). Two international collaborative projects, the Diabetes Mondiale study (DiaMond) (9) and the Europe and Diabetes study (EURODIAB) (19) have monitored trends in incidence. The incidence of T1D has increased all over the world (9), but it seems that the increase has been strongest in low incidence countries (20). The encouraging observation in some recent studies is that the incidence of childhood T1D in some countries has ceased to increase after a period of accelerated increase (11-13). Even though T1D is diagnosed in all age groups, it seems that the incidence increases with age until puberty (10-14 years) (9). The incidence of T1D among children under the age of 14 years varies greatly between countries and between different ethnic populations within countries (9). Finland has the highest recorded incidence in children < 15 years of 64.9 per 100 000 person-years (in 2006) (11). China has among the lowest incidences between 0.1 and 4.5 per 100 000 person-years (in 1990-1996). Norway, Canada, the USA and Australia are high incidence countries, while Argentina is intermediate incidence and India and countries in Sub-Saharan Africa are low incidence countries (9).

#### **Etiology and pathogenesis for type 1 diabetes**

The characteristic feature of T1D is the selective destruction of the insulin producing  $\beta$ -cells of the pancreas. This leads eventually to complete insulin deficiency. The etiology is not completely understood, but serological markers are present in 85-90% of individuals when hyperglycemia is

detected (1, 21). These markers include islet cell antibodies, GAD, IA-2, IA-2 $\beta$  and insulin autoantibodies. Susceptibility to autoimmune T1D is determined by multiple genes, human leukocyte antigen (HLA) genes having the strongest known association. The environmental triggers (chemical and/or viral) which initiate pancreatic beta cell destruction remain largely unknown, but the process usually begins months to years before the manifestation of clinical symptoms (1). T1D becomes clinically symptomatic when approximately 90% of pancreatic  $\beta$ -cells are destroyed (22).

## Type 2 Diabetes

T2D is a growing disease among children and adolescents. It used to be a disease among the middle-aged and older generation, but in the latest decade more young people have been affected. Obese children and adolescents with newly onset T1D can be misdiagnosed having T2D (23). Both genetics and lifestyle are factors that are involved in the pathogenesis of T2D. A positive family history of T2D gives a two to fourfold increased risk to develop T2D, and 15% to 25% of first-degree relatives of persons with T2D develop impaired glucose tolerance (IGT) or diabetes (24). Obesity and lack of physical activity is also a big contribution to the increased incidence of T2D in the world (25).

T2D is a condition which results in both hyperglycemia and hyperinsulinemia. This is due to insulin resistance in peripheral tissue, reduced ability to glucose transport over the cell membranes, increased glucose production by the liver and deranged insulin secretion by the pancreatic beta cells. Over time, usually a few years, the pancreatic beta cells will be exhausted and fail to produce insulin (25, 26).

Treatment for T2D depends on the symptoms, severity of the hyperglycemia and whether ketosis is present or not. To control BG levels it may be sufficient to make a lifestyle change with weight-loss through physical activity and dietary management. Along with normalization of the BG it is important to control co-morbidities, such as hypertension, dyslipidemia, nephropathy, retinopathy

and hepatic steatosis. If control of BG is not achieved by lifestyle change alone, pharmaceutical therapy such as oral tablets to increase insulin sensibility must be added. Failure of treatment after three months with oral tablets, indicate the need to start insulin therapy for T2D patients (23).

## Diagnostic criteria

ISPAD diagnostic criteria for T1D are based on both BG measurements and the presence of symptoms. Presenting symptoms of diabetes in children are usually polyuria, polydipsia, weight loss and blurring of vision in association with glycosuria and ketonuria. Four ways to diagnose diabetes are possible (1, 27):

1. Symptoms of diabetes plus casual plasma glucose concentration  $\geq 11.1$  mmol/l (200mg/dl).  
Casual is defined as any time of day without regard to time since last meal.  
**or**
2. Fasting plasma glucose  $\geq 7.0$  mmol/l ( $\geq 126$  md/dl). Fasting is defined as no caloric intake for at least 8 hours.  
**or**
3. 2 hour post load glucose  $\geq 11.1$  mmol/l ( $\geq 200$  mg/dl) during an oral glucose tolerance test (OGTT). The test should be performed as described by WHO (28), using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water or 1.75 g/kg body weight to a maximum of 75g.  
**or**
4. Glycosylated hemoglobin (HbA1c)  $\geq 6.5\%$  (Presented in the 2011 ISPAD guidelines).

ADA and CDA have similar diagnostic criteria for T1D (29, 30).



## Treatment

Children and adolescents with T1D require lifelong insulin substitution from the time of diagnosis. Before the discovery of insulin in 1921, few patients with T1D survived more than a year or two because of the acute effects of the disease (31). The aim with insulin treatment is to replace the missing physiological insulin and have as close to normal glycemic control as possible. Since insulin is destroyed in the gastrointestinal tract it must be given as injections, either subcutaneously or intravenously. Several insulin formulations and regimes are available. The choice depends on the resources available and the children and their families preferences. It is important to optimize compliance to prevent the imbalance between hypo- and hyperglycemia which results in the acute and late complications of the disease (32, 33).

Three different types of insulin may be used. They are classified by their onset, peak and duration of action:

- Rapid-acting and short-acting types.
  - Usually given before meals as a bolus based on the BG level and the carbohydrate content of the food.
  - When delivered by continuous subcutaneous infusion via an insulin pump they provide a basal insulin level.
- Intermediate-acting type:
  - Usually given two or three times a day.
  - Can also be given in combination with long-acting insulin.
- Long-acting type:
  - Usually given once or twice a day.
  - Provides a basal insulin level in the fasting state that suppresses glucose production by the liver and maintains a glucose level near normal.

Insulin can be administered through syringes, pen or insulin pump.

Different insulin regimens are available for adolescents and children. ISPAD recommends at least two injections of insulin a day and that all children should have available rapid – acting or regular insulin for crisis management (33).

- Conventional regimen:
  - “Two injections daily” or “three injections daily” regimen.
  - Administration of an intermediate-acting insulin at least twice a day, at breakfast and either at dinner or bedtime, combined with at two or three times a day injection of rapid – or short- acting insulin also at breakfast or dinner, sometimes at lunch or bedtime depending on the BG concentrations (32, 33).
  - This traditionally regimen is fixed. The children and their family have to live after a planned schedule and adjust meals and physical activity to fit this regimen.
- Intensive regimen, the basal bolus concept, multiple injection therapy (MIT):
  - Multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII).
  - The aim with this regimen is to imitate normal physiologic insulin secretion by providing a basal insulin level through the day with bolus of rapid-or short acting insulin before meals and snack to prevent postprandial elevation of BG.
  - The bolus is based on the carbohydrate content of the meal, physical activity level after the meal and current BG level.
  - This gives more flexibility than a conventional regimen, but depends on a stricter commitment from the children and their family with increased BG monitoring, carbohydrate counting, judging the impact of exercise on insulin requirements and increased frequency of insulin administration to obtain the benefits.
  - MDI can require six to seven injections daily, and therefore insulin pump (CSII) is often preferred (32).

The Diabetes Control and Complications Trial (DCCT) compared the intensive regimen with the conventional regimen through a randomized clinical trial over a mean period of 6.5 years, with regard to their effect on the microvascular and macrovascular complications of T1D. Results of the trial showed that intensive therapy effectively delays the onset and slows the progression of retinopathy, nephropathy and neuropathy in patients with T1D (5).

Insulin treatment is lifesaving for children and adolescents with T1D, but to achieve optimal effect and prevent long term complication a comprehensive diabetes management must be followed. This includes education, nutritional management, physical activity, rules for sick days and psychosocial support (33). There are large differences in the diabetes management all over the world. In some countries this is free, including self-care tools and insulin, but in others the patients must pay 40-60% of the health care expenditures themselves (10, 34).

## **Treatment target**

Self blood glucose monitoring (SBGM) is an important tool to better daily glycemetic control and reach treatment target for T1D patients. SBGM gives immediate information about the BG level, depending on this the patients and their caregivers can immediately adjust insulin injections to optimal treat. Frequency of SBGM correlates with glycemetic control and should be performed four to six times a day. BG targets with the goal of achieving as normal as possible BG (3.6-5.8 mmol/L) and avoiding severe hypoglycemia and also mild to moderate hypoglycemia, is individually determined for each child (35).

HbA1c is used as a long-term monitor for glycemetic control and late complications (5). HbA1C is hemoglobin to which glucose is attached. Through the lifecycle of the red blood cell of approximately 120 days glucose get irreversible bound to the hemoglobin, and HbA1C can therefore be used as an indicator for the average BG level over the past three months (35).

DCCT and other studies have shown that through better glycemic control measured with a low HbA1c the patients will get fewer or delayed microvascular complications. Based on this ISPAD recommend the target HbA1C for age-groups up to 18 years to be < 7.5% (5, 35).

ADA and CDA recommends considering age when calculating glycemic goals for children and adolescents with T1D to prevent the increased risk of hypoglycemia associated with lower HbA1C.

**Table 3:** American Diabetes Association recommendations for target glycosylated hemoglobin (HbA1c) for children and adolescents with type 1 diabetes (36)

Age (years)	HbA1c (%)	Rationale
< 6	< 8.5	<ul style="list-style-type: none"> <li>• Caution regarding vulnerability to hypoglycemia and insulin sensibility.</li> <li>• May be unpredictable in dietary intake and physical activity.</li> <li>• Reasonable with a lower target (&lt; 8.0%) if achieved without excessive hypoglycemia.</li> </ul>
6-12	< 8	<ul style="list-style-type: none"> <li>• Caution regarding vulnerability to hypoglycemia.</li> <li>• Reasonable with a lower target (&lt; 7.5%) if achieved without excessive hypoglycemia.</li> </ul>
13-19	< 7.5	<ul style="list-style-type: none"> <li>• Reasonable with a lower target (&lt; 7.0%) if achieved without excessive hypoglycemia.</li> </ul>

**Table 4:** Canadian Diabetes Association recommendations for target glycosylated hemoglobin (HbA1c) for children and adolescents with type 1 diabetes (37, 38)

Age (years)	HbA1c (%) 2013	HbA1c (%) 2008	Considerations
< 6	< 8.0*	< 8.5	Caution is required to minimize hypoglycemia because of the potential association between severe hypoglycemia and later cognitive impairment.
6-12	≤ 7.5**	≤ 8.0	Targets should be graduated to the child's age
13-18	≤ 7.0	≤ 7.5	Appropriate for most adolescents.

\* Consider target of < 8.5% if excessive hypoglycemia occurs.

\*\* Consider target of < 8.0% if excessive hypoglycemia occurs.

## Complications

### Acute complications

Patients with T1D on insulin treatment can experience that the BG can become either too high or too low. If too much insulin is given the patient becomes hypoglycemic and can eventually become unconscious with or without convulsions. With total or relative lack of insulin the patient can become hyperglycemic and reach a state of diabetic ketoacidosis (DKA). Both conditions are associated with both short term (39) and serious life -threatening challenges (40).

**Table 5:** The biochemical criteria for diabetic ketoacidosis used by ISPAD\*and ADA\*\* (41):

	ISPAD*	ADA**
Hyperglycemia	Blood glucose > 11 mmol/L (≈200 mg/dl)	Blood glucose: >14 mmol/L (> 250 mg/dl)
Venous pH	< 7.3	< 7.3
Bicarbonate	< 15 mmol/L	-
Ketones	Ketonemia and ketonuria	Ketonemia and ketonuria

\*International Society for Pediatric and Adolescent Diabetes \*\*American Diabetes Association

Australian Pediatric Endocrine Group (APEG) follow the criteria stated by ISPAD(42). CDA acknowledges the same characteristics and biochemical values as ISPAD and ADA(30).

### Late complications

After the introduction of insulin in treatment, diabetes is no longer an acute threat to life. It is still associated with increased morbidity and mortality of other reasons, especially after many years of disease. Elevated plasma glucose predisposes to micro- and macrovascular complications such as retinopathy, nephropathy, neuropathy, angiopathy and myocardial- and cerebrovascular insults. Intensive diabetes treatment, with as close to normal as possible BG, decreases the incidence of microvascular- (5) and macrovascular complications (43). Screening for late complications is

important in patients with T1D because the microvascular complications have early, asymptomatic and reversible stages before the end stage damages (5, 44).

**Table 6:** ISPAD\* recommendations from 2009 concerning screening for microvascular complications in children with type 1 diabetes (45)

	<b>When to commence screening</b>	<b>Screening methods</b>
<b>Retinopathy</b>	Annually from age 11 years with 2 years diabetes duration and from 9 years with 5 years diabetes duration	Fundal photography or mydriatic ophthalmoscopy (less sensitive)
<b>Nephropathy</b>	Annually from age 11 years with 2 years diabetes duration and from 9 years with 5 years diabetes duration	Urinary albumin/creatinine ratio or first morning albumin concentration
<b>Neuropathy</b>	Unclear	History and physical examination

\*International Society for Pediatric and Adolescent Diabetes

The ISPAD/IDF guidelines from 2011 recommend that peripheral and autonomic neuropathy should be assessed by history and physical examination from age 11 years with two years diabetes duration.

Diabetic retinopathy (DR) presents as non-proliferative DR which is the first reversible stage of eye affection from DM. It will, without intervention, progress to proliferative diabetes retinopathy (PDR) which is an irreversible threat to vision. The severity of DR is related to higher levels of HbA1c (46).

When DR has progressed to PDR, laser treatment called photocoagulation has a good chance of reducing further vision loss (47). If discovered in the phase of microalbuminuria; tougher treatment for hypertension, hyperglycemia and the microalbuminuria itself can prevent or delay progression to end stage renal failure (48, 49).

**Table 7:** Definition of diabetic nephropathy (50)

	<b>Definition</b>
<b>Microalbuminuria*</b>	Albumin excretion rate (AER) between 20 and 200 µg/min or AER 30 – 300 mg/24 h in 24-h urine collections <b>or</b> Albumin concentration (AC) 30 – 300 mg/L (on early morning urine sample) <b>or</b> Albumin/creatinine ratio (ACR) 2.5 – 25 mg/mmol or 30 – 300 mg/gm (spot urine) in males and 3.5 – 25 mg/mmol in females (because of lower creatinine excretion)
<b>Proteinuria*</b>	Persistent proteinuria greater than 500 mg/24 hours or albuminuria greater than 300 mg/24 hours <b>or</b> Albumin concentration (AC) > 300 mg/L <b>or</b> Albumin/ creatinine ratio (ACR) > 25 mg/mmol

\*In two out of three consecutive urine samples

## Part 2: Diabetes in a global perspective

WHO have listed diabetes along with other non-communicable diseases such as; cancer, cardiovascular diseases and chronic respiratory diseases as the leading cause of mortality in the world (51). Diabetes is a chronic disease that gives a social and economic burden to the affected individuals and their families (10).

### Population and economy

Our study compares data from eight countries which all is different in social and economic development. Gross domestic product (GDP) per capita can be used as an indicator for the country's standard of living. The World Bank's definition of GDP is: "the sum of gross value added by all resident producers in the economy plus any product taxes and minus any subsidies not included in the value of the products. It is calculated without making deductions for depreciation of fabricated or for depletion and degradation of natural resources". GDP per capita is GDP divided with midyear population in the country. Norway is one of the world's richest country with a GDP per capita of 100 US\$ and a population just over 5 million people in 2012. India, on the other hand, had a population counting 1.2 billion people and a GDP per capita on 1.5 US\$ in 2012. Four of the countries in this study; Norway, Australia, Canada and the USA are defined as high income countries with a GDP per capita ranging from 50 to 100 US\$. The other four countries; Argentina, South Africa, India and Rwanda are defined as middle- and low- income countries with GPD per capita from almost 0.6 to 11.5 US\$ (52).



**Table 8:** Population and gross domestic product in 2012 in studied countries

Country	Population (*)	Overall proportions of ethnicities (**)	Gross domestic product (GDP) per capita (current US\$ 05.09.13) (*)	Gross domestic product (GDP) (Current US\$ per 05.09.13), in 10 <sup>9</sup> , billion (*)
Norway	5,018,869	Norwegian 94.4% (includes Sami, about 60,000), other European 3.6%, other 2% (2007 estimate)	99.6	499
Argentina	41,086,927	White (mostly Spanish and Italian) 97%, mestizo (mixed white and Amerindian ancestry), Amerindian, or other non-white groups 3%	11.6	475
Australia	22,683,600	White 92%, Asian 7%, aboriginal and other 1%	67	1520
Canada	34,880,491	British Isles origin 28%, French origin 23%, other European 15%, Amerindian 2%, other, mostly Asian, African, Arab 6%, mixed background 26%	52	1821
India	1,236,686,732	Indo-Aryan 72%, Dravidian 25%, Mongoloid and other 3% (2000)	1.5	1841
Rwanda	11,457,801	Hutu (Bantu) 84%, Tutsi (Hamitic) 15%, Twa (Pygmy) 1%	0.6	7
South-Africa	51,189,306	Black African 79%, white 9.6%, colored 8.9%, Indian/Asian 2.5% (2001 census)	7.5	384
USA	313,914,040	White 79.96%, black 12.85%, Asian 4.43%, Amerindian and Alaska native 0.97%, native Hawaiian and other Pacific islander 0.18%, two or more races 1.61% (July 2007 estimate) <sup>5</sup>	50	15684

(\*) Numbers from The World Bank(53)

(\*\*) The World Factbook, Central Intelligence Agency (54) <sup>5</sup>A separate listing for Hispanic is not included because the US Census Bureau considers Hispanic to mean persons of Spanish/Hispanic/Latino origin including those of Mexican, Cuban, Puerto Rican, Dominican Republic, Spanish, and Central or South American origin living in the US who may be of any race or ethnic group (white, black, Asian, etc.); about 15.1% of the total US population is Hispanic

## Health economy

All the member states of WHO made in 2005 a commitment to work for universal health coverage. They believed that all people should have access to the health services they needed without the risk of impoverishment and financial ruin. WHO stated that working towards universal health coverage is a powerful mechanism for achieving better health and well-being, and for promoting human development (55). In the USA, the GDP was calculated to be approximately 15500 billion US\$ in 2012. Their total expenditure on health was approximately 18% of their GDP in 2011. The same year, 46% out of total expenditure on health was general governmental expenditure. Along with India and South Africa, the USA is one of the countries in our study where the health expenditures are less financed by the general governmental expenditures. India's GDP was approximately 1800 billion US\$ in 2012. In 2011 they used 4% of their GDP on health expenditures, and out of the total expenditure on health, 31% was general governmental financed. South Africa's GDP in 2012 was approximately 384 billion US\$. Total expenditures on health in this country were 8.5% of GDP in 2011. Out of their total expenditure on health in 2011, 48% was general governmental expenditures. In our study, the countries where most of the total expenditure of health is financed from the general government expenditures are Norway, Canada, Australia and Argentina. Their general governmental expenditure was respectively 86%, 70%, 66% and 61% of the total expenditure on health in 2011.

**Table 9:** Health economics in 2011 in studied countries <sup>(\*)</sup>

Country	Total expenditure on health as a % of the GDP	General government expenditure on health as % of total expenditure on health	General government expenditure on health as % of total government expenditure
Norway	9	86	18
Argentina	8	61	20
Australia	9	69	17
Canada	11	70	18
India	4	31	8
Rwanda	11	57	24
South-Africa	8.5	48	13
USA	18	46	20

<sup>(\*)</sup> Numbers from the World Health Organization (56)

## Mortality and average life expectancy

Infant mortality -, child mortality- and life expectancy rates also reflect the degree of development in a certain country. Infant mortality rate is the number of infants dying before reaching one year of age, per 1000 live births in a given year. India, estimated with 47 deaths/ 1000 live births in 2011, had the highest infant mortality among the countries in our study that year. Norway is on the other side of the scale with 3 deaths/1000 live births. Child mortality rate is the number of children who die before the age of five, per 1000 live births per year. In 2011 in India, the child mortality rate was 61 deaths/ 1000 live births. The child mortality rate in Norway the same year was 3 deaths/ 1000 live births. Estimated life-expectancy rate in 2011 was calculated to be 67 years for women and 64 years for men in India. In Norway, the rate was estimated to be 84 for women and 79 for men the same year.

In 2011, Australia, Canada and the USA also had low infant mortality, like Norway. Their infant mortality rate was 4, 5 and 6 deaths/1000 live births respectively. Rwanda and South Africa with 38 and 35 deaths/ 1000 live births had lower infant mortality rate than India, but it is still defined as high, and is much higher than the other countries in our study. The infant mortality rate in Argentina was 13 deaths / 1000 live births in 2011.

The child mortality rate follows the same trend as the infant mortality rate among the countries in our study in 2011. Australia, Canada and the USA had a child mortality rate at 5, 6 and 7 deaths/ 1000 live births respectively. In Rwanda and South Africa the rate was 54 and 47 deaths/ 1000 live births. The child mortality rate in Argentina was 14 deaths/ 1000 live births.

The country with the highest life expectancy rate in 2011 was Australia with 84 years for women and 80 years for men. Australia was followed by Norway, Canada, the USA and Argentina. The life expectancy rate in these countries varied from 80 – 84 years for women and 72 – 79 for men. The country with the lowest life expectancy rate in 2011 was South Africa with 53 for women and 52

men. Along with South Africa, Rwanda and India was the countries with the lowest life expectancy in 2011.

**Table 10:** Average life expectancy and mortality in 2011 in studied countries<sup>(\*)</sup>

Country	Average life expectancy for women, (years)	Average life expectancy for men, (years)	Infant mortality deaths/ 1,000 live births	Child mortality deaths under 5 years/ 1,000 live births
Norway	84	79	2.6	3.1
Argentina	80	72	12.6	14.1
Australia	84	80	4.1	4.5
Canada	83	79	4.9	5.6
India	67	64	47.2	61.3
Rwanda	57	54	38.1	54.1
South-Africa	53	52	34.6	46.7
USA	81	76	6.4	7.5

<sup>(\*)</sup> Numbers from the World Bank (57)

## National health

WHO follows the situation and trends on the world's health workforce. In The World State Report 2006 – “Working together for health”, they stated that there are an unevenly distribution of health workers across the globe. The smallest health workforce is in the countries with the highest burden of disease, while the countries with less needs have the highest numbers of health workers. Less than 1% of the world's financial resources are in the African region and they suffer from more than 24% of the global burden of disease. Nevertheless, this region only has 3% of the world's health workforce (58). Table 11 shows the physician density per 1000 population in the countries in our study. Norway, Argentina, Australia, Canada and the USA had the highest density. India and the Sub-Saharan countries, Rwanda and South Africa, had the lowest density of physicians.

The national health systems are different in all the eight countries studied. Medical expenditures for individuals with diabetes are two to three times more than for those without diabetes (59). Several

studies have shown that the disease presents a high burden, not only for the individuals, but also for the society. This is due to costs caused by loss of productivity from disability and premature mortality (34, 60, 61). Some of the countries had a health system that finances all or parts of treatment necessary for children and adolescents with T1D. Table 11 gives an overview of the financial support an individual with diabetes could get in the countries in our study.

**Table 11:** Physician density and national health support systems for diabetes in studied countries

Country	Physicians density (physicians/ 1,000 population) <sup>1</sup> in 2006	Are there any support system that finance the costs associated with diabetes medication and equipment?	If there are any support systems; which medication is financed?	If there are any support systems; which materials is financed?	If there are any support systems; does the patient have to pay anything? If so, how much %
Norway	3.13	Yes. All citizens are member of the Norwegian Health Insurance. This gives all citizens equal right to help services <sup>2</sup> .	Insulin <sup>2</sup> antidiabetic drugs and glucagon.	Syringes, needles, insulin pen, insulin pump, materials for the insulin pumps, home BG meters, BG test strips, finger-pricking devices, lancets for finger-pricking, SBGM devices, urine sticks <sup>2</sup> .	It is a deductible on health supplies and support on 1980 nok (ca 330 USD) per year. When reached this amount health support and supplies is free of charge <sup>2</sup> .
Argentina	3.01	Yes, public health services are free for all individuals making use of them regardless of health insurance <sup>3</sup> .	Insulin <sup>4</sup> .	Pharmaceutical industry provides BG meter and strips to measure BG x3 per day <sup>5</sup> .	No data available.
Australia	2.47	Yes, if registered in the National Diabetes Service Scheme (NDSS) <sup>5</sup> or having a Health Care Card <sup>6</sup> .	Health care card and Pharmaceutical Benefits Scheme gives cheaper prescription medicine <sup>6</sup> .	Subsidized testing strips for checking BG levels, free insulin syringes and pen-needles (if require insulin or non-insulin inject able BG lowering medications), information services on managing life with diabetes subsidized insulin pump consumables (IPCs) <sup>5</sup> .	No data available.
Canada	2.14	Yes, but data for criteria not available.	Insulin.	No data available.	No data available.

**Table 11:** Physician density and national health support systems for diabetes in studied countries

Country	Physicians density (physicians/ 1,000 population) <sup>1</sup> in 2006	Are there any support system that finance the costs associated with diabetes medication and equipment?	If there are any support systems; which medication is financed?	If there are any support systems; which materials is financed?	If there are any support systems; does the patient have to pay anything? If so, how much %
India	0.60	Yes, philanthropic: Individual donations, Pharmacy companies, non-governmental organizations. The support is for selected patients depending on age, socio-economic status etc <sup>7</sup> .	Insulin <sup>7</sup> .	Glucometers, stripes, injection devices (pens, syringes), patient education material, demo kits, material for different recreational activities and events <sup>7</sup> .	Yes, majority of the times, partly. (Up to 50%) <sup>7</sup> .
Rwanda	0.05	No.	Some private organizations provide free insulin. Patients still has to pay the OPC registration fee of 1 EUR once a month to get the insulin prescription.	No data available.	No data available.
South – Africa	0.77	Yes <sup>8</sup> .	Insulin, antidiabetic drugs and glucagon <sup>8</sup> .	Syringes, needles, insulin pen, home BG meters, BG test strips, finger-pricking devices, lancets for finger-pricking and urine sticks to check for ketonuria <sup>8</sup> .	Child <5 years: parents do not need to pay anything for the medication and the equipment. >5 years: parents have to pay. How much depends on they having a job or not and the income <sup>8</sup> .
USA	2.56	No data available.	No data available.	No data available.	No data available.

<sup>1</sup>The World Health Report 2005, WHO(62).<sup>2</sup>The Norwegian Diabetes Association(63)<sup>3</sup>UN Refugee Agency(64). Public hospitals provide care to the poor with or without insurance, subsidizes obras sociales and occasionally those with high income and private insurance who preferred a particular institution or personnel(65).<sup>4</sup>Personal communication with Dr. Lidia Caracotche.<sup>5</sup>Diabetes Australia(66)<sup>6</sup>Australien Government, Human Service Department(67). <sup>7</sup>Personal communication with professor Chittaranjan Yajnik, Pune. <sup>8</sup>Personal communication with the pediatrician endocrinologist doctor Ekkekard Zöllner.

## Incidence of Type 1 Diabetes

In 2007, IDF estimated incidence of T1D among children less than 15 years of age in countries all over the world, Table 12. According to the estimates from IDF, Norway had the highest incidence of T1D with 27.9 per 100 000 among the countries in our study. Norway was accompanied by Canada with

21.7 per 100 000, Australia with 20.9 per 100 000 and the USA with 16.1 per 100 000 as high incidence countries. The country in South America, Argentina, had an intermediate incidence on 6.8 per 100 000. The Asian country, India, had the lowest incidence of the countries who had data in our study with 4.2 per 100 000. This trend of incidence among the countries follows the trend found by the DIAMOND project group (9). The DIAMOND study points out that in their data they lack information about incidence in the countries with the largest child populations and the lowest GDP. When 1 out of 10 children die before the age of five it is difficult to get reliable data on the incidence of diabetes among children. This is the situation for the countries in Africa and South- and East Asia. When the children die of acute respiratory infections or diarrhea this can mask the symptoms of diabetes and whether the children had diabetes or not, remain unrecognized (9).

Table eight; population and gross domestic product in 2012 in studied countries, shows that there are different ethnic groups in the studied countries. Genetics and environmental factors influence the incidence of DM, both T1D and T2D(9).

**Table 12:** International Diabetes Federation incidence on type 1 diabetes (T1D) in children 0-14 years, for 2007 <sup>(\*)</sup>

Country	Incidence of T1D among children <15 years of age
Norway	27.9 per 100 000
Argentina	6.8 per 100 000
Australia	20.9 per 100 000
Canada	21.7 per 100 000
India	4.2 per 100 000
Rwanda	No data available
South-Africa	No data available
USA	16.1 per 100 000

<sup>(\*)</sup> IDF estimates for 2007 (68).

## Prevalence of Type 1 Diabetes

According to Table 12, Norway was estimated to have the highest incidence of T1D among children less than 15 years of age in 2007. The country also had the highest percentage of the childhood population between 0 – 14 years with T1D in 2007, Table 13. However, Norway, which is a small country in population compared to India, had the lowest number of children, less than 15 years of age, with T1D in our study. India which had the lowest incidence of T1D in our study had the highest population of children between 0 - 14 years, and therefore the highest number of children under 15 years of age with T1D. The prevalence numbers are from the IDF Diabetes Atlas estimates for 2007. Due to lack of national registers, which register prevalence of T1D, we could only find official data from Norway, Canada and the USA. The data from Canada and the USA do not distinguish between T1D and T2D or give data on the age group less than 15 years of age as a whole.

**Table 13:** Prevalence of diabetes mellitus in studied countries

COUNTRY	TOTAL PREVALENCE OF TYPE 1 DIABETES IN CHILDREN <15 YEARS		
	IDF estimates for 2007 (000'S) <sup>1</sup>	IDF estimated prevalence per population 0 -14 years,~ %, 2007 <sup>2</sup>	NATIONAL DIABETES REGISTER
Norway	1,6	0.18	Ca 2500 <sup>3</sup>
Argentina	4,4	0.04	No data available
Australia	5,2	0.13	No data available
Canada	8,4	0.15	2008/2009, T1D and T2D, 1-9 years: 0.2 %, 5201 children. 10-19 years: 0.5 %, 20492 children. > 1 - < 20 years: 0.3 %, 25693 children and adolescents <sup>4</sup> .
India	92,3	0.003	No data available
Rwanda	0,2	0.05	No data available
South-Africa	5,0	0.03	No data available
USA	62,6	0.10	No data available form register *215 000 <20 years have DM, T1D or T2D. 2010. 0.26 % of all people in this age group in US <sup>5</sup> .

<sup>1</sup>IDF estimates for 2007(68). <sup>2</sup>Estimated prevalence per 2007 divided to estimated child population 0 – 14 years. Numbers are rounded to two decimals. <sup>3</sup>Personal communication with Senior Consultant Torlid Skriverhaug MD PhD. <sup>4</sup>Public Health Agency Canada (69). <sup>5</sup>National Diabetes Factsheet, US(70).



## Patient organizations

In all the countries in our study there were patient organizations for people with T1D. All the patient organizations were members of IDF. There were differences among the organizations in the studied countries. However, all of them worked for better knowledge and treatment of T1D among people with T1D, their families and among health personnel. Some of the organizations also arranged diabetes camps and different social happenings, and had local organizations to support their members where they live. Social networking and support for children and adolescents with T1D could be important for better compliance in treatment and also better social wellbeing. Patient organization for people with chronically diseases is an important tool to complement the treatment and follow up from the national health care systems. Patient organization for patient with T1D may also be an important tool to integrate use of ISPADs guidelines for children and adolescents with T1D.

**Table 14:** Patient organizations for patients with diabetes mellitus in the countries studied.

COUNTRY	PATIENT ORGANIZATIONS		
	National organizations for patients with T1D? <sup>1</sup>	Local organizations for patients with T1D?	Support offered the children and their parents?
Norway	Yes, the Norwegian Diabetes Association <sup>2</sup> .	Yes. Norwegian Diabetes Association is divided into 19 county branches which are divided into several small local groups.	Diabetes magazine and websites with information about diabetes and diabetes management (including a websites on young diabetes). Camps. Advocacy help, courses, educational programs, social happenings.
Argentina	Yes, Federación Argentina de Diabetes (The Argentine Diabetes Federation) <sup>3</sup> .	No data available.	Diabetes magazine and websites with information about diabetes and diabetes management. Camps.
Australia	Yes, Diabetes Australia <sup>4</sup> .	Diabetes Australia is divided into departments in each state. Local community support group only available in certain states.	Diabetes magazine and websites with information about diabetes and diabetes management. Camps. Preferred access and discounts for diabetes products and services, discounts on publications, travel, health insurance and footwear, amongst others. Sales and advice on blood glucose meters.
Canada	Yes, Canadian Diabetes Association <sup>5</sup> .	Yes. The Canadian Diabetes Association is divided into regional departments.	Diabetes magazine and websites with information about diabetes and diabetes management. Camps. Special offers and discount on diabetes products, contact centre available on phone for information about diabetes, local events.
India	Yes, Diabetic Association of India <sup>6</sup> .	No data available.	Diabetes journal which include educational section for non-medical members. Education for diabetics patient, courses for family physicians.
Rwanda	Yes, Rwanda Diabetes Association <sup>7</sup> .	No data available.	Publish free of charge leaflets providing basic information about diabetes to hospitals, dispensaries, and health care centers. Works for insulin accessibility for people with diabetes. The first diabetes camp was held January 2013. Education of health personell.
South-Africa	Yes, Diabetes South Africa <sup>8</sup> .	Yes, Diabetes South Africa is divided into 8 branches.	Publications and literature, websites with information about diabetes and diabetes management. Camps. Lectures and workshops, support groups.
USA	Yes, American Diabetes Association <sup>9</sup> .	Yes, there are local offices.	Diabetes magazines and websites with information about diabetes and diabetes management. Camps. Local events, website for kids and parents.

<sup>1</sup> All the patient organizations are found through IDF web pages (71). <sup>2</sup>The Norwegian Diabetes Associations web pages (72). <sup>3</sup>The Argentine Diabetes Federation web pages (73). <sup>4</sup>Diabetes Australia Web pages (74). <sup>5</sup>Canadian Diabetes Association (75). <sup>6</sup>Diabetic Association of India web pages (76). <sup>7</sup>Rwanda Diabetes Association web pages (77). <sup>8</sup>Diabetes South Africa web pages (78). <sup>9</sup>American Diabetes Association web pages (79).

## National diabetes register

In some of the countries and hospitals that have been compared in this study, it has been difficult to find the exact data about diabetes and the effect of the disease for the patients. Four out of eight countries in this study have a national diabetes register. These countries are Norway, Australia, Canada and India. The register in Canada, however, does not register acute and late complications for children and adolescents less than 15 years of age. The data which the register in India registers was not available.

In the report “Good health registries – good health” from The Norwegian government and the Norwegian Institute of Public health, 2010, it says that: “One of the most important sources to new knowledge about disease, treatment effect and quality services, are national health registries.” This report includes a plan for improving all health registries in Norway from 2010-2020 (80).

**Table 15:** Registers for diabetes in studied countries

COUNTRY	REGISTER FOR DIABETES	
	Is there a national diabetes register?	If yes, what data is registered?
Norway	The Norwegian Childhood Diabetes Register, the Norwegian Diabetes Register for adults. <sup>1</sup>	Incidence, annual data on diabetes care, quality indicators for diabetes care: HbA1c, acute complications, screening for late complications, screening for associated diseases.
Argentina	No	----
Australia	National Diabetes Register (obtain information from the National Diabetes Services Scheme and the Australasian Pediatric Endocrine Group (APEG) State-based registers. <sup>2</sup>	Collects information about people who use insulin in the treatment of their diabetes. Incidence, acute and late complications
Canada	National Diabetes Surveillance System (NDSS) <sup>3</sup> .	Incidence, prevalence, other.
India	Indian Council of Medical Research, Registry of People with Diabetes with Young Age at Onset <sup>4</sup> .	Data not available.
Rwanda	No	----
South-Africa	No	----
USA	No	----

<sup>1</sup>National service environment for medical quality register (81, 82). <sup>2</sup>Australian Institute of Health and Welfare (83). <sup>3</sup>Public Health Agency of Canada (84). <sup>4</sup>Personal communication with professor Chittaranjan Yajnik, Pune.

## Part 3: Results

### Diabetic ketoacidosis at diagnosis

DKA is unfortunately a quite common presentation of T1D in children. Only studies and diabetes registries can state the incidence exactly.

**Table 16:** Proportion of children having diabetic ketoacidosis (DKA) at diagnosis

Country, Hospital	Proportion (%) of children having DKA at diagnosis
Norway, OUH, 2011	13
Norway, SUH, 2011	6
Norway, Buskerud Central Hospital, 2010	33
Norway, Elverum, 2011	24
Argentina, Hospital de Niños, 2011	30
Argentina, Hospital Narciso Lopes, 2011	90
Australia, Royal Childrens Hospital (Melbourne), 2009	28
Australia, Alice Springs Hospital, 2009	Data not known
Australia, John Hunter Hospital (Newcastle), 2010	Data not known
Canada, British Colombia Children's hospital, 2010	20
Canada, Hospital for Sick Children, 2010	18
South Africa, Tygerberg Hospital, 2010	Most
Rwanda, University Teaching Hospital of Butare, 2010	100
USA, Childrens Hospital of Orange County, 2009	20-25
USA, University of Minnesota Amplatz Children's Hospital, 2009	< 15
India, King Edward Memorial Hospital, 2013	80

All hospitals visited, except from UTHB (Rwanda), used the ISPAD criteria for DKA, as shown in Table 5. At UTHB (Rwanda) they did not have a specific protocol for diabetes care and based their diagnostics on clinical symptoms such as impaired consciousness, dehydration, acidotic breathing, hyperglycemia, glucosuria and on occasion ketonuria in acutely ill patients. Bicarbonate and pH were not measured of unknown reasons.

The proportion of children presenting with DKA varied considerably among the different hospitals visited. SUH (Norway) reported in 2011 the lowest proportion of 6%, while UTHB (Rwanda) reported

that all children diagnosed with T1D had DKA. Close by, TH (South-Africa) reported that most of their patients presented with DKA and at Hospital Narciso Lopes (Argentina), 90% of children had DKA at diagnosis. At KEM (India), 80% of the children had DKA at diagnosis. Between these extremes the proportions from the remaining 9 hospitals with known data varied from 15% (UofM (Minnesota, USA) reported < 15%) to 33%. The mean proportion when adjusting the answer from CHOC (California, USA) to 23%, the answer from U of M (Minnesota, USA) to 15% and the answer from TH (South Africa) to 100%, was 41%.

## Acute complications

**Table 17:** Annual proportion of diabetic ketoacidosis (DKA) and severe hypoglycemia among children with type 1 diabetes

Country, Hospital	DKA, annually proportion (%)	Severe hypoglycemia with unconsciousness with/without convulsions, annually proportion (%)
Norway, OUH, 2011	6	6
Norway, SUH, 2010	4	9
Norway, Buskerud Central Hospital, 2010	6	3
Norway, Elverum, 2010	4	1
Argentina, Hospital de Niños, 2011	10	< 1
Argentina, Hospital Narciso Lopes, 2011	20	10
Australia, Royal Childrens Hospital (Melbourne), 2009	Data not available	Data not available
Australia, Alice Springs Hospital, 2009	Data not available	Data not available
Australia, John Hunter Hospital (Newcastle), 2010	Data not available	Data not available
Canada, British Colombia Children's hospital, 2010	Data not known	Data not known
Canada, Hospital for Sick Children, 2010	5-12	10-15
South Africa, Tygerberg Hospital, aug-nov 2010	16	Hardly ever
Rwanda, University Teaching Hospital of Butare, 2010	Data not known	Data not known
USA, Childrens Hospital of Orange County, 2009	< 1	5
USA, University of Minnesota Amplatz Children's Hospital, 2009	4	8
India, KEM Hospital, 2013	< 5	< 5

The annual proportion of children admitted with DKA varied from < 1% to 20% among the hospitals visited in our trial.

The annual proportion of children admitted with severe hypoglycemia varied from none (hardly ever) at TH (South Africa) to 15% at SickKids (Toronto, Ontario, Canada). In Rwanda this number was unknown.

In Argentina and South Africa, children with DKA presented more often than children with severe hypoglycemia. In Canada and the USA, it was the other way around. Children with severe hypoglycemia were admitted more often than children with DKA.

### **Treatment and treatment goals**

Seven out of 15 hospitals reported that 100% of their patients were on MIT. Ten hospitals out of 15 reported that more than 50% of their patients were on MIT.

In Norway, none used syringes and the majority of patients used insulin pumps. Syringes were not in use at UofM (Minnesota, USA) either. At ASH (Northern Territory, Australia) and at UTHB (Rwanda), 100% of patients used syringes in treatment. At both hospitals visited in Argentina, ASH (Northern Territory (Australia), TH (South Africa) and UTHB (Rwanda) insulin pumps were not available for children with T1D.

**Table 18:** Proportion of patients with type 1 diabetes on various treatment regimens

Country, Hospital	Syringes (%)	Insulin pen (%)	Insulin pump (%)	Proportion of patients on multi-injection therapy (%)
Norway, OUH, 2011	0	30	70	100
Norway, SUH, 2011	0	49	51	100
Norway, Buskerud Central Hospital, 2010	0	23	77	100
Norway, Elverum, 2011	0	79	21	100
Argentina, Hospital de Niños, 2011	Data not available	Data not available	0	100
Argentina, Hospital Narciso Lopes, 2011	Data not available	Data not available	0	90
Australia, Royal Childrens Hospital (Melbourne), 2009	Data not available	Data not available	30	50
Australia, Alice Springs Hospital, 2009	100	0	0	0
Australia, John Hunter Hospital (Newcastle), 2010	Data not available	Data not available	38	94
Canada, British Colombia Children's hospital, 2010	Data not available	Data not available	32	36
Canada, Hospital for Sick Children, 2010	Data not available	Data not available	30 (-40)	40 (-50)
South Africa, Tygerberg Hospital, 2010	25	75	0	100
Rwanda, University Teaching Hospital of Butare, 2010	100	0	0	0
USA, Childrens Hospital of Orange County, 2009	52	18	30	45
USA, University of Minnesota Amplatz Children's Hospital, 2009	0	33	67	100
India, KEM Hospital, 2013	100 (in combination with insulin pen)	100 (in combination with syringes)	0*	> 95

\*10 children used insulin pump

The treatment goal stated by ISPAD is HbA1c < 7.5%. Out of 16 hospitals visited, 11 followed ISPAD's goal. The two hospitals visited in Canada used Canadian treatment goals. CHOC (California) in the USA used American treatment goals (Table 3). At UTHB (Rwanda) there was, as mentioned earlier, no specific protocol for diabetes care. At John Hunter Hospital (Newcastle, Australia) the treatment goal for children was < 7%.

**Table 19:** Proportion of patients reaching the treatment goal of HbA1c < 7.5% as stated by ISPAD\*

Country, Hospital	Proportion (%) of patients achieving treatment goals
Norway, OUH, 2011	23
Norway, SUH, 2011	33
Norway, Buskerud Central Hospital, 2010	23
Norway, Elverum, 2010	20
USA, University of Minnesota Amplatz Children's Hospital, 2009	22
Argentina, Hospital Narciso Lopez, 2011	60
Argentina, Hospital de Niños, 2011	65
South Africa, Tygerberg Hospital, 2010	9
Australia, The Royal Children's Hospital in Melbourne, 2009	~ 30
Australia, Alice Springs Hospital, 2009	< 50
India, KEM Hospital, 2013	15-20

\*International Society for Pediatric and Adolescent Diabetes

**Table 20:** Guidelines used and proportion of patients reaching the treatment goal in hospitals not using ISPAD's\* treatment goal

Country, Hospital	Guidelines or treatment target used	Proportion (%) of patients achieving treatment goals
USA, Children's Hospital of Orange County, 2009	ADA guidelines	30
Canada, British Columbia Children's Hospital, 2010	CDA Guidelines	Data not available
Canada, Hospital for Sick Children, 2010	CDA Guidelines	Data not available
Australia, John Hunter Hospital, Newcastle, 2010	HbA1c <7 %	Data not known
Rwanda, University teaching hospital of Butare, 2010	No specific protocol for diabetes care	Data not known

\*International society for pediatric and adolescent diabetes

The treatment target used by ADA and CDA are age specific, as presented in Table 3 and Table 4. Children over the age of 13 years strive to achieve HbA1c below 7.5%. Younger children have a higher treatment target. Different treatment targets between different hospitals make it harder to compare results. It must be taken into account when comparing



the amount of children reaching treatment goals at for instance CHOC (California, USA) and JHH (Newcastle, Australia).

At UTHB (Rwanda) it was not possible to measure HbA1c, and therefore impossible to estimate a proportion of patients achieving ISPAD's target. The BG measured indicated, however, an HbA1c above 7.5%.

The results varied in general from 9% at TH (South Africa) to 65% at Hospital de Niños (Argentina). The number from TH (South Africa) was based on a few case reports and the number from Hospital de Niños (Argentina) was an estimate. Uncertainty about the true value must be assumed. The proportions reported from hospitals with registries varied from 22% to 33%.

### **Long-term complications**

As showed in table 6, ISPAD has detailed guidelines concerning the screening for DR and diabetic nephropathy. The guidelines from 2009 are unclear on recommended screening for neuropathy in children with T1D.

Alice Springs Hospital (Northern Territory, Australia) and UTHB (Rwanda) were the only two hospitals without any screening programs for late complications.

Out of the three complications screened for, neuropathy was most often omitted. Five hospitals did not screen for neuropathy, even though they screened for DR and nephropathy. RCH (Melbourne, Australia) and JHH (Newcastle, Australia) followed Australian guidelines when it came to screening for late complications. They evaluated peripheral nerve function annually in the presence of poor metabolic control. This is in accordance with Australian guidelines.

At Hospital for SickKids (Toronto, Ontario, Canada) they screened for retinopathy when indicated.

Our study didn't answer what the indications were. It must be assumed that they screened in case of poor compliance and metabolic control. Screening for nephropathy was done yearly from 12 years of age.

At CHOC (California, USA) they screened for retinopathy and nephropathy annually five years after diagnosis independently of age at diagnosis.

At KEM (India), fundoscopy was done annually to screen for DR. At what age or duration of T1D screening was started, is unknown. Nephropathy was screened for using albumin-creatinine-ratio in urine combined with serum creatinine. In screening for neuropathy, foot examination, including testing for sensation of pain and vibration, was used. How often screening for nephropathy and neuropathy was done, is unknown.

**Table 21:** Screening programs for long-term complications among children with type 1 diabetes

<b>Country, Hospital</b>	<b>Retinopathy</b>	<b>Nephropathy</b>	<b>Neuropathy</b>
Norway, OUH, 2011	X	X	No
Norway, SUH, 2011	X	X	No
Norway, Buskerud Central Hospital, 2010	X	X	X
Norway, Elverum, 2011	X	X	No
Argentina, Hospital de Niños, 2011	X	X	X
Argentina, Hospital Narciso Lopes, 2011	X	X	X
Australia, Royal Childrens Hospital (Melbourne), 2009	X	X	In risk patients
Australia, Alice Springs Hospital, 2009	No	No	No
Australia, John Hunter Hospital (Newcastle), 2010	X	X	In risk patients
Canada, British Colombia Children's hospital, 2010	X	X	Data not available
Canada, Hospital for Sick Children, 2010	When indicated	X	Data not available
South Africa, Tygerberg Hospital, 2010	X	X	X
Rwanda, University Teaching Hospital of Butare, 2010	No	No	No
USA, Childrens Hospital of Orange County, 2009	X	X	No
USA, University of Minnesota Amplatz Children's Hospital, 2009	X	X	No
India, KEM Hospital, 2013	X	X	X

**Table 22:** Proportion of children with type 1 diabetes having long term complications

Country, Hospital	Retinopathy	Nephropathy	Neuropathy
Norway, OUH, 2011	0	0	0
Norway, SUH, 2011	0	0	0
Norway, Buskerud Central Hospital, 2010	0	0	0
Norway, Elverum, 2011	0	0	0
Argentina, Hospital de Niños, 2011	< 1%	15 %	12 %
Argentina, Hospital Narciso Lopes, 2011	0	3-4 %	2 %
Australia, Royal Childrens Hospital (Melbourne), 2009	Data not available	Data not available	Data not available
Australia, Alice Springs Hospital, 2009	Data not known	Data not known	Data not known
Australia, John Hunter Hospital (Newcastle), 2010	Data not available	Data not available	Data not available
Canada, British Colombia Children's hospital, 2010	Data not available	Data not available	Data not available
Canada, Hospital for Sick Children, 2010	Data not available	Data not available	Data not available
South Africa, Tygerberg Hospital, 2010	Data not known	Data not known	Data not known
Rwanda, University Teaching Hospital of Butare, 2010	Data not known	Data not known	Data not known
USA, Childrens Hospital of Orange County, 2009	0	0	0
USA, University of Minnesota Amplatz Children's Hospital, 2009	0	0	0
India, KEM Hospital, 2013	Data not available*	Data not available*	Data not available*

\*Ten years after diagnosis, 20-25% of children with type 1 diabetes was reported to have late complications. Distribution is unknown.

Our data show that even if most hospitals visited did screening for late complications, few registered and kept record of the data. It might be registered in the patient's journal and used in follow up of the individual patient, but not possible to observe in an overall view for patients from that area.

KEM (India) and the two hospitals in Argentina were the only hospitals reporting late complications in children with T1D. At Hospital de Niños (Argentina), all three late complications were observed.

CHOC (California, USA) followed up some patients with microalbuminuria, but no one with diabetes nephropathy (see Table 7 for definitions).

Hyperglycemia, hyperlipidemia and hypertension are examples of risk factors for late complications.

Hypertension is seen in children with T1D. It is therefore important to screen for and treat if present.

ASH (Northern Territory, Australia) and UTHB (Rwanda) did not screen for hypertension. Our study didn't find out whether KEM (India) and the hospitals in the USA and Canada did screening for

hypertension or not. At ASH (Northern Territory, Australia), TH (South Africa) and UTHB (Rwanda) the amount of children with hypertension was unknown. Hypertension in children is defined as blood pressure above the 95% percentile.

**Table 23:** Proportion of children with type 1 diabetes having hypertension

Country, Hospital	Proportion of children having hypertension
Norway, OUH, 2011	2 %
Norway, SUH, 2011	7 %
Norway, Buskerud Central Hospital, 2010	4 %
Norway, Elverum, 2011	1 %
Argentina, Hospital de Niños, 2011	5 %
Argentina, Hospital Narciso Lopes, 2011	1-3 %
Australia, Royal Childrens Hospital (Melbourne), 2009	Data not available
Australia, Alice Springs Hospital, 2009	Data not known
Australia, John Hunter Hospital (Newcastle), 2010	Data not available
Canada, British Colombia Children's hospital, 2010	Data not available
Canada, Hospital for Sick Children, 2010	Data not available
South Africa, Tygerberg Hospital, 2010	Data not known
Rwanda, University Teaching Hospital of Butare, 2010	Data not known
USA, Childrens Hospital of Orange County, 2009	5-10%
USA, University of Minnesota Amplatz Children's Hospital, 2009	1 %
India, KEM Hospital, 2013	< 5%

The reported proportion of children with hypertension at the four hospitals in Norway gives a mean value of 4%. The Norwegian hospitals reported both among the highest and the lowest proportions in our study. The lowest proportion reported was 1%. U of M (Minnesota, USA) reported that between five and 10% of children with T1D had hypertension. This, along with the SUH's (Stavanger, Norway) proportion of seven percent, is the highest proportions reported.

## Diabetes team

**Table 24:** Multidisciplinary diabetes teams in the different hospitals

Country, Hospital	Diabetes team	Doctor	Diabetes nurse	Nutritionist	Social worker	Psychologist	Diabetes educator
ISPAD recommendations	Y	Y	Y	Y	Y	Y	
Norway, OUH, 2011	Y	Pediatrician	Y	Y	Y	Y	
Norway, SUH, 2011	Y	Pediatrician	Y	Y	Y	Y	
Norway, BCH, 2010	Y	Pediatrician	Y	Y	Y	Y	
Norway, Elverum, 2011	Y	Pediatrician	Y	Y	Y	None	
Argentina, Hospital de Niños, 2011	Data not available	Y, specialised in diabetes	Data not available	Data not available	Data not available	Data not available	
Argentina, Hospital N. Lopes, 2011	Data not available	Y, specialised in diabetes	Data not available	Data not available	Data not available	Data not available	
Australia, RCH, 2009	Y	Pediatrician	Y	Y	Y	On request	
Australia, ASH, 2009	No	Pediatrician	None	Y	None	On request	Y
Australia, JHH, 2010	Y	Pediatrician	None	Y	Y	On request	Y
Canada, BCCH, 2010	Y	Y (unknown speciality)	Regular nurse	Y	Y	On request	
Canada, SickKids, 2010	Y	Pediatrician	Y	Y	Y	Y	
South Africa, TH, 2010	Y	Pediatrician	Y	Y	Y	None	
Rwanda, UTHB, 2010	No	Pediatrician	Regular nurse	None	None	None	
USA, CHOC, 2009	Y	Y (unknown speciality)	Y	Y	Y	Y	
USA, U of M, 2009	Y	Y (unknown speciality)	Y	Y	Y	Y	
India, KEM Hospital, 2010	Y	Pediatrician	Regular nurse	Y	None	None	Y

UUH: Ullevål University Hospital, SUH: Stavanger University Hospital, BCH: Buskerud Central Hospital, RCH: Royal Children's Hospital, ASH: Alice Springs Hospital, JHH: John Hunter Hospital, BCCH: British Columbia Children's Hospital, SickKids: Hospital for Sick Children, TH: Tygerberg Hospital, UTHB: University Teaching Hospital of Butare, CHOC: Children's Hospital of Orange County, U of M: University of Minnesota Amplatz Children's Hospital, KEM Hospital: King Edward Memorial Hospital. Y = yes, profession part of the multidisciplinary team

Because ASH (Northern Territory, Australia) followed up very few children with DM they did not have a fixed multidisciplinary team. Nevertheless, whenever a child visited the outpatient clinic or was admitted, a pediatrician, a diabetes educator and a dietician at the hospital functioned together as a team. If the family was aboriginal, an aboriginal liaison officer also participated in the team.

At UTHB (Rwanda) there were no endocrinologists, specialized diabetic nurses, psychologists, nutritionists or social workers at the hospital.

The nurses working at BCCH (Vancouver, British Columbia, Canada), UTHB (Rwanda) and KEM (India) were not specialized in diabetes like ISPAD recommends. At KEM (India) they also lacked a psychologist and a social worker.

Out of the professions ISPAD recommends to constitute the treatment team, psychologists were most often missing. Seven hospitals had a psychologist at least in a part time job. At all but four hospitals, psychologists were available on request.

All but the two hospitals in Argentina had access to interpreters if needed, among the hospitals we have that information about. We miss information about interpreters from UTHB (Rwanda), KEM (India) and the two hospitals in Canada. At Alice Springs Hospital (Northern Territory, Australia) they had access to an interpreter at the hospital if the patient was indigenous. Otherwise, interpreters were available in town.

## Part 4: Discussion

### Use of guidelines in general

Among the 16 hospitals visited, 15 hospitals used guidelines in their care for children with T1D. At UTHB (Rwanda) there was no specific protocol for diabetes care. Hospitals in the USA followed American guidelines. Hospitals in Canada followed Canadian guidelines. Hospitals in Australia followed Australian guidelines. The remaining hospitals reported that they followed the guidelines stated by ISPAD. ADA and CDA have age-dependent treatment goals. Besides that, there are no major differences between these different guidelines related to the subjects of this thesis.

At UTHB (Rwanda) the doctor was in charge of everything concerning the treatment when a child with T1D was admitted. For acute management of DKA, the guidelines used at UTHB were described in the book "Pediatric Emergencies" by Francois DeVilliers. Because of the low incidence of T1D in Rwanda, the physicians at UTHB saw few children with T1D. Only four cases of new onset T1D were registered at UTHB (Rwanda) between November 2008 and October 2010. Naturally, a doctor will improve his/her clinical experience if seeing a large quantity of children with diabetes. One could think that guidelines would be especially important when clinical experience is limited. Because of lack of medical equipment and financial challenges this might, however, be hard to practice. At UTHB (Rwanda) it was not possible to measure HbA1c due to lack of equipment. Home BG monitoring was not used and simple urine glucose testing was not performed regularly. Physicians and nurses in Rwanda deserve credibility for the effort and work despite lack of frequent experience and technological equipment.



## Variations in diabetic ketoacidosis at diagnosis

The proportion of children with DKA at diagnosis does not tell anything about the diabetes care in the hospitals. However, it can tell something about the pre-hospital health care and might also tell something about the knowledge about DM in an area. Incidence may correlate to knowledge. In Rwanda and South Africa, where 100% of newly diagnosed children with T1D had DKA, there was unfortunately no data available on the incidence of childhood DM. India was reported to have 80 % of the children less than 15 years of age presenting with DKA at diagnosis. The proportion of children presenting with DKA is generally lower in western, high incidence countries (Table 12 and Table 16).

Incidence of T1D among children has in some studies been found to correlate with the proportion of children having DKA at diagnosis in a country (85, 86). The studies show that in countries with high incidence of T1D there were lower percentages of children having DKA at diagnosis and vice versa. The same trend was seen in this study. The high incidence countries for T1D among children under 15 years of age in our study was Norway on the top followed by Canada, Australia and the USA, while Argentina and India are reported as intermediate- and low incidence countries. There are no data available from Rwanda and South Africa in our study, but data from the DIAMOND project group shows that Africa is a low incidence area for T1D among children (9). In an area with low incidence of T1D there may be less knowledge about the disease, and therefore less awareness of the symptoms both among the general population and among health professionals. Less knowledge may lead to people seeking medical help later in the process or medical delay at the general physician or at local health centers. Medical delay may be due to misinterpretation of the symptoms for DKA. DKA in undiagnosed children might for example be misinterpreted as gastroenteritis or cerebral malaria.

Physician density may also be an explanation for the variations in frequency of DKA at diagnosis. If the doctor is far away, patients may wait longer until they seek help and their situation might be more critical when seeing the doctor. The patients followed up at UTHB (Rwanda) could live in a five hour walking distance from the hospital. One can expect that patients with this acute complication

never reach hospital. In our study, the country with the lowest physician density, Rwanda, also had the highest frequency (100%) of DKA at diagnosis among children. The same trend could be seen in South Africa and India. In Argentina, however, where Hospital N. Lopez reported 90% DKA at diagnosis among children, they had the second highest physician density among the countries in our study. Along with physician density per population, the geographical distribution of physicians in rural and urban areas must be considered. The high frequency of DKA at Hospital N. Lopez despite Argentina's high physician density could be due to an unequal distribution of physicians among the population.

Other factors such as social, economical and geographical differences may also explain why there is this big variation in DKA at diagnosis between the hospitals and the countries in our study.

### **Treatment regimens and financial support**

ISPAD recommend MIT as insulin replacement therapy. The aim with the therapy is to be as close to physiological insulin production as possible. This is best managed through insulin pump (33). Use of insulin pump has been showed to have greater treatment satisfaction compared to MDI. However, the outcome on metabolic control is the same when using insulin pump as when using MDI (87).

Despite the guidelines, there were differences among the hospitals in how insulin was administered. MIT administered through insulin pump is more expensive than use of insulin pen or syringes. MDI is also more expensive than a two-injection daily regimen which requires less insulin and insulin administration tools.

Five hospitals did not offer insulin pumps to their patients. These hospitals were; Hospital de Niños and Hospital N. Lopez in Argentina, ASH (Northern Territory, Australia), TH (South Africa) and UTHB (Rwanda). The main reason for treatment without insulin pump was lack of financial support from the government or others to cover the cost for this expensive regimen. In Argentina, insulin pumps

were only available for those who had private health insurance or could pay for the pump themselves. In Australia, it was almost impossible to afford this regimen for patients without a private health insurance. The children and adolescents with diabetes in Australia needed to have the private health insurance one year prior to applying for the pump. Therefore, despite having health insurance, the patients had to wait before they could start with an insulin pump. In South Africa, insulin pumps were not financed through the public health care system. In Rwanda there was no national support system and the patients had to pay for all the diabetes treatment themselves. In India, they had 10 patients who used insulin pump. Why only these patients were using insulin pump is unknown, but may be due to financial reasons. India had no governmental financed support system for patient with diabetes.

Among the countries in our study, it seemed like the countries with the best national support system for diabetes treatment had most patients on the more expensive treatment regimens, like MIT administered through insulin pump and insulin pen. In Norway all the diabetes treatment was financed through the national health system. The patients only had to pay a standard deductible each year. When reaching this deductible, all the treatment was free of charge. At the hospitals in Norway all the patients followed the MIT regimen and were either on insulin pump or used insulin pen.

In Canada however, the government financed the pump and some of the pump supplies when the child had had T1D for a year and when certain criteria were met. The government also supplied syringes, insulin pens and insulin. Despite the good national support system most children at the visited hospitals in Canada used the two-injection daily regimen due to other reason than economy.

In the USA, private health insurances financed the diabetes treatment, including insulin pumps. The patients at CHOC (California, USA) and U of M (Minnesota, USA) had insurances to cover the expenditure related to pump therapy. Nevertheless, our study found a great difference between the numbers of patients using insulin pumps at these two hospitals. There was also a great difference

between the number of patients on MDI and two-injection daily regimen. These differences were related to other reasons than economy.

## **Multi injection therapy**

Nine hospitals (56%) reported that they treat some of the children with insulin only two times per day.

At RCH (Melbourne, Australia), most toddlers and young children were treated with twice daily insulin injections. The reason for this choice of treatment was partly to avoid focus on diabetes in the youngest. Most schools did not have school nurses to help with insulin administration. This made it hard to take injections during school hours. Furthermore, the youngest children had a quite regular schedule concerning meals and activity. It was therefore believed that insulin twice daily combined with an appropriate diet was optimal care for the youngest.

At CHOC (California, USA), all children started with a two-shot regime. Eventually, the strategy for therapy was age dependent. Between the age of five and 14 years, patients injected insulin only twice daily. The reason was partly to do as few injections as possible and partly because of strict rules concerning who could give insulin. Only school nurses, parents and the child itself were allowed to set insulin at school and there weren't enough nurses to administer insulin during school hours. With a two-shot regime, the child didn't have to take insulin at school.

In Canada, as in California, school personnel were not allowed to press the button on the insulin pump or give injections of insulin. This was the main reason reported from both BCCH (Vancouver, British Columbia) and SickKids (Toronto, Ontario) for children not on MIT.

In Rwanda, all patients were given two injections of insulin per day. When recommending three injections per day, poorer compliance and outcome had been observed. Home BG monitoring was not used and dose adjustments were rarely performed due to difficulties in educating patients.

At ASH (Northern Territory, Australia), JHH (Newcastle, Australia), KEM (India) and Hospital Narciso Lopez (Argentina), no reason for choice of treatment regime was given.

### **Treatment target, long term complications and national register**

ADA and CDA have higher limits for treatment target measured with HbA1c than ISPAD (Table 3 and 4). This could be a reason for higher percentage of patients reaching treatment target in the countries using ADA and CDA guidelines.

The prevalence of late complications should correspond to the average HbA1c (5). In our study, the hospitals in Argentina had the highest percentage of patients reaching treatment target. These hospitals were also the only hospitals, along with KEM (India), who reported long term complications among children with T1D. KEM (India) reported long term complications in children with more than 10 years from diagnosis. The numbers from Argentina were based on estimates from health personnel, and not from local databases or a national register. At the hospitals in Norway, the data were collected from the NCDR. Here, they did not report any long term complications among children with T1D. However, they reported approximately half of the percentage of children with T1D reaching treatment target, compared with Argentina. RCH (Melbourne, Australia) and CHOC (California, USA) reported numbers that showed the same correspondence between late complications and average HbA1c as in Norway. At the other hospitals, either the data on long term complication or the data on proportion reaching treatment goals among children with T1D was missing or unknown due to different reasons.

Norway had the only hospitals in this study where the data was collected from a national register. Among the other hospitals, TH (South Africa) and U of M (Minnesota, USA) kept local databases on the patients' HbA1c. At TH (South Africa) they started to register in August 2010 and they could not give any number regarding patients with long term complications. At U of M (Minnesota, USA) the

database registered patients with HbA1c < 7.5% and > 10%. This register did not register long term complications. All the other values, regarding treatment target and long term complications, at the other hospitals in our study are based on estimates from health personnel.

Conclusions cannot be made based on these observations in our study alone. Still, we can discuss some theories around our results. While using estimates based on clinical practice it might be easier to under- or overestimate the results. Before pediatricians in Norway started with systematic registering of diabetes care in Norway, at hospitals and on national basis, they often overestimated the results of children reaching treatment target (88). This might influence on further treatment and follow-up, and can give a higher risk for developing long term complications. As several studies have shown, strict monitoring of treatment in diabetes can prevent long term complications (5). The discrepancy between the amount of children reaching treatment goals and the amount of children with late complications in Argentina, constitute a logical gap. This indicates that the estimate on children reaching treatment target is too high, as seen in Norway before registration was started. This might show that a diabetes register at the hospitals and/or a national diabetes register, via awareness and increased focus, can help to prevent long term complications in children with diabetes.

## **Limitations**

Our study had some limitations.

The questionnaires used when interviewing health personnel working with diabetes care all over the world were not validated. Validation would increase the quality and reduce the chance of misunderstanding. In the work with making the questionnaire, it was tried out several times on diabetes nurses at OUH, and improved and corrected where needed before travelling abroad. We hope and believe that this work reduced the need for validation.

Another limitation is that different interviewers went to the different hospitals visited. Different focus and different personal qualities may influence the information collected. On the other side a standardized questionnaire was a strength in this study and reduced the challenge of using several different interviewers.

A challenge, but not a limitation, is that information was collected in different years. We believe that this is of minor importance. A more limiting factor is the fact that some data have been hard to find. Some of this data isn't known due to lack of registers, and some are not easily available, at least not to us. This complicates comparison between different hospitals and makes it harder to draw conclusions.

## **Treatment strategy and compliance**

We have good indications to say that the approaches to treatment were very different in different countries visited. In Norway, the therapist communicated with the patient through motivational interviewing. The patients were in charge of their own treatment and the goal was to make the patient an expert on his/her own disease. The therapist coached and guided the patient when needed. If the metabolic control wasn't satisfying, the patient was reminded of the possible long-term complications and reeducated. The seriousness of T1D was in some cases neglected by the children and their parents so that they could be able to live their life as normal as possible. In Argentina, the therapists confronted the children more directly with the fact that they had a serious disease with possible complications, both now and later in life. In Rwanda, no information was given to the children and their families about the effect and complications of the disease. Because of the lack of equipment, children in Rwanda were in a lesser extent able to take control of the disease themselves. Home blood glucose monitoring was not used. In contrast, home blood glucose monitoring was the cornerstone and most essential part of treatment of T1D in Norway. Patients got equipment to measure their BG as many times as they wanted for free. The children in Argentina

were provided, by the pharmaceutical industry, with equipment to measure their BG three times a day. If more strips were needed, they had to pay themselves.

Our study cannot answer which treatment strategy is the most effective in reaching treatment goals. The important point, and the huge difference between treating DM and other diseases, is the fact that the therapist can do no more than guiding the patient in treatment. It is the patients' day to day responsiveness, adjustments and actions that decide the long term outcome of the disease. The number of free BG strips doesn't alone decide the prognosis. Compliance in treatment is everything.

### **Diabetes mellitus – a model for management of chronic diseases**

There are extensive and thorough international guidelines concerning care for patients with DM. Still, it is hard to achieve that this care reaches all patients. It is even harder to achieve treatment goals because of the importance of compliance. No other chronic disease has such detailed international guidelines. When the criteria for good treatment and registration are objective, benchmarking between units is an important tool to learn between different treatments clinics and to adjust and improve practice. In this sense, diabetes care is a model for other chronic diseases.



## **Conclusion**

Among chronic diseases in children, diabetes is in a special position by having good international guidelines. Guidelines highlights important parameters in diabetes care and give a basis for establishing diabetes registers which can be compared internationally. Diabetes registers give objective data which can be used in highlighting challenges and in benchmarking. Benchmarking can influence diabetes care units to strive towards better results through increased awareness. Increased awareness can motivate diabetes care units to exchange experiences concerning diabetes care where guidelines, because of geographical and economical reasons, are hard to follow. We can achieve great results by learning from each other, both domestically and internationally.

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## Appendix

Questionnaire – Diabetes in children



**Universitetet i Oslo  
Det medisinske fakultet**

### QUESTIONNAIRE – DIABETES (T1D and T2D) IN CHILDREN: A GLOBAL PERSPECTIVE 17.11.10

The questionnaire is designed to gather information about children with diabetes  $\leq 15$  years of age. The interview is in two parts. Each part should not last more than 1 hour.

The first part is designed to map diabetes in children at a national or regional level. Each country has a number code (see list). The regions/counties/states are indicated by names. The interviewer fills out this first part of the interview based on information available on the internet and other available sources. The information will then be quality assessed with the local informant.

The second part is designed to map how children with diabetes are followed up at the local hospital/treatment centre. The interview contains multiple open, qualitative questions. The interview will therefore be tape-recorded. The tape recordings will be transcribed before the analysis takes place.

**The questionnaire does not ask for personal sensitive information.**

#### QUESTIONNAIRE – DIABETES IN CHILDREN

##### PART 1

- Incidence
- Prevalence
- Mortality
- National health
- Patient organizations
- Register for diabetes
- Complications

##### PART 2

- Hospitalizations and number of beds
- Diagnostics
- Treatment and follow up
- Treatment goals
- Quality of life and mental health
- Complications

Country (code):

Region/county/state:

Date:

Informant: name/occupation

Interview by:

## PART 1

### Incidence

1. The annual incidence of the different types of diabetes in this country (enter the number and percentage)
  - Type 1 diabetes (T1D)
  - Type 2 diabetes (T2D)
  - Gestational diabetes
2. The incidence of T1D and T2D among children under 15 years of age
  - The total incidence:
  - How is the distribution in the following groups of ages (estimated):
    - <5 years
    - 5-<10 years
    - 10-<15 years
    - > 15 years
3. What is the gender distribution among children with T1D and T2D in the country?
4. What are the overall proportions of the following ethnicities in this country:
  - White / European background (non-Hispanic whites)
  - Black / African background
  - Middle-East / North-African
  - Indian subcontinent
  - East-Asia
  - Middle- and South American (Hispanics)
  - Indigenous (specify)
  - Mixed (or unclassified)
5. How many children with diabetes in this country are
  - White / European background (non-Hispanic whites)
  - Black / African background
  - Middle-East / North-African
  - Indian subcontinent
  - East-Asia
  - Middle- and South American (Hispanics)
  - Indigenous (specify)



- Mixed (or unclassified)

#### Prevalence

6. What is the prevalence of T1D and T2D among children in the following groups of age?
- <5 years
  - 5-<10 years
  - 10-<15 years
  - ≥ 15 (adults)

#### Mortality

7. What is the average life expectancy in the country?
- Women:
  - Men:
8. What is the average life expectancy among patients diagnosed with T1D before the age of 15?
- Women:
  - Men:

#### National health

9. How many doctors per citizen? (This will differ depending on location; city, rural, town etc)
10. Is there a geographical difference in availability of doctors?
11. What is the gross domestic product (GDP) of the county?
12. What is the total expenditure on health as a percentage of the GDP?
- Which proportion is financed by the public?
  - Which proportion is financed by private actors?
13. Which proportion of the national budget is spent on health?
14. Does the public health care system finance the costs associated with diabetes medication and equipment?
- Yes
  - No
15. If the answer is yes on question 14, which *medication* is financed?
- Insulin
    - Yes
      - \_\_\_\_\_% financed
    - No
  - Antidiabetic drugs
    - Yes

- \_\_\_\_\_% financed
  - No

Glucagon

- Yes
- \_\_\_\_\_% financed
- No

16. If yes on question 14, which of the following *materials* is financed

- Syringes:
- Needles:
- Insulin pen:
- Insulin pump:
- Materials for the insulin pump: (needle, catheter, reservoir etc):
- Home Blood Glucose meters:
- Blood glucose test strips:
- Finger-pricking devices:
- Lancets for finger-pricking:
- Continuous subcutaneous glucose monitoring devices:
- Urine sticks to check for ketonuria:
- Other:\_\_\_\_\_

17. If the answer is yes on question 14, does the patient have to pay anything? If so, how much? (%)

- Syringes:
- Needles:
- Insulin pen:
- Insulin pump:
- Materials for the insulin pump: (needle, catheter, reservoir...):
- Home Blood Glucose meters:
- Blood glucose test strips:
- Finger-pricking devices:
- Lancets for finger-pricking:
- Continuous subcutaneous glucose monitoring devices:
- Urine sticks to check for ketonuria:
- Other:\_\_\_\_\_

18. Who brings the child to their check-ups?

- Mum
- Dad
- Other:\_\_\_\_\_ (specify)

19. Are there any laws/public rights for parents to get extra time off work to take their children to check ups?

- Yes
- No

20. Are parents with chronic ill children allowed to take additional days off compared to the general population?

- Yes (\_\_\_\_\_ number of additional days)
- No

21. Are there national guidelines for the management of children with T1D and T2D?

- Yes
- No

#### Patient organizations

22. Are there any national organizations for patients with diabetes?

- Yes
  - For children?
  - For children and adults?
  - For adults only?
- No

23. Are there any local organizations for patients with T1D?

- Yes
  - For children?
  - For children and adults?
  - For adults only?
- No

Comment:

24. What do the patient organizations offer the children and their parents?

- Websites
- Telephone
- Courses
- Information meetings
- Holiday offers / camps
- Other: \_\_\_\_\_

#### Register for diabetes

25. Is there a national diabetes register?

- Yes, for children
- Yes, for adults
- Yes, for adults and children
- No

26. If yes, what data is registered? Does it include both T1D and T2D?

#### Complications

27. What is the incidence of acute diabetes complications among children under 15 years of age?

- Diabetic ketoacidosis (with hospitalization)

- Severe hypoglycemia (unconscious with or without convulsions)

28. What is the incidence of late diabetes complications among children under 15 years of age?  
(estimated percentage)

- Retinopathy
- Nephropathy
- Neuropathy

Country (code):

Region/county/state:

Local treatment center (name and type):

Date:

Informant: name/occupation

Interview by:

## PART 2

Hospitalizations and number of hospital beds

29. How many children <15 years with diabetes are admitted to hospital annually in the following wards (The total number of hospitalizations including rehospitalization)

- Paediatric ward
- Adolescents ward
- Internal medical ward

30. To what age are the children managed in the paediatric wards? \_\_\_\_\_

31. If there is an adolescent department, when do the children start attending and how long can they attend there?

32. What is the maximum number of beds in the ward? \_\_\_\_\_

33. How often has the ward been full during the last 6 months? (regardless of the reason for the hospitalisation)

34. How many children with diabetes are followed up at the local hospital today?

35. How is the gender distribution among the children that are followed up at the local hospital?

36. Who takes over the responsibility for the treatment and follow-up after the diagnosis of diabetes?

- Specialist \_\_\_\_\_ (which type)
- General practitioner (GP)
- Other : \_\_\_\_\_

## Diagnostics

37. Who usually make the diagnosis?

- General practice
- Specialised health service
- Nurse
- Other: \_\_\_\_\_

38. What is the average age at diagnosis?

39. What are the classical symptoms that make the patient and his or her parents contact a doctor?

40. Which diagnostic criteria have to be fulfilled to set the diagnose of diabetes?

### *T1D*

- International guidelines; ISPAD (Blood glucose)
- Other guidelines: \_\_\_\_\_

### *T2D*

- International guidelines; ISPAD (Blood glucose)
- Other guidelines: \_\_\_\_\_

41. Where are recently diagnosed juvenile diabetics treated the first time?

### *T1D*

- Out-patients clinic
- Hospital ward with beds

### *T2D*

- Out-patients clinic
- Hospital ward with beds

42. If the patient is admitted to hospital, what is the average length of stay?

T1D:

T2D:

43. Which diagnostic criteria do you use for DKA?

- Hyperglycemia
- Standard Bicarbonate (< 15 mmol)
- pH (< 7,3)
- Ketonuria / ketonemia

44. What proportion of children has DKA at diagnosis?

T1D:

T2D:

## Treatment and follow up

45. Who participates in the treatment and follow up of children with diabetes?

- Nurse
- Doctor
- School nurse
- Social worker
- Nutritionist
- Psychologist
- Other: \_\_\_\_\_
- Multidisciplinary team

46. Does the child with diabetes have one particular contact person? If yes, specify:

- Yes: \_\_\_\_\_
- No

47. When the diagnosis is made who is responsible for the follow-up?

- Specialist (doctor / diabetologist)
- Hospital doctor
- Nurse
- General practitioner
- Other: \_\_\_\_\_

48. Who are educated (at the time of the diagnosis, and after discharge)?

- The child
- Parents
- School
- School nurse
- Nursery
- Activity leaders/coaches
- Others: \_\_\_\_\_
- No one

49. Does the hospital have access to interpreters when they have patients that do not speak/understand English?

50. How is the education organized?

- Training in groups
- Individual training
- A combination of both

51. When is a new education organized? (re-education)

52. Is carbohydrate counting used systematically when calculating the insulin bolus in relation to food?

53. How is the education organized?

- Training in groups
- Individual training
- A combination of a and

Comment:

54. How much do parents participate in the treatment and follow up?
55. Do the adolescents get contraceptive counselling?
- Yes (comment ; )\_\_\_\_\_
  - No
56. Have you experienced unintended pregnancies in this group of patients?
- Yes (how many? what are the characteristics of these patients; ethnicity, socioeconomic status etc?)
  - No
57. What types of treatment/treatment regimens are available for children with diabetes at the local hospital?
- Syringes
  - Needles
  - Insulin pen
  - Insulin pump
  - Continuous Subcutaneous Glucose Monitoring
  - Others: \_\_\_\_\_
  - None
58. How many patients use multi injection (insulin > 3 times a day) therapy?
59. What proportion of the patients (in number and percentage) follow the different treatment regimens listed
- Insulin pump:
  - Others:
  - None:
60. Among the children under multi injection therapy what type of insulin preparations are used? (%)
- Premixed insulin preparations
  - Intermediate-acting insulin + rapid-acting insulin
  - Analogues
    - Which combinations: \_\_\_\_\_
  - Are there any different strategies for insulin therapy concerning the child's age?
61. Who does the patient and his or her parents contact if the child is acute ill?
- Specialist
  - Contact person
  - GP
  - Emergency room
  - Other: \_\_\_\_\_



## Treatment goals

62. Are the ISPAD treatment goals adhered to?

(ISPAD = International Society for Paediatric and Adolescent Diabetes)

- Yes
- No
  - If no, which guidelines are used \_\_\_\_\_

63. What are the treatment goals

- HbA<sub>1c</sub> < 7,5 %
- Other: \_\_\_\_\_

64. What proportions (%) of patients achieve the treatment goals?

65. How often do the children attend diabetes health check ups?

T1D: \_\_\_\_\_ T2D: \_\_\_\_\_

66. What proportions (%) of the patients attend their appointment?

- Most patients
- 50 %
- Only a few

67. Who does not attend? Why? What are the characteristics of these patients?

68. Is there a screening program for autoimmune diseases?

- Yes
- No

69. If yes, witch diseases are included in the screening

- Celiac disease
- Hypothyroidism / hyperthyroidism
- Others: \_\_\_\_\_

70. If yes, how often is the screening performed

- At each check up
- Annually
- Other: \_\_\_\_\_

71. Are there any screening program concerning late diabetes complications among children with diabetes?

- Yes
- No

72. If yes, what kind of late diabetes complications are included in the screening program among children with diabetes? And which methods are used in the screening

- Retinopathy: \_\_\_\_\_
- Nephropathy; \_\_\_\_\_
- Neuropathy: \_\_\_\_\_
- Angiopathy: \_\_\_\_\_
- Others: \_\_\_\_\_

73. If yes on question 70, how often is the screening performed

- At every check up:
- Annually:
- Other: \_\_\_\_\_

#### Quality of life and mental health

74. What assistance do the children with diabetes and their parents receive in relation to:

- School
- Hobbies
- Sports

75. Are there social activities arranged for the children and their parents?

76. What kind of social activities are arranged? And who organises them?

77. Have you conducted/do you conduct research on the quality of life in the children with diabetes?

- Yes
  - If yes, can you elaborate
- No

78. Are intoxicants a problem among children with T1D and T2D?

- Yes
  - What kind of intoxicant?
  - What are the characteristics of these patients (gender, ethnicity, socioeconomic status etc)
- No

Comment:

## Complications

79. What is the incidence (percentage) of acute diabetes complications among children with T1D and T2D under the age of 15?

### *Type 1 diabetes*

- Diabetic ketoacidosis
- Severe hypoglycaemia with unconsciousness and/or convulsions
- Other: \_\_\_\_\_

### *Type 2 diabetes*

- Diabetic ketoacidosis
- Severe hypoglycaemia with unconsciousness and/or convulsions
- Other: \_\_\_\_\_

80. What is the incidence (%) of long-term complications among children under the age of 15 years? And how old are they?

### *Type 1 diabetes*

- Retinopathy:  
How many have been treated with laser?
- Nephropathy:
- Neuropathy:
- Hypertension  
How many get anti hypertension treatment?

### *Type 2 diabetes*

- Retinopathy:  
How many have been treated with laser?
- Nephropathy:
- Neuropathy:
- Hypertension  
How many get anti hypertension treatment?

81. What is the incidence (%) of long-term complication among adults who got the diagnosis of diabetes before they turned 15 years?

### *Type 1 diabetes:*

### *Type 2 diabetes:*

The following must be discussed:

- How old were the patients when they were diagnosed with diabetes?
- How many years diabetes duration at onset of the late complication?
  
- Retinopathy:
- Nephropathy:
- Neuropathy:

82. Is overweight a problem among children with diabetes?

*Type 1 diabetes*

- If yes:
  - Are there any differences between gender, ethnicity, socioeconomic background etc?
  - In which group is the prevalence of overweight highest?
  - What kind of prevention and treatment regimens does the hospital have?
  - Are the treatment regimens effective?
  - Do children with overweight in practice have significant more complications than children with normal weight?
  - Are there other problems related to overweight and diabetes?

*Type 2 diabetes*

- If yes:
  - Are there any differences between gender, ethnicity, socioeconomic background etc?
  - In which group is the prevalence of overweight highest?
  - What kind of prevention and treatment regimens does the hospital have?
  - Are the treatment regimens effective?
  - Do children with overweight in practice have significant more complications than children with normal weight?
  - Are there other problems related to overweight and diabetes?