

Childhood diabetes in Argentina and Norway

A comparative study of guideline
implementation and follow-up



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Abstract

Aims: To compare and illustrate the treatment of diabetes in Norway and Argentina using the International Society for Pediatric and Adolescent Diabetes (ISPAD) and American Diabetes Association (ADA) guidelines.

Methods: *Part one:* Literature review of diabetes using the ISPAD and ADA guidelines and non-systematic search on Pubmed.

Part two and three: Literature review of information about Argentina and Norway. Comparison of Drammen and Buenos Aires (BA) based up on a semi structural questionnaire used to interview health personnel at two public hospitals in BA (Hospital de Niños and Hospital Narciso (N.) Lopez) and one public hospital in Drammen (Buskerud Central Hospital).

Results and discussion: In 2011 all three hospitals used the ISPAD guidelines as a basis for diagnosis and treatment of children with diabetes. The reported treatment results, patients reaching HbA1c < 7.5 %, were better in BA compared to Drammen (65 % at Hospital de Niños and 60 % at Hospital N. Lopez compared to 23 % at Buskerud Central Hospital). In Drammen 80 % of the children used insulin pump while this is not offered to the children at public hospitals in BA due to financial causes. In BA the majority of the children use MDI. The children in BA get a limited number of blood glucose (BG) strips for free (enough to measure three times a day) and have to buy the rest themselves. In Norway the children get unlimited numbers of BG strips for free. All three hospitals provide education, regular checkups and screening for complications as recommended by the ISPAD and ADA guidelines. The children in Drammen are admitted to the pediatric ward together with both their parents the first two weeks after diabetes onset. In BA the children get education at the out patients clinic at diabetes onset. Unlike Drammen, both hospitals in BA report long term complications among children/ adolescents < 15 years of age. The numbers we got in BA concerning treatment results as well as acute- and long term complications where all based on clinical experience, while numbers from Norway are from the Norwegian Childhood Diabetes Registry where all children/adolescents with diabetes in Norway are registered.

Conclusion: All three hospitals use the ISPAD guidelines as basis for their treatment of children/adolescents with diabetes. Both the economic systems and health care systems are very different in Argentina and Norway. Even a higher proportion of the patients in BA reached treatment goal compared to Drammen, late diabetes complications were only seen in BA. Generally registration is a good tool for monitoring a disease; both incidence, treatment and treatment results.

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Abbreviations

ADA	American Diabetes Association
AER	Albumin excretion rate
BA	Buenos Aires
BG	Blood glucose
CSII	Continuous subcutaneous insulin infusion
CVD	Cardio vascular disease
DCCT	Diabetes Control and Complications Trial
DSME	Diabetes self- management education
DKA	Diabetic ketoacidosis
EMA	Elevated endomysial autoantibody
ESRF	End stage renal failure
GAD	Glutamic Acid Decarboxylase autoantibodies
GDP	Gross domestic product
GFR	Glomerular filtration rate
GP	General practitioner
HbA1c	Glycated hemoglobin A1c
HDI	Human Development Index
Hospital N.Lopez	Hospital Narciso Lopez
IAA	Insulin Autoantibodies
ICA	Islet Cell Autoantibodies
IgA	Immunoglobulin A
ISPAD	International Society for Pediatric and Adolescent Diabetes
IDF	International Diabetes Federation
IMF	International Monetary Fund
MDI	Multiple daily injections
NCDR	The Norwegian Childhood Diabetes Registry
NPH	Neutral Protamine Hagedorn Insulin
OGTT	Oral glucose tolerance test
SHI	Social health insurance
SMBG	Self-monitoring of blood glucose
SMR	Standardized mortality ratio
TSH	Thyroid- stimulating hormone
tTG	Transglutaminase
T1D	Type 1 diabetes
T2D	Type 2 diabetes
T4	L-thyroxin
USD	US Dollars
WHO	World Health Organization

Introduction

In 2011 the total population of children in the world was 1,900,000,000, and out of these 490,100 had Type 1 diabetes (T1D) (12). In Norway, a country located in Scandinavia in Northern Europe (79), the total population is 4,691,849 (July 2011) (79) and the incidence of T1D is 33.0 per 100,000 in the young (0-14 years) (86). Argentina is the second largest country in South America and the total population is 41,769,726 (July 2011) (91). According to International Diabetes Federation (IDF) Diabetes Atlas, the incidence of T1D in the young (0-14 years) is 6.8 per 100,000 (2011) (84). The incidence of T1D has had a rapid increase almost worldwide, both in low- and high- incidence populations during the last few decades (7, 8). More research is needed to explain this trend. The DIAMOND Group concluded in their study “Incidence and trends of childhood Type 1 diabetes worldwide 1990-1999” that “The rising of Type 1 diabetes globally suggests the need for continuous monitoring of incidence by using standardized methods in order to plan or assess prevention strategies” (10).

Several guidelines have been developed to ensure optimized diabetes care all over the world, but there are still many challenges to solve, especially in diabetes treatment. Before insulin was first introduced in 1922, diabetes was a fatal disease (23). Today insulin therapy has been used in almost a hundred years as treatment for diabetes, but still the major cause of death amongst children with diabetes globally is lack of insulin (26).

In this thesis we access how the clinical practice consensus guidelines made by the ISPAD and the American Diabetes Association (ADA) are implemented in the treatment of children with diabetes in Argentina and Norway; two countries very far apart from each other with huge differences both in economy and health care systems. We will compare our results from the questionnaire used in interviewing health personnel working with childhood diabetes at hospitals in Buenos Aires and Drammen as-well as discuss some theories that could help explain the differences we found, especially concerning treatment results. While reading this thesis it is worth remembering that most figures and percentages presented from the Argentinean hospitals are based on clinical experience by the doctors, while the same data from Norwegian hospitals are based on registries both at the hospital and the Norwegian Childhood Diabetes Registry (NCDR).

Aims

The aim of this thesis is to compare the treatment of children and adolescents with diabetes in Buenos Aires to the treatment in Drammen. Our main focus has been the public hospitals in Argentina compared to public hospitals in Norway. The thesis is part of the bigger project “Diabetes in children; a global comparative study”. Several medical students have visited different countries to access how the international clinical practice consensus guidelines made by the ISPAD and ADA are implemented in the treatment of children with diabetes in different parts of the world, and the alternative strategies followed.

Methods

A semi structural interview was based on a questionnaire. The questionnaire was made by some of the other students who have participated in the same project, but visited other countries. They made an electronic questionnaire based on the 2009 ISPAD's and ADA's guidelines. ISPAD is a professional organization whose aims are to promote clinical and basic science, education and advocacy in childhood and adolescent diabetes. The strength of ISPAD lies in the scientific and clinical expertise in childhood and adolescent diabetes of its members. ISPAD is the only international society focusing specifically on all types of childhood diabetes (1). ISPAD guidelines from 2011 are made in collaboration with the International Diabetes Federation (IDF). ADA is a USA organization working to prevent, cure and manage diabetes in the best way for all people affected by diabetes. ADA Clinical Practice Guidelines are based on a review of the relevant literature by a diverse group of trained clinicians. The recommendations are revised on a regular basis and published in the journal *Diabetes Care* (2). Our questionnaire was designed to collect information about T1D in children less than 15 years of age. Dr. Adriana Rousaus, specialist in diabetes and nutrition at Hospital de Niños in BA, helped us transform the questionnaire from English to Spanish. Both of us speak Spanish to some extent, but all the doctors we interviewed in BA spoke English well and we were therefore able to use both the English and Spanish questionnaire to make sure we had a common understanding of the questions asked. The questionnaire contains two parts. The 1st part is made to get an overview over the condition in the country/state in general, and the 2nd part is made to map how the treatment of children with diabetes is at specific hospitals.

We visited three hospitals, two in Argentina and one in Norway, where we interviewed various health personnel who work with children with diabetes on a daily basis and the interviews were taped. The survey contains no personal identifiable data. We also participated in the daily work at the hospitals.

1. PART ONE: Literature review

1.1 Diagnosis of diabetes mellitus

One should consider diabetes when elevation of blood glucose is found, whatever the measurement. Some children have a rapid onset of the disease and present themselves with severe symptoms of ketoacidosis, while others have an onset over several months (3).

Diagnostic criteria of diabetes mellitus according to the IDF/ISPAD guidelines:

Diagnostic criteria for diabetes are based on blood glucose measurements and the presence or absence of symptoms. The criteria according to IDF/ISPAD Guidelines 2011 are based on the World Health Organization (WHO) and ADA reports (5, 6). The criteria are as follows (3, 4):

1. Symptoms of diabetes plus casual plasma glucose concentration ≥ 11.1 mmol/l.
 - Casual is defined as any time of day without regard to time since last meal.
 - Corresponding values are ≥ 10.0 mmol/l venous blood and ≥ 11.1 mmol/l capillary blood.

OR

2. Fasting plasma glucose ≥ 7.0 mmol/l
 - Fasting is defined as no caloric intake for at least 8 hours.
 - Corresponding values are ≥ 6.3 mmol/l for both venous and capillary blood

OR

3. 2-hour postload glucose ≥ 11.1 mmol/l during an Oral Glucose Tolerance Test (OGTT)
 - An OGTT is an oral glucose tolerance test using a glucose load containing the equivalent of 75 g glucose dissolved in water, or 1.75 g/kg body weight to a maximum of 75 g (5).
 - Rarely indicated in diagnostics among children and adolescents (5).

4. Glycated hemoglobin A1c (HbA1c) ≥ 6.5 .

There are difficulties with assay standardization and individual variation in the relationship between blood glucose and HbA1c, which may outweigh the convenience of this test.

The diagnosis should not only be based on a single plasma glucose concentration, but may require “continued observation with fasting and/or 2 hour post-prandial blood glucose and/or an OGTT.” (3).

An OGTT should not be performed if one can diagnose diabetes using other measurements. Also, if the child represent with severe fasting hyperglycemia and symptoms of ketoacidosis, one needs to start treatment with insulin immediately, and cannot wait for further test results (3).

1.2 Diabetes mellitus type 1

Epidemiology of T1D

The total population of children in the world is 1,900,000,000 (2011) and out of these 490,100 have T1D (12). The incidence is rising, and is seems to be increasing with age (10).

AT A GLANCE	2011
Total child population (0-14 years, billions)	1.9
TYPE 1 DIABETES IN CHILDREN (0-14 YEARS)	
Number of children with type 1 diabetes (thousands)	490.1
Number of newly-diagnosed children per year (thousands)	77.8
Annual increase in incidence (%)	3.0

Table 1: *Total child population (0-14 years) in the world in 2011. Prevalence and incidence of type 1 diabetes among children and adolescents (0-14 years) in 2011, Diabetes Atlas 5th edition (12).*

The incidence of T1D has had a rapid increase almost worldwide, both in low- and high- incidence populations, during the last few decades (7,8). The WHO program, Multinational project for childhood diabetes (Diamond project group), studied global childhood diabetes from 1990-1999 (9), and their results showed that the incidence of T1D has increased by 2.8 % on average per year from 1990-1999 worldwide (10). In 70 % of the Asian countries the incidence was <1 per 100,000/year, in most African countries the incidence was between 1-9 per 100,000 /year, and in South American countries the incidence varied between very low, <1 per 100,000/year, to high, 10 per 100,000/year (10). In Europe the incidence was found to vary from low, 4 per 100,000/year, to very high, 41 per 100,000/year, with the Northern countries Finland, Sweden and Norway showing very high incidence with ≥ 20 per 100,000 per year (10). In 2011 the numbers in the Northern countries are even higher, with an incidence ≥ 24 per 100,000 per year (12). The incidence is rising, and more research is needed to explain this trend. "The increasing incidence of T1D globally emphasize the need for

continuous monitoring of incidence by using standardized methods in order to plan or assess prevention strategies” (10).

Map 2.5. New cases of type 1 diabetes (0-14 years per 100,000 children per year), 2011

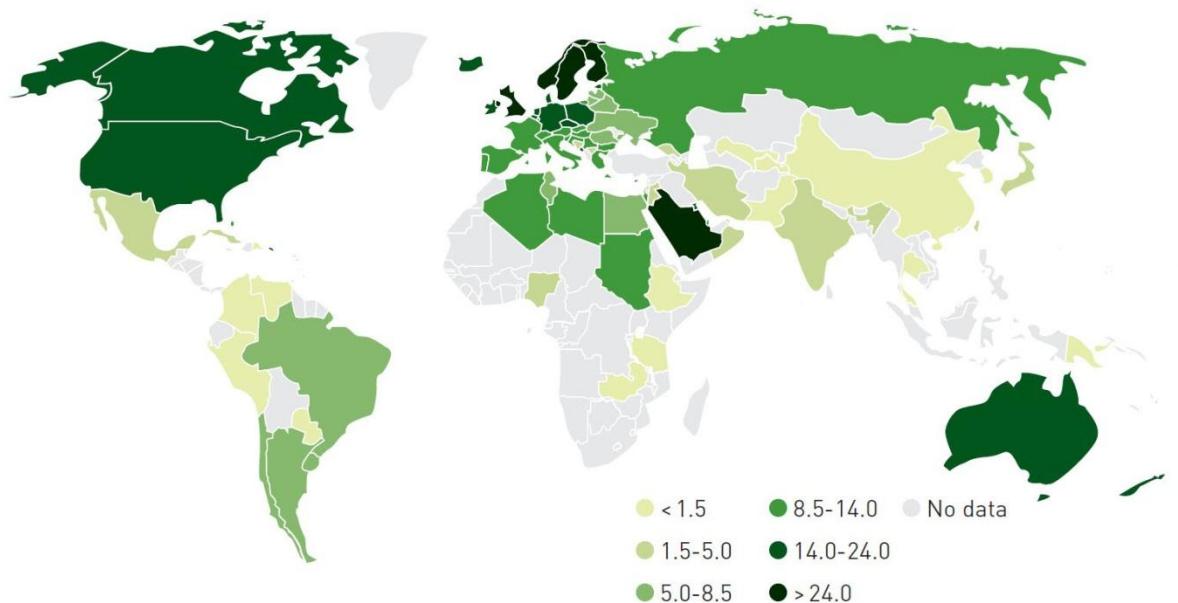


Figure 1: Incidence of type 1 diabetes per 100,000 among children and adolescents 0-14 years of age in the world, 2011. International diabetes federation, Diabetes Atlas 5th edition. Available at URL: <http://www.idf.org/diabetesatlas/5e/diabetes-in-the-young> (13).

Etiology of T1D

The Diamond Project Group stated in their study “Incidence of the Childhood Type 1 diabetes worldwide” that “continuing and expanding surveillance for childhood diabetes across the world represents one of the most potent strategies for understanding the multi factorial etiology of the disease and ultimately preventing it.” (11). From this statement we understand that there might still be a lot to be discovered when it comes to understanding the etiology of T1D. Here we will give a short presentation of what is known today:

Most cases of T1D are caused by a selective β -cell destruction in the pancreas due to T-cells. This occurs at a variable rate, and becomes clinically symptomatic when approximately 90 % of the β -cells are destroyed (4). More than 40 genomic locations have been associated with T1D, and HLA genes have the strongest association (16). When fasting hyperglycemia is detected, one might find

markers of an autoimmune pathological process in 85- 90 % of the individuals. These include islet cell autoantibodies (ICA), glutamic acid decarboxylase autoantibodies (GAD), IA-2, IA-2 β , or insulin autoantibodies (IAA) (17). It is suggested that the age of onset of T1D is determined by the intensity of the β -cell destructive process, which again is modulated by both genetic and environmental factors (14). The environmental factors which trigger the destruction of β - cells remain largely unknown. Triggers might be chemical, bacterial and/or viral, and the process often begins months to years before clinical symptoms manifest. Enterovirus infections have been associated to development of autoantibodies in T1D (15).

Diagnosis and the different phases of T1D

The date of onset of T1D is defined as the date of the first insulin injection (3).

The different phases of T1D

The IDF/ISPAD guidelines of 2011 suggest that T1D may be divided into these phases (3):

Preclinical phase T1D: Is a phase lasting from months to years before clinical manifestation of the disease. In this period autoantibodies can be detected, which indicate beta cell autoimmunity.

Presentation of T1D: When first diagnosed, T1D can present itself with severe symptoms requiring acute treatment (ketoacidosis), with mild symptoms, or by accident in the absence of symptoms.

Partial remission or Honeymoon phase of T1D: In many children and adolescents, the requirements of insulin may decrease transiently after the initiation of insulin treatment, due to the remaining β - cells that are still functioning. This phase of remission usually starts within days or weeks after introducing insulin treatment, and may last for weeks or months. The definition of this phase is insulin requirements less than 0.5 units/kg/day with HbA1c \leq 7 %. Blood glucose is stable despite fluctuations in diet and exercise.

Chronic phase of T1D: Gradually the functioning β -cells will decrease even further, and so the insulin production in the pancreas will diminish, and the disease will develop from a remission phase to a chronic phase with lifelong treatment with insulin.

Clinical presentation of T1D:

In children, diabetes mellitus usually presents itself with characteristic symptoms such as polyuria, polydipsia, blurring of vision and weight loss, in association with glycosuria and ketonuria (4). The child might also suffer from irritability and decreasing school performance, recurrent skin infections, enuresis and vaginal candidiasis in prepubertal girls. In severe cases, children may present with some of the symptoms caused by ketoacidosis; severe dehydration, vomiting, polyuria despite dehydration, weight loss, flushed cheeks, acetone detected in the breath, hyperventilation, disorientation/semicomatose/comatose, decreased peripheral circulation with rapid pulse, hypotension and shock with peripheral cyanosis (3).

Treatment of T1D

In 1922 insulin therapy was introduced, using regular insulin before each main meal and one injection during the night. During the following years, intermediate- and long-acting insulin was developed, and after 1935 most diabetic patients used one or two insulin injections per day (23). In 1960 a published study showed that patients diagnosed between 1935 and 1945, which were using the regimen with one or two injections per day, had a much higher risk of retinopathy after 15 years of diabetes duration, compared to those who were diagnosed before 1935 and used multiple daily injections (MDI) (61 % vs. 9%) (25). Today, insulin therapy has been used in almost a hundred years as treatment for diabetes, but still the major cause of death amongst children with diabetes globally is lack of insulin (26).

Glycemic control:

Monitoring glycemic control includes both daily monitoring of glucose as-well as periodic monitoring of overall glycaemia. The aim is to prevent acute complications in the form of hypoglycemia and hyperglycemia, and minimize chronic complications of microvascular and macrovascular disease. Daily monitoring of blood glucose is best determined by self-monitoring of blood glucose (SMBG). This will give the patient instant information of blood glucose levels and the patient can determine the correct insulin requirements and also detect hypoglycemia and hyperglycemia (17). HbA1c reflects average plasma glucose over the previous 2-3 months in one single measure (5, 17) however the last week before measurement is not included because the most recent glycation is reversible (22). HbA1c measurements can be performed at any time of the day, and the patients do not have to consider any special preparations such as fasting (5). Elevated HbA1c predicts long-term

microvascular and macrovascular complications, and it is clear evidence that lower HbA1c reflects better metabolic control, and is associated with fewer and delayed microvascular complications (19, 20). The frequency of SMBG is associated with improved HbA1c, most likely because this will make the insulin adjustment for consumed food better, and the patient will be able to quickly correct glucose values that are out-of-target (21).

Among the recommendations made by IDF/ISPAD Guidelines 2011 are (18):

- SMBG should be prescribed at a frequency to optimize each child's diabetes control, usually four to six times a day.
- Ketone testing should be available and performed: During illness with fever and/or vomiting, when blood glucose value above 14 mmol/l in an unwell child or when persistent blood glucose levels above 14 mmol/l are present, when there is persistent polyuria with elevated blood glucose, especially if abdominal pains or rapid breathing are present.
- Facilities for the measurements of HbA1c should be available to all centers caring for young people with diabetes.
- HbA1c should be monitored four to six times per year in younger children, and three to four times per year in older children.
- When urine glucose testing is used, as many urine tests as possible should show no glycosuria without occurrence of frequent or severe hypoglycemia.

Targets of treatment:

Target HbA1c for those under the age of 18 years is a value less than 7.5 % (17-19). This value is based upon clinical trials made in the Diabetes Control and Complications Trial (DCCT) (19).

Insulin treatment:

Over the last years, insulin analogues have been developed, both rapid and long-acting. The debate whether these analogues give better results than regular insulin is ongoing (23). Regular (soluble) insulin, porcine or bovine insulin and insulin analogues are available for use in treatment. Porcine or bovine preparations are cheaper in some parts of the world, they are not inferior in efficiency, but they have greater immunogenicity (29). These insulins from animal species are however currently being withdrawn from the market, and most manufacturers are producing insulin analogs instead. The regular soluble insulin is usually

identical to human insulin and is short acting; it is still used in many daily regimens in many parts of the world (23). Several rapid acting insulin analogs have been developed, and the advantage is that these insulins can both be given before and after meals (30), can be given immediately before a meal, they give a quicker effect when needed for treatment of hyperglycemia and are often used in insulin pumps (23). The intermediate acting insulins include Isophane Insulin, also called Neutral Protamine Hagedorn (NPH) insulin, and Crystalline zinc acetate insulin. These are suitable for twice daily regimens and for pre-bed dosage in basal-bolus regimens (23). New basal long-acting analogs, glargine and detemir, show less day to day variation compared to NPH insulin, but they are however 50- 100 % more expensive. There is evidence for reduced rate of hypoglycemia and a greater treatment satisfaction (31, 32).

Because children and adolescents with diabetes are dependent on insulin treatment for survival, ISPAD and IDF are working together to make insulin available for all children and adolescents with diabetes and they should as a minimum have access to adequate amounts of at least regular and NPH- insulin (23).

According to ISPAD Guidelines from 2009, frequently used regimens in insulin therapy all over the world are currently (23):

Two injections daily: A mixture of short or rapid and intermediate acting insulins (before breakfast and the main evening meal).

Three injections daily: Using a mixture of short or rapid and intermediate acting insulins before breakfast; rapid or regular insulin alone before afternoon snack or main evening meal; intermediate acting insulin before bed or variations of this.

Basal-bolus regimen: Of the total daily insulin requirements, 40- 60 % should be basal insulin, the rest pre-prandial rapid-acting or regular insulin. The regimen includes injection of regular insulin 20-30 minutes before each main meal, injections of rapid acting insulin analog immediately before (or after) each main meal, intermediate- acting insulin or basal/long-acting analog at bedtime, probably before breakfast and sometimes at lunchtime or twice daily (mornings and evenings).

The basal-bolus regimen has the best possibility of imitating the physiological insulin profile. According to several randomized trials, the use of MDI and pumps will give better control of blood glucose than a treatment with injections two times per day (27, 28).

Insulin dosage: Daily insulin dosage is based on several factors such as age, weight, stage of puberty, duration and phase of diabetes, state of injection site, nutritional intake and distribution, exercise, daily routine, results of blood glucose monitoring and intercurrent illness (23). During partial remission phase, total daily insulin dose is often < 0.5 IU/kg/day. After this phase, prepubertal children usually require 0.7-1.0 IU/kg/day, and during puberty insulin requirements may rise up to 1-2 IU/kg/day (23, 24).

IDF/ISPAD Guideline 2011 include these recommendations for insulin therapy (24):

- Insulin treatment must be started as soon as possible after diagnosis in all children with hyperglycemia.
- The insulin treatment modality should be as physiological as possible, but with consideration of the patient's and caregiver's preferences.
- Rapid- and long-acting insulin analogues should generally be available, alongside with Regular (soluble) and NPH insulin.
- Comprehensive care: Insulin pump therapy should be available and considered.

Nutritional management in T1D

Nutritional management is one of the cornerstones of diabetes care and education (33). Successful implementation of meal planning with appropriate insulin adjustments has been shown to improve glycemic control (34). It is also necessary to ensure optimal growth and development. Dietary recommendations for children with diabetes are based upon healthy eating principles suitable for all children and families and does not only improve glycemic control, but also reduce cardiovascular risk factors and improve general health.

Carbohydrate counting is a tool that focuses on improving glycemic control and to allow a greater flexibility of food choices. For the children using MDI or pump, insulin doses can be calculated based upon the amount and type of carbohydrate intake. With the determined insulin, both carbohydrate ratios and adjustment of pre-meal insulin according to the estimated carbohydrate content of the meal or snack is enabled (33).

The ISPAD guidelines recommend that a specialist dietitian with experience in childhood diabetes should be part of the interdisciplinary pediatric diabetes team. The dietitian should be available at diagnosis and in the first year thereafter to provide a minimum of two to four follow-up sessions (35).



1.3 Diabetes mellitus type 2

Epidemiology

Diabetes type 2 (T2D) used to be a disease of the middle- aged and older generation, but during the last decades T2D has had a rising incidence among children and adolescents. In the USA between 8 and 45 % of children and adolescents with newly presenting symptoms of diabetes have T2D (40). T1D still remains the most common form of childhood onset diabetes worldwide, but T2D is all-ready the main form of diabetes in many ethnic groups (38). In Japan, T2D already accounts for 80 % of diabetes in children (39). There are still no clear criteria for defining insulin resistance in children (37).

Etiology

Information on etiology of T2D in pediatric medicine is sparse (38). It seems clear however that in the pathogenesis of T2D in the young, insulin resistance and impaired β - cell function are the two main components (36), and T2D occurs when insulin secretion is inadequate to meet the increased demand due to insulin resistance (43). Insulin secretion can vary from delayed, but highly elevated in response to a glucose challenge, to absolutely diminished (43). Risk factors in the young are both modifiable; obesity, low physical activity, low socioeconomic status, and non-modifiable; ethnicity (Pima Indians, Hispanics, Asians and Afro-Caribbeans), family history of T2D, low birth weight,

gestational diabetes in the mother and female sex. Puberty is an additional risk factor which contributes to insulin resistance (41).

Diagnosis

Some children are being misdiagnosed as T1D (38), and the fact that up to one third of T2D- patients may present with ketoacidosis, makes it even more difficult to distinguish the two (42). With more children developing T2D, it becomes even more important to recognize the correct diagnosis, so that appropriate therapy can be induced (40).

The clinical diagnosis of T2D in an asymptomatic individual requires at least two abnormal glucose values, diagnostic of diabetes (see Diagnostic criteria of T1D), on two separate days (44). One should test for autoantibodies, especially in areas where T1D is more common and in obese children over the age of 13 where clinical symptoms resemble T1D. Also one might measure C-peptide levels, but this is most valuable done when the diabetes is established and not in the acute phase. Persistent elevated C-peptide levels are unusual in T1D after 12-14 months (44).

Treatment and managing

Initial treatment is determined by symptoms, the severity of hyperglycemia, and the presence or absence of ketoacidosis. Treatment goals are weight loss, increased exercise, normalization of glycaemia and control of co-morbidities such as hypertension, dyslipidemia, nephropathy and hepatic steatosis (44).

Diet and exercise can improve insulin sensitivity (37) and are essential parts of the treatment. Other treatment may be added if treatment goals are not reached with diet and exercise alone. Metformin is the initial pharmacological treatment (44), and the aim is to decrease insulin resistance and increase insulin secretion (44). If therapy with metformin alone fails over a period of 3 months, this indicates the need of adding insulin alone, or in combination with other agents. In the majority of countries only metformin and insulin are approved for use in children and adolescents (44).

1.4 Monogenic diabetes

Monogenic diabetes results from the inheritance of a mutation or several mutations in a single gene; this could be a dominant or recessive inheritance or a de novo mutation. Monogenic diabetes is confirmed by molecular genetic testing. Genetic testing should be considered in all children presenting with diabetes before six months of age (45).

There are several types of diabetes in the monogenic group, each associated with different mutations, and here are some of them shortly presented:

Neonatal diabetes: Insulin requiring diabetes diagnosed usually in the first three months of life. There are two groups; one transient group where 50 % of the cases ultimately relapses, and one permanent group where continuous insulin treatment is needed.

Familial diabetes: The most common cause is *MODY 3*; Hepatocyte nuclear factor 1-alpha gene mutations. Clinical characteristics are young-onset of diabetes that is not insulin-dependent, good glycemic control on a small dose of insulin or detectable C-peptide measured when on insulin with glucose over 8 mmol/l, and family history of diabetes.

MODY 1: Hepatocyte nuclear factor 4 alpha gene mutations. This is a less common mutation, but is similar to mutations of HNF-1 α gene (47).

MODY 2: Mild fasting hyperglycemia due to glucokinase mutations. HbA1c is usually just below or just above the upper limit of normal (5.5- 5.7 %) (45).

Most children with monogenic diabetes are first misdiagnosed as T1D or T2D (46). According to the 2011 guidelines of IDF and ISPAD, monogenic diabetes should be considered with these clinical presentations (45):

- Neonatal diabetes or diabetes diagnosed within 6 months of life.
- Familial diabetes with an affected parent.
- Mild (5.5- 8.5 mmol/l) fasting hyperglycemia especially if young or familial.
- Good glycemic control on a small dose of insulin and not developing ketoacidosis in the absence of insulin.
- Diabetes associated with pancreatic features.

1.5 Diabetes education

Education is a critical element for children and adolescents with diabetes and their families. It is necessary for improving patient outcomes (48, 49). "Diabetes self-management education (DSME) is the ongoing process of facilitating the knowledge, skill and ability necessary for diabetes self-care" according to a study published in Diabetes Care 2007 (48). Patients who do not receive any education, are more likely to suffer from complications related to diabetes (48).

The diagnosis of T1D gives rise to dramatic changes in lifestyle, the need for acceptance of a chronic illness and understanding the possibility of long-term complications. There is evidence that psychological problems are increased in children with diabetes, and this is also often associated with poor metabolic control (50). It is a widely accepted fact that diabetes education needs to include behavioral modification in order to be managed successfully (50). Because of this there is a need for training diabetes teams in behavioral change management, including counseling techniques, in addition to structured education of the disease itself (48, 49).

Recommended diabetes education according to the IDF/ISPAD guidelines 2011 include (51):

- Every young person with diabetes and their parents/caregivers have a right to accessible, planned diabetes self-management education.
- Initial learning, started as soon as possible after diagnosis, should include immediate knowledge-based education and practical survival skills. This should be followed by graduate levels of education reinforced whenever possible by diagrams, drawings, written guidelines, booklets and other visual media appropriate to the child's age, maturity and environmental circumstances.
- Diabetes education should be delivered by a pediatric diabetes team (as a minimum a doctor, nurse and dietitian), acknowledging their different skills with a clear understanding of the special and changing needs of young people and their families as they grow through different stages of life.
- Diabetes education must be given by someone with experience and expertise in pediatric diabetes management.
- Diabetes education needs to be learner- centered and thus be adaptable to suit individual needs.
- Diabetes management, facilitated by education, is unlikely to be successful without some degree of behavioral change in children, adolescents and their parents/carers.
- The diabetes team should receive training in teaching and counseling techniques.
- Diabetes education needs to be a continuous process and repeated for it to be effective.

1.6 Complications of diabetes mellitus

Acute complications

Diabetic ketoacidosis (DKA)

DKA is a life-threatening complication that results from lack of insulin. Absolute deficiency can occur if T1D is undiagnosed or if the patients for some reason do not take insulin. Relative insulin deficiency occurs in situations when the concentrations of counter regulatory hormones such as catecholamines, glucagon, cortisol and growth hormone increase in response to stress. This can happen in conditions such as sepsis, trauma, or gastrointestinal illness with diarrhea and vomiting. The increase of counter regulatory hormones leads to an insulin resistance (52). The catabolic state caused by the combination of low levels of insulin and high levels of counter regulatory hormones causes the liver and kidney to produce glucoses via glycogenolysis and gluconeogenesis. There is also increased lipolysis and ketogenesis, which leads to ketonemia and metabolic acidosis.

The hyperglycemia and hyperketonemia cause osmotic diuresis, dehydration, acidosis and loss of electrolytes. The clinical manifestations and signs of DKA include (53):

- Dehydration, nausea, vomiting
- Abdominal pain mimicking an acute abdomen
- Rapid and deep sighing (Kussmaul respiration)
- Increased leukocyte count and non-specific elevation of serum amylase and fever if infection is present
- In severe cases of DKA; loss of consciousness, cerebral edema and death can also occur

The biochemical criteria for the diagnosis of DKA used by ISPAD and ADA are: (54)

	ISPAD	ADA
Hyperglycemia	Blood glucose >11 mmol/L (≈200 mg/dL)	Blood glucose 14 mmol/L (>250 mg/dL)
Venous pH	<7.3 or bicarbonate <15 mmol/L	<7.3 or bicarbonate <15 mmol/L
Ketones	Ketonemia and ketonuria	Ketonemia and ketonuria

Table 2: *Biochemical criteria for the diagnosis of diabetic ketoacidosis used by ISPAD and ADA.* DUNGER DB, SPERLING MA, ACERINI CL, BOHN DJ, DANEMAN D, DANNE TP, et al. ESPE/LWPES consensus statement on diabetic ketoacidosis in children and adolescents. Arch Dis Child 2004 Feb; 89(2):188–94. (54).

There is wide geographic variation in the frequency of DKA at onset of diabetes. DKA at diagnosis is more common among younger children (<5 years of age) and in children whose families do not have easy access to medical care because of social or economic reasons (55, 56).

Hypoglycemia

Hypoglycemia is a common acute complication for children with diabetes. There is a mismatch between the food consumed, amount of exercise and the insulin dose (57). In the interest of avoiding hypoglycemia and maintaining consistency in reporting hypoglycemia, 3.9 mmol/L (70 mg/dL) is the recommended lower target for BG levels in children and adults with insulin-treated diabetes (58). The symptoms vary and can be embarrassing, unpleasant and potentially dangerous. It is important to avoid these symptoms, both for the wellbeing of the patients and to avoid limitations due to treatment and achievement of normal BG (59).

The children can get a wide variety of symptoms: (57)

- From the autonomic neural system: trembling, pounding heart, cold sweatiness, pallor, neuroglycopenic signs and difficulty concentrating.
- Disturbance of vision, hearing and speech.
- Behavioral signs and symptoms: irritability, nightmares, hunger, headache, tiredness and nausea.
- In the worst case hypoglycemia can lead to loss of consciousness, seizures and death.

Younger children and their parents are typically not good at sensing the early signs of hypoglycemia and parents therefore need to measure BG level regularly, especially in situations when hypoglycemia is likely to occur such as after exercise or when the treatment regimen is altered (60).

Long term complications

There are several long term complications associated with diabetes. A good BG control is important to avoid these potentially harmful complications. It is usually rare among children and adolescents. However early functional and structural abnormalities may be present a few years after the onset of the disease (61).

The hyperglycemia affects blood vessels in different parts of the body. The long term complications are divided into microvascular and macrovascular complications.

Microvascular complications

Microvascular alterations due to influence of hyperglycemia may lead to retinopathy, nephropathy or neuropathy.

Diabetic retinopathy: Diabetic retinopathy is the most common cause to loose of sight in working age worldwide. The risk increases with age, longer duration of diabetes and during puberty. Adolescents have a higher risk of progression to vision threatening retinopathy compared to adult patients with diabetes. The progression may be rapid, especially in those with poor glycemic control (61). Retinopathy is associated with micro aneurisms, hemorrhages, ischemia and occlusions of the vessels in retina. If the central part of retina is affected this is called maculopathy and will affect vision. The retinopathy will, if it continues to develop, lead to proliferation of the vessels in the retina, called neovascularization. These vessels can rupture or bleed into the vitreoretinal space which is threatening to the vision (62). Because diabetic retinopathy starts to develop without any symptoms, it is very important to screen for early signs of diabetic retinopathy. Ideally, this is done with fundal photography or alternatively with ophthalmoscopy. If vision threatening retinopathy has been detected this can be treated with photocoagulation, also called “laser therapy”. This can cause a delay of further development of the retinopathy.

Diabetic nephropathy: Diabetic nephropathy is according to ISPAD defined as persistent proteinuria greater than 500 mg/24 hours or albuminuria greater than 300 mg/24 hours. The first sign of renal affection is micro albuminuria, which develop further into albuminuria and eventually proteinuria. It is therefore important with regular screening to delay development of renal failure. It is also important with regular screening of blood pressure.

Micro albuminuria is defined by any of the following criteria: (63)

- Albumin excretion rate (AER) between 20 and 200 µg/min, or AER 30-300 mg/24 h in 24-h urine collections.
- Albumin concentrations (AC) of 30-300 mg/L (in early morning urine sample).
- 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).

Micro albuminuria is confirmed by consistent findings; meaning abnormal findings in two or all of three samples over a period of 3–6 months. Persistent micro albuminuria has been shown to predict the progression to End stage renal failure (ESRF) and is associated with an increased risk of macro vascular disease. Albuminuria is often associated with hypertension and reduction in Glomerular filtration rate (GFR). ESRF may occur many years later and requires dialysis or kidney transplantation. Diabetic nephropathy is a major cause of morbidity and mortality amongst young adults with T1D (63).

Diabetic neuropathy: Diabetes can affect both the somatic and the autonomic nervous system (61):

In the somatic nervous system the affection can be focal and/or affect several nerves in polyneuropathy. Focal neuropathies can for instance cause carpal tunnel syndrome with affection of the median nerve or palsy of the third cranial nerve. The polyneuropathy is often referred to as “diabetic neuropathy” because this is the most common form of nerve affection in patients with T1D. It causes a diffuse damage to all peripheral nerve fibers; first it will lead to sensory loss and later loss of motor function.

Autonomic neuropathy can for instance cause postural hypotension, vomiting, diarrhea, bladder paresis, impotence or sweating abnormalities (61).

Macrovascular complications

The mortality and morbidity of cardiovascular disease (CVD) are markedly increased in diabetic individuals compared to the non-diabetic population (64). Diabetic patients are more

prone to develop atherosclerosis, and hypertension has a greater impact on cardiovascular disease in patients with diabetes compared to others (65). To help prevent macrovascular complications it is important with good control of blood pressure and treatment with statins if cholesterol levels are elevated. Short term trials have shown that simvastatin, lovastatin and pravastatin are effective and safe to use in children and adolescents (66).

Other complications and associated conditions with diabetes in children and adolescents

Impaired growth and development

Increased height at diagnosis of T1D has been frequently reported (67). The precise mechanism for this and whether or not this increased height is maintained is unclear. Some studies report that poorly controlled patients show a decrease in height standard deviation score over the next few years, whilst better controlled patients maintain their height advantage. Others have not shown this relationship with diabetic control (68, 69).

Associated autoimmune conditions

Hypothyroidism: Primary hypothyroidism due to autoimmune thyroiditis occurs in approximately 3–8% of children and adolescents with diabetes (70). Clinical features may include the presence of a painless goiter, increased weight gain, retarded growth, tiredness, lethargy, cold intolerance and bradycardia. Diabetic control may not be significantly affected.

The treatment is based on replacement of L-thyroxin (T4) to normalize the thyroxin levels, and usually this allows regression of goiter (71).

Celiac disease: Celiac disease is an autoimmune disease that causes gluten intolerance. Celiac disease occurs in 1-10 % of children and adolescents with diabetes (72). Any child with gastrointestinal signs or symptoms including diarrhea, abdominal pain, flatulence, dyspeptic symptoms, recurrent aphthous ulceration, unexplained poor growth or anemia should be investigated. Undiagnosed celiac disease has also been associated with increased frequency of hypoglycemic episodes and a progressive reduction in insulin requirement over a 12 month period prior to diagnosis (73).

Recommendations from the ISPAD and ADA guidelines concerning complications

Screening for diabetes complications aims to detect subclinical complications which may be treated to delay progression to clinical disease (74).

Screening for acute complications

To detect DKA, ketones are determined in urine or blood. Blood ketone determination has been shown to be most helpful in avoiding emergency room visits. ISPAD recommends that ketone testing should be performed during illness with fever and/or vomiting, when BG value above 14 mmol/L (250 mg/dL) in an unwell child, when the BG levels are persistent elevated and when there is persistent polyuria with elevated BG or urine glucose, especially if abdominal pain or rapid breathing is present (75).

Screening for micro- and macro vascular complications

Improvement in glycemic control will reduce the risk for onset and progression of diabetes vascular complications (76).

Screening for macrovascular complications:

		Screening method	Frequency
Dyslipidemia	ISPAD	Assessment of fasting blood lipids.	Should be performed soon after diagnosis in all children with T1D aged over 12 years. Should be repeated every 5 years.
	ADA	Assessment of fasting blood lipids.	At 10 years of age and every 5 years.
Hypertension	ISPAD	Blood pressure measurement	Annually
	ADA	Blood pressure measurement	Annually

Table 3: *Screening for macrovascular complications according to the ISPAD/ADA guidelines*

(Donaghue KC, Chiarelli F, Trotta D, Allgrove J, Dahl-Jorgensen K. Microvascular and macrovascular complications associated with diabetes in children and adolescents. *Pediatric Diabetes* 2009; 10 (Suppl. 12): 195–203.

Screening for microvascular diseases:

		Screening method	Frequency
Retinopathy	ISPAD	Ophthalmoscopy	Annually from -11 years, with two years duration of diabetes -9 years with five years duration of diabetes.
	ADA	Fundal photography or ophthalmoscopy	Annually from age ≥ 10 years with 3–5 years duration
Nephropathy	ISPAD	Urinary albumin/- creatinine ratio OR first morning albumin concentration	Annually from -11 years, (with two years duration of diabetes) -9 years, (with five years duration of diabetes)
	ADA	Urinary albumin/- creatinine ratio	Annually from 10 years (with 5 years duration)
Neuropathy	ISPAD	History and clinical examination	No recommendations made by ISPAD
	ADA	-Clinical examination for distal polyneuropathy -History and clinical examination for autonomic neuropathy	Annually

Table 4: *Screening for microvascular diseases according to the ISPAD/ADA guidelines*

(Donaghue KC, Chiarelli F, Trotta D, Allgrove J, Dahl-Jorgensen K. Microvascular and macrovascular complications associated with diabetes in children and adolescents. *Pediatric Diabetes* 2009; 10 (Suppl. 12): 195–203)

Screening for associated conditions:

Monitoring of growth and physical development and the use of growth charts is an essential element in the continuous care of children and adolescents with T1D (77).

Screening for autoimmune diseases:

		Screening method	When
Hypo-thyroidism	ISPAD	Analyzing circulating thyroid-stimulating hormone (TSH), T4 and antibodies	Is recommended at the diagnosis of diabetes, and thereafter every second year in asymptomatic individuals.
	ADA	Analyzing circulating TSH, T4 and antibodies	Every 1-2 year or if thyroid disease is suspected.
Celiac disease	ISPAD	Normal Immunoglobulin A (IgA) antibodies and IgA antibodies against tissue transglutaminase (tTG) or elevated endomysial autoantibody (EMA)	At the time of diagnosis, annually for the first five years and every second year thereafter.
	ADA	Normal IgA antibodies and IgA antibodies against tissue tTG or EMA	At the time of diagnosis. Periodic rescreening if negative antibodies.

Table 5: *Screening for autoimmune diseases according to the ISPAD/ADA guidelines*

(Kordonouri O, Maguire AM, Knip M, Schober E, Lorini R, Holl RW, Donaghue KC. Other complications and conditions associated with diabetes in children and adolescents. *Pediatric Diabetes* 2009; 10 (Suppl. 12): 204–210.)

Complications and mortality

The article: “Long term mortality in a nationwide cohort of childhood-onset type 1 diabetic patients in Norway” was published in 2006 (78). All Norwegian patients who were diagnosed with T1D between 1973 and 1982 and were under 15 years of age at diagnosis was included (n=1,906). During follow up 103 individuals died. The mortality was 2.2/1000 person years. . The standardized mortality ratio (SMR) was based on national background statistics. The overall SMR was 4.0 (95% CI 3.2-4.8) and was similar for males and females. Acute metabolic complications of diabetes were the most common cause of death under 30 years of age. Cardiovascular disease was responsible for the largest proportion of deaths from the age of 30 years onward. The study concluded that childhood-onset T1D still carries an increased mortality risk when compared with the general population, particularly for cardiovascular disease. This shows how important it is to prevent short- and long term complications in children with early onset T1D.

2. PART TWO: An international perspective; diabetes in Argentina and Norway

2.1 Diabetes in Norway

2.1.1 Presentation of Norway

Geography and demography

Norway is located in Northern Europe, and has country boundaries to Sweden in the east, Russia and Finland in the north (79).



Figure 3: Map of Norway and Europe. CIA, The World Factbook 2011. Available at URL: <https://www.cia.gov/library/publications/the-world-factbook/geos/no.html> (80).

The population is 4,691,849 (July 2011), and consists of 94.4 % Norwegians, 3.6 % other Europeans and 2 % others (2007). 18 % of the population is between 0-14 years. In the capital of Oslo the population is 875,000 (2009) (79).

Economic situation

Norway is a welfare state and the Norwegian economy is an example of a mixed economy, with a combination of free market activity and large state ownership in certain key sectors. The income from the petroleum production is significant. Large reserves of petroleum and natural gas were discovered in the 1960s. Norway has a large amount of natural resources

compared to the size of the population. This has led to one of the highest standards of living in the world.

Gross domestic product (GDP) per capita is \$ 54,200 in 2011, and puts Norway as number 8 in a world ranking (79). Unemployment rate the same year was 3.3 % (79). Another ranking system, the Human Development Index (HDI), is a comparative measure of life expectancy, literacy, education, standards of living, and quality of life for countries worldwide presented by United Nations annually, and Norway was ranked number 1 in 2011 (81).

2.1.2 Health care system in Norway (83)

WHO ranked the health systems of its 191 member states in the World Health Report 2000, and Norway was then ranked as number 11 (82). The rankings are based on different factors such as (82):

- Health: disability-adjusted life expectancy
- Responsiveness: speed of service, protection of privacy, and quality of amenities
- Fair financial contribution

Health expenditure is 9.7 % of GDP, and this ranks Norway as number 35 in a world comparison (79). There are 4076 medical doctors per 100,000 inhabitants, which rank Norway as number 10 in the world (79). Life expectancy at birth is 80.32 years (female: 83.14 and male: 77.65) (84), the child mortality rate is 3.5 per 1000 per year (79). The national health system in Norway provides healthcare to all citizens. The fundamental principle is that all citizens should have the same right to receive health services no matter age, sex, where they live and economic status. The health care system in Norway is mainly based on taxes taken directly from salaries. When you undergo a health check or receive medical treatment in Norway, you are obliged to pay a minor user fee. If the user fee exceeds a certain amount within one year (approximately 350 US Dollars (USD)), you are entitled to a health care exemption card. This amount also includes certain medical equipment and medicines that are essential for a longer period of time, which means that these medicines will be free of charge for the rest of the year once the set amount of 350 USD is reached.

The health system is divided into three levels:

1. The central management
2. The specialist healthcare system
3. The primary healthcare system

The central health management is run by the government and is responsible for the overall planning and controlling of the healthcare system. The Ministry of Health and Care Services has the overall responsibility for government policy on health care services in Norway. They make sure that the healthcare system is operated according to Norwegian law, controls the economics and the quality of the health services.

The specialist healthcare system in Norway is divided into four health regions; The Northern-, Central-, Western- and South-Eastern Norway Regional Health Authority. These four health regions are responsible for operating the public hospitals in Norway.

The primary health care system is organized and run by the 430 municipalities in Norway. Most of the patients are treated at this level. In Norway there are more than 4000 general practitioners (GPs). Most GPs and specialists working outside hospitals are private, but work under contract within the public system in return for grants and fees for services. In 2001 Norway started a new system called "Fastlegeordningen" which includes an arrangement giving all inhabitants in Norway one specific GP that they should always seek in need of medical assistance (except for emergency situations outside of the GPs opening hours, or when direct admission to the hospitals are required). Each GP is responsible for 1200 patients in average. This new system has worked well for the doctors as well as for the patients.

There are also private options in Norway, where the patient will have to pay for the whole treatment himself. Some specialized doctors run their own clinics and there are a few private hospitals. In order to reduce waiting lists, some public hospitals have contracts with private hospitals. The main reason that patients seek private hospitals is because of long waiting lists in the public hospitals.

2.1.3 The Norwegian Childhood Diabetes Registry

The Norwegian Childhood Diabetes Registry (NCDR) was established in 2006. NCDR collects data of all new cases of diabetes amongst children and adolescents under the age of 18 in Norway. It includes data retrospectively from 1973-1982 and prospectively from 1989.

The main aim of NCDR is to monitor the incidence of T1D in children 0-14 years of age as-well as ensure the quality of and standardize diabetes care in children and adolescents in Norway. This is done by registering all new cases of diabetes, optimize diagnostics and classification of the disease to learn more about the disease and optimize treatment, register acute and chronic complications due to diabetes, ensure equality and optimize treatment according to international standards for all

children and adolescents and also continue research on diabetes. NCDR also perform an annually examination of children and adolescents with diabetes; this is a standardized examination according to WHO standards of quality in diabetes care. For children and adolescents registration in the NCDR is voluntary. The patient has to give a signed consent twice; both at the time of diagnosis (child or parents, or both) and also when he/she is 18 years old.

Since 2008, all 27 pediatric departments in Norway participate in NCDR, 22 of these treat new cases of diabetes and all 26 participate with annual examinations. NCDR annually analyze data and publishes a report, mainly addressed to the different hospitals and pediatric departments responsible for diagnostics, treatment and follow-up. Hospitals can compare their own results with other hospitals, and the process is made anonymous by giving the hospitals different codes in the report. In 2010, 2457 patients participated in the annual control, which is estimated to be 95 % attendance (86).

2.1.4 Epidemiology of diabetes in Norway

T1D is the second most common chronic disease, and the most common of the different types of diabetes amongst children and adolescents in Norway (86).

In 2010, 325 new cases of diabetes in children and adolescents under 18 years of age were registered in the NCDR. 99 % (323/325) of these had T1D. 93 % (303/325) of children with all types of diabetes were diagnosed under the age of 15, and 99 % (301/303) of these had T1D. These numbers gives us an incidence of childhood onset T1D of 33.0 per 100,000 in the young (0-14 years) (86). If we look at the figures from 1990-1999 with an average incidence of 20.8 per 100,000 per year (10), we can see that the incidence has increased the last years. Norway is today one of those countries with the highest incidence of T1D before 15 years of age.

2.1.5 Diabetes in Drammen

Hospital presentation – Drammen

In December 2010 we visited the children department at Buskerud Central Hospital in Drammen.



Photo 1: *Buskerud Central Hospital.*

Available at URL:

<http://www.vestreviken.no>

Buskerud Central Hospital is part of Vestre Viken Health Authority which is owned by The South-Eastern Norway Regional Health Authority.

The hospital is situated in Drammen, which is a city and municipality located in Buskerud, approximately 35 kilometers from the capital Oslo. Buskerud is a county with 14927 square meters and consists of 21 municipalities.

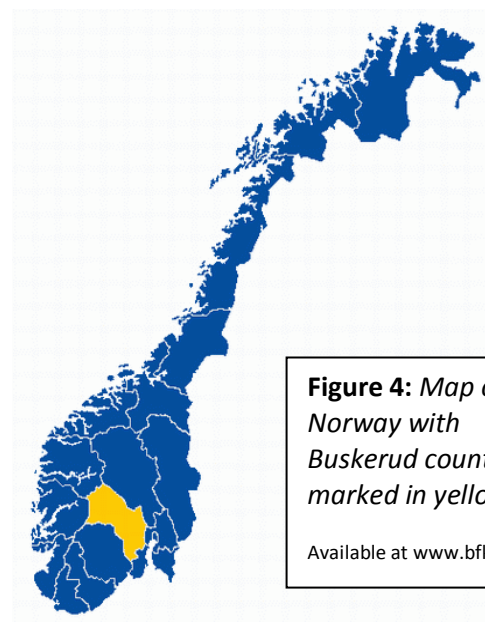


Figure 4: *Map of Norway with Buskerud county marked in yellow.*

Available at www.bfk.no (87)



Figure 5: *Map of Buskerud county with its 21 municipalities named. Drammen is seen in the middle at the bottom of the map.*

Available at www.bfk.no (88).

There are 261,110 inhabitants in Buskerud (01.01.2011) including 64,055 (01.01.2011) inhabitants in Drammen. The children's department at Buskerud Central hospital is responsible for treating 92,000 children from the 26 municipalities in Buskerud (89). During our research we interviewed two nurses who are specialized in working with children and adolescents with diabetes; Åse Løkkeberg Figenschau and Wenche Helene Wang.

In Drammen the treatment of children and adolescents with diabetes is either in a pediatric ward or pediatric outpatient clinic. The pediatric ward consists of 32 beds. Annually they have approximately 47 children with diabetes admitted to the pediatric ward and the nurses report that the ward rarely is full. All the children get treatment and follow up by a pediatrician at the hospital.

Epidemiology

There are 130 children with diabetes who are being followed up at the hospital in Drammen (December 2010).

Diagnosis

The hospital in Drammen uses the diagnostic criteria made by ISPAD as listed at page 8. The reason for seeking a doctor is typically that the children have classical symptoms such as thirst, polyuria, great appetite and impaired general condition. Usually the diagnosis is first made by the GP and in Drammen all the children are then admitted to the pediatric ward at onset of diabetes. The children stay at the hospital 10-14 days together with their parents. Their parents get time off from work, while still getting paid from the government, to stay at the hospital. During this period of time treatment is being initiated, while at the same time the child and its parents get education about diabetes and how to handle the disease. During this stay they are encouraged to also spend time together at home. This way the children and their families get thorough follow-up, education and time to adjust to the alterations in their lives.

The average age at diabetes onset is 8.8 years at Buskerud central hospital.

The hospital in Drammen uses the ISPAD's biochemical criteria for DKA as described in table 2 at page 21. They report that 33 % of the children have DKA at diagnosis, and because this is registered both at the hospital and also in the NCDR they are able to give us this exact number.

Treatment

A multidisciplinary team participates in the treatment and follow-up of children with diabetes at Buskerud central hospital. There are two nurses who are specialized in working with children/adolescents with diabetes and three pediatricians. A psychiatrist is always involved in the beginning and can participate in treatment if necessary. School nurses and social workers are contacted when needed.

The types of treatment regimens available at Drammen hospital are insulin pen, insulin pump and insulin pump and continuous subcutaneous glucose monitoring. 80 % of the children are treated with insulin pumps.

All patients have one specific contact person; one of the nurses who are specialized in working with childhood diabetes, that they can ask if they have questions. They can seek help at the emergency room at the hospital whenever needed if they get acute ill.

In Drammen the children attend diabetes checkups every third or fourth month, or more often if needed. Most of the patients attend to their appointment. The few patients who do not attend are most often due to poor follow-up by parents.

Treatment goals

Buskerud Central Hospital uses the ISPAD treatment goal of HbA1c < 7.5 %. The percentage of children achieving the treatment goals are 23 % (2011). This is registered at the hospital and reported to the NCDR. The level is also registered in the patient's electronic journal system. This way they can easily follow HbA1c over time and keep control of the exact number of children achieving the treatment goals at the hospital.

As part of the annual examination in NCDR, HbA1c from all the children and adolescents with diabetes are measured centrally at a DCCT-laboratory located in Oslo, at Aker University Hospital. This is to make sure the test has a good quality and to avoid analytic variation. In the annual examination 2010, 97 % of the children in NCDR had HbA1c measured at Aker Hospital (90).

In addition control of lipids and quality of life are added to their treatment goals.

Nutritional management

Carbohydrate counting is used systematically when calculating the insulin bolus in relation to food.

Education

Education is provided to the child, parents and school/kinder garden. They also arrange education for siblings and sometimes for grandparents. The child receives education individually. A school nurse will be going to the kindergartens and/or schools to inform teachers and others who will be in contact with the child.

The Norwegian Diabetes Association arranges camps for children and adolescents with diabetes.

If needed the hospital have access to interpreters when they have patients that do not speak/understand Norwegian.

Complications

Buskerud Central Hospital screens for celiac disease and hypothyroidism/hyperthyroidism. They also have screening programs concerning late diabetes complications among children with diabetes; they have tests for retinopathy, nephropathy, neuropathy and angiopathy. The testing is done annually. The results from the testing are registered in a scheme; the Norwegian version of the WHO DiabCare Basic information sheet for children and adolescents. All the results are reported to the NCDR.

In Drammen they report that 15 % of the patients have DKA annually. The number of patients with severe hypoglycemia is from 1 to 5 annually. There are no long-term complications among the children followed up at the hospital in Drammen.

2.2 Diabetes in Argentina

2.2.1 Presentation of Argentina

Geography and demography

Argentina is the second largest country in South America after Brazil and share land boundaries with five other countries: Bolivia, Chile, Brazil, Uruguay and Paraguay (91). Argentina is integrated by 23 provinces and the Federal Capital of Buenos Aires (85).



Figure 6: Map of Argentina, CIA The world Factbook 2011.

Available at: <https://www.cia.gov/library/publications/the-world-factbook/geos/ar.html> (91).

The population in Argentina is 41, 769, 726 (July 2011) and 25.4 % of these are between 0-14 years old (91). The capital, Buenos Aires, has 12, 988 million inhabitants. Approximately 89.4 % of the total population lives in urban areas (numbers from 2001) (92). The population consists of 97 % white (of Italian and Spanish origin), and the remaining 3 % are mestizo (mixed white and Amerindian ancestry), Amerindian and others (91).

Economic situation

Argentina has a vast amount of fertile land and at the beginning of the 20th century Argentina was the 10th wealthiest nation per capita in the world due to great exploitation of the pampas which strongly pushed the economy. However, by 1998 the country had fallen to 36th. Despite the involvement of the International Monetary Fund (IMF), the country has experienced a great reversal in economy like no other country in recent history (92). From the 1930s, there was political instability in the country and various governments depended on a strategy with import substitution to decrease their independency on other countries. This however turned the industry away from agriculture which fell dramatically over the years. In 1976, the era of import substitution ended, but at the same time a huge inflation was created because of great government spending, large wages increases and an inefficient industry (93). For the next years, several loans were granted the country from neighboring countries as-well as IMF, but unfortunately Argentina failed to pay its debts (94). Between 1999- 2002, the country suffered from a devastating economic crisis because of several external factors, amongst some of them leading to low prices for agricultural exports (95). Finally from 2001/2002, economic growth has resumed with the economy growing over 6 % per year for several years, partly because of a huge growth in export of soybeans, soybean oil and meal.

If we look at the real growth rate of Argentina today, they had a growth of 8.9 % in 2011, and the same year GDP per capita was \$ 17,400 (data are in US dollars), which ranks Argentina ad number 69 in a world comparison (91). Unemployment rate in 2011 was 7.2 %, and population below poverty line was estimated to be 30 % (91). According to Index, the Argentinean Statistics bureau, 8.7 % of the population was below the extreme poverty line in 2004 (98). According to the HDI ranking system, Argentina was ranked number 45 in 2001 out of 180 countries in total (compared to Norway who was number 1 the same year) (81).

2.2.2 Health situation and health care system in Argentina

Health expenditures in Argentina is 9.5 % of GDP, and in 2004 they had 3.155 medical doctors per 1000 people, which ranks Argentina as number 34 in a world comparison (84). Life expectancy at birth is 76.95 years (female: 80.36 and male:73.71) (84), but the country has a very high child mortality rate of 14.4 per 1000 per year for the whole country (2004), and some of the provinces in the north have considerably higher rates, varying from 20.5/1000 in Tucumán to 25.1/1000 in Formosa (98).

Argentina's health care system consists of three separate components; one sector that is publicly funded, one sector which consists of social insurance funds known as the obras sociales and finally private plans (98).

The public sector: In this system the public hospital is the cornerstone. It provides care to both the poor who either don't have any insurance or have insufficient insurance, it also subsidizes the obras sociales (social works funds), and occasionally serves those with high income and private insurance plans who are attracted by the reputation of one particular institution or medical personnel. The public hospitals are also responsible for health emergency services, training professionals to the graduate and post-graduate level and biomedical research (99). Officially, public health services are free for all individuals making use of them no matter if they have health insurance or not. There is a long wait in public facilities, with over 74 % of low-income clients forced to wait more than 24 hours for a consultation with a health professional (98).

Social health insurance (SHI): This system evolved at the start of the twentieth century. The sector came under supervision of the Ministry of Labour and Welfare in 1946. In 1970 affiliation became compulsory for formal sector workers. By 1990, the SHI consisted mostly of more than 300 different obras sociales, which were largely run by trade unions. Each of these funds had monopolistic rights over one demarcated sector of the labor force and workers were not able to choose which fund to join. Most of these funds, obras sociales, were too small to provide health services themselves, and therefore contracted out to private clinics and hospitals, and this gave rise to the private sector. According to the World Bank, this system led to a chaotic system of contracting and sub-contracting. Perhaps this was caused by the absence of state regulation (98).

The publicly funded sector had during the 1940s and the 1950s developed a national network of publicly funded hospitals and health facilities, under the government of the Ministry of Health. This led to rivalry between the labour unions with their obras sociales and the Ministry of Health and their public funded sector; both wanted to dominate the national health care system. Over a few years, one might say that the SHI (or obras sociales) won this competition and state funding to the Ministry of Health was poor. Another factor in this is that both the obras sociales and private insurers were allowed to send their affiliates to public hospitals. In principle they had to pay for this service, but hospitals rarely received any money. State law today says that public hospitals are obliged to treat any patient, and a penalty can be given if someone is denied treatment. This fact has reduced the resources available for the uninsured people of Argentina even more, as they are dependent on the public system. By 1990 people became more and more dissatisfied with the quality of care the obras sociales provided, and so sector of private health insurance grew. In 1997 it is estimated that 10

% of the population had private health insurance, and 4 of these 10 % also affiliated to an obra social (98). In 2003 there were still 271 obras sociales, and 196 of these were still run by labour unions in theory. Many of these had started to contract out their administration to private firms, and therefore served as fronts for private insurers. The social health insurance system is therefore becoming gradually more private (98).

In 1996-1997 a National Survey on Household Expenditure was done in Argentina, and some of the results are presented here: According to the survey about 35 % of the population in Argentina was not covered by any health insurance, 50 % had social health insurance, 10 % had private health insurance, and 5 % had both social and private health insurance. Among the population with the lowest income 57 % had no health insurance. The previous 30 days before the survey was done 23 % of the population experienced illness or injuries. Out of these 80 % went to see a physician, 2 % obtained self-treatment or traditional medicine and 18 % did not receive medical help. In the last 3 months before the survey, 22 % of the population had been prescribed medical examinations or tests by a physician; 10 % of these people could not undergo the tests when required, and 38 % of these claimed that financial difficulties was the reason (100).

2.2.3 Epidemiology of diabetes in Argentina

According to IDF Diabetes Atlas, the incidence of T1D in the young (0-14 years) was 6.8 per 100,000 in 2011 (84).

2.2.4 Diabetes in Buenos Aires



BA is the largest city and the capital of Argentina. It is located on the southeastern coast of the South American continent.

Figure 7: Map of Argentina and Buenos Aires.

Available at: <http://www.britannica.com/EBchecked/media/54714/Buenos-Aires-Argentina> (102).

The city BA is 203 square kilometers and has a population of 2,891,082 (2010). Greater BA refers to the city BA and the conurbation around it that spreads to the south, west and north of BA. It consists of 24 municipalities, called *partidos* in Spanish. The Greater BA is 3820 square kilometers and has a total population of 12,801,365 (2010) (101). There are several hospitals in BA, both public and private. We visited two public hospitals in January 2011, Hospital de Niños and Hospital N Lopez.

Hospital presentation

Hospital de Niños



Photo 2: *Hospital de Niños in Buenos Aires 2011, Private picture.*

Hospital de Niños Dr. Ricardo Gutierrez is a children's hospital located in Recoleta in the center of BA. Patients mostly come from Buenos Aires, but there are also patients coming from other parts of Argentina and even from other countries in South America. The hospital is required to help every child that seeks help, regardless of what country they come from.

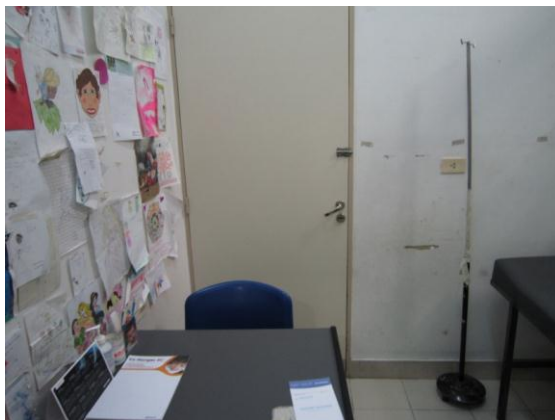


Photo 3: *Examination room at Hospital de Niños 2011, Private picture.*

There are close to 600 children with diabetes who are followed up at the outpatient clinic at Hospital de Niños. Approximately 30 children with diabetes are admitted to the pediatric ward annually. The pediatric ward has 100 beds, none of which are exclusively for children with diabetes. The doctors at the diabetes and nutrition department report that the ward, that is the same for all the patients at the hospital, has been constantly full during the last six months.

Hospital Narciso Lopez

Hospital N. Lopez is a small hospital located in the municipality Lanús Partido, which is part of Greater BA and located south of the capital BA. Lanús partido has a total population of 459,263 (2010) (103). At Hospital N Lopez about 11-12 children with diabetes are admitted to the pediatric ward annually. There are 22 beds for children; none of them are exclusively for children with diabetes. Approximately 26 children with diabetes are followed up at the hospital. Dr. Lidia Caracotche is specialized in diabetes and nutrition and is the only doctor who works with children with diabetes at hospital N Lopez. Dr. Caracotche also treated some adult patients with diabetes at the pediatric outpatient clinic, and our impression was she kept following up some of the patients which she had treated as children, and also that her reputation as a specialist in diabetes and nutrition made her popular amongst the patients.



Photo 4: From the left: Anja Kwetzinsky, Dr. Lidia Caracotche and Heidi Lehmann, 2011. Private picture.

Both Hospital de Niños and Hospital N Lopez have doctors who are specialized in “diabetes and nutrition” and the children with diabetes get treatment at the outpatient’s clinic in the nutrition and diabetes department.

The hospitals in BA are not as modern as the hospitals in Norway because of the difference in economic situations. The journal system is written by hand and the locals are smaller than and not as equipped as in Norway. This gives the doctors in BA a disadvantage that they handle exceptionally. They are knowledgeable and dedicated to their work.

We participated in the treatment of children with diabetes one week at the outpatient's clinic at each hospital.

Epidemiology

Because there are no diabetes register in BA/Argentina it has not been possible to find the total number of children with diabetes in BA.

Diagnosis

Both the hospitals in BA use the diagnostic criteria made by ISPAD as listed at page 9. The reason for seeking a doctor is usually that the children have classical symptoms such as thirst, polyuria and impaired general condition. The children in BA normally get their first treatment and information about diabetes at the out-patients clinic. The exception is children younger than three years old and those who have DKA at time of diagnosis, who will be admitted to the pediatric ward. The parents in Argentina do not get time off from work the first period after their child has been diagnosed. In BA the child and the family can come to the out-patients clinic every day in the first days after the diagnosis to get education and the opportunity to ask questions. The average age at diabetes onset is 9.0 years at both Hospital N. Lopez and Hospital de Niños.

The hospitals in BA use ISPAD's biochemical criteria for DKA as described in table 2 at page 21. At Hospital de Niños 30 % of the children have DKA at the time of diagnosis. The number at Hospital N Lopez is much higher with a percentage of 90 %. These numbers are not written down or registered, but are based upon clinical experience of the doctors we interviewed.

Treatment

The treatment regimens at the hospitals in BA are syringes, needles, insulin pen and continuous subcutaneous glucose monitoring. At Hospital de Niños all patients use MDI and at Hospital N. Lopez 90 % of the patients use MDI. The patients are not offered insulin pumps at the public hospitals in BA. This is only an option for those who are able to pay for the pump themselves or have health insurance.

The children in Argentina get the BG meter for free from the pharmaceutical industry, and the industry also provides the hospitals with strips. According to Dr. Lidia Caracotche the children get enough strips to measure BG three times a day. If more strips are needed they have to pay themselves. Not everyone has the opportunity to buy more strips.

At both the hospitals the children have one of the doctors as a contact person who can be contacted if the child is acute ill or have any questions. In BA several doctors give their private cell phone number to the patients, so that they can call if they have any questions at any time.

In Buenos Aires both hospitals reported that most of the patients meet to their appointment and also that they need to attend in order to get insulin and strips to measure BG. Those who do not meet are usually due to problems in the families or because they cannot afford the travel. Unfortunately, we were not able to get any information about what happens to these children.

The children attend diabetes check-ups every second month at hospital de Niños and once a month at hospital N. Lopez.

Treatment goals

Both the hospitals in BA use the ISPAD treatment goals; HbA1c < 7, 5 %. The reported treatment goals at both hospitals were respectively 60 % at Hospital N. Lopez and 65 % at Hospital de Niños. At hospital de Niños and Hospital N. Lopez they don't have a computer-based electronic system and they do not keep an overview over the patients all together. The number of patients they reported is therefore based on clinical experience. At Hospital de Niños, they had recently started to register the number of patients, and Dr. Liliana Trifone told us they were working towards a computer-based registration system.

Nutritional management

Both hospitals use carbohydrate counting systematically when calculating the insulin bolus in relation to food. Because some of the patients have limited possibility to measure BG this is very important in order to achieve good BG control.

Education

At time of diagnosis the child and usually one of the parents are educated. Hospital de Niños sends information in writing to schools and activity leaders/ coaches. Hospital N. Lopez arranges education at the hospital for teachers and activity leaders /coaches. At time of diagnosis education to the children and their parents are arranged individually. Later the education is given in groups with approximately 15 children and their parents per group. Hospital de Niños arranges these groups every second month and Hospital N. Lopez every month.

The Argentinean Diabetes Federation also arranges diabetes camps for the children/adolescents.

Written information is also handed out to the children. This is provided to the hospital by the pharmaceutical industry. This contains information to the patients about different topics such as; carbohydrate counting, BG measurements, how to handle different life situations and so on. The information is presented in a child friendly way with colors and figures.

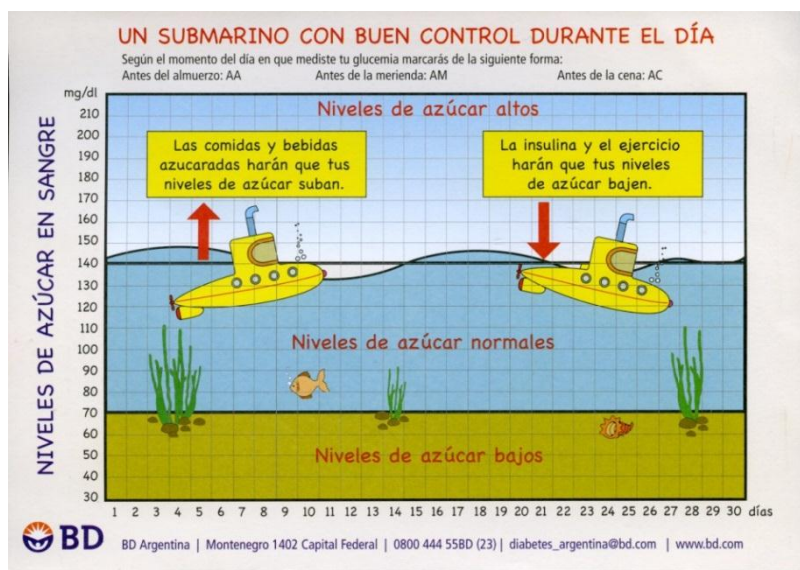


Figure 8: Example of written explanation of BG levels, handed out at the hospitals in Buenos Aires. Private example.

None of the hospitals in BA have access to interpreters when they have patients/families that do not speak and/or understand Spanish. This is usually solved by letting a family member interpret.

Complications

The hospitals screen for the autoimmune diseases celiac disease and hypothyroidism/hyperthyroidism annually. They also have screening programs concerning late diabetes complications among children with diabetes. Both hospital annually tests for retinopathy, nephropathy, neuropathy and angiopathy. The incidence of acute complications among children under the age of 15 with T1D varies among the hospitals. The percentage with DKA annually at Hospital N. Lopez is 20 % and at Hospital de Niños 10 %. The number of patients with severe hypoglycemia is less than one percent at Hospital de Niños and 10 % at Hospital N. Lopez.

Complication	Hospital N. Lopez	Hospital de Niños
DKA	20 %*	10 %*
Severe hypoglycemia	10 %*	<1 %*

Table 6: Number of patients with acute complications at the hospitals in BA. *All numbers are based on clinical experience of the doctors interviewed.

The hospitals in BA reported long term complications among children under the age of 15 as listed in the table below:

Complication	Hospital N. Lopez	Hospital de Niños
Retinopathy	None	< 1 %*
Nephropathy	3-4 %*	15 %*
Neuropathy, subclinical	2 %*	12 %*
Hypertension	1-2 %*	5 %*

Table 7: Number of patients with long term complications at the hospitals in BA. *All numbers are based on clinical experience of the doctors interviewed.

3. PART THREE: Discussion and conclusion

3.1 Discussion and comparison

Epidemiology

The NDCR in Norway provided us with the exact number of children/adolescents with diabetes in Drammen; 130 in 2010. They do not have any diabetes register in BA and therefore we are not certain about the number of children/adolescents with diabetes in BA. Additionally the hospitals in BA treat patients from all over South America, and this makes it even harder to find an exact number for BA.

Hospitalizations and number of hospital beds

All the hospitals, both in BA and Drammen, treat the children/adolescents with diabetes in pediatric wards or pediatric outpatient clinics. They all get treatment and follow- up by a specialist at the hospital.

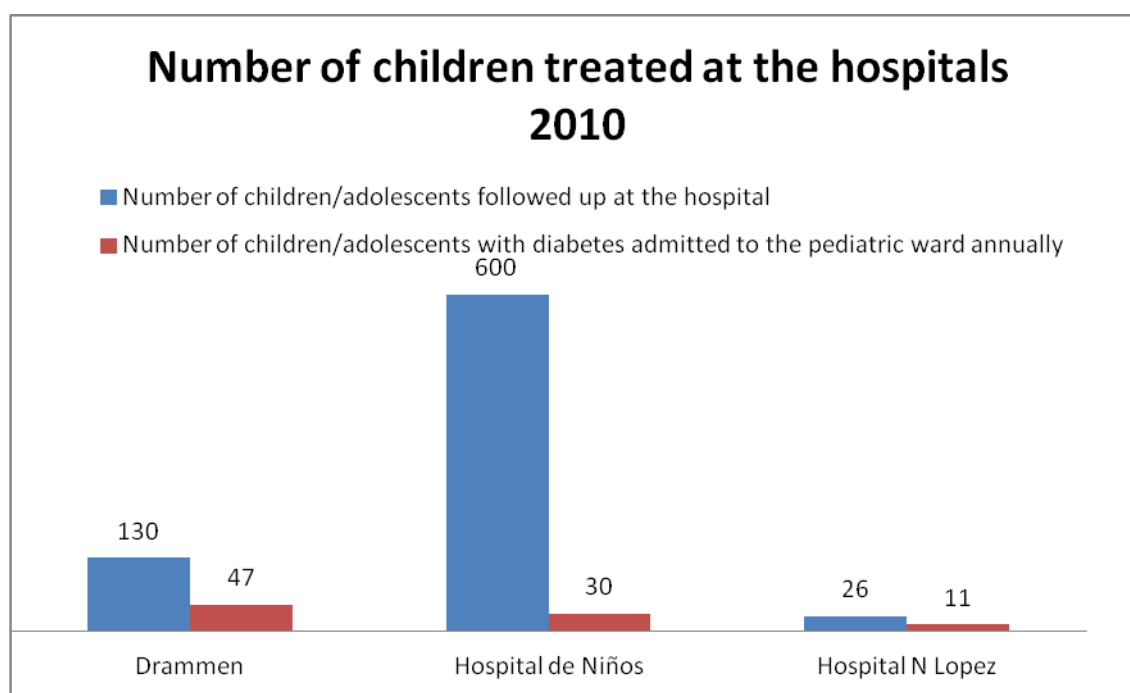


Table 8: *Number of children/adolescents followed up and admitted to the hospitals annually.* Based on our results.

In Drammen at Buskerud Central hospital they have the highest number of children (<15 years) admitted to the pediatric ward per year. Approximately 47 children are admitted annually compared

to 30 at Hospital de Niños and 11 at Hospital N. Lopez. In Drammen they currently follow up 130 children with diabetes (December 2010), at Hospital N. Lopez they have 26 children (January 2011) and at Hospital de Niños they have 600 children with diabetes (January 2011). Compared to the 600 patients that are followed up at Hospital de Niños, the number of children admitted to the pediatric ward per year seems low. There could be several reasons for this; one of them could be that children/adolescents who are recently diagnosed with diabetes in Drammen are always admitted to a hospital ward with beds, while they are mostly treated in out-patients clinics in BA. In 2010 16 new children/adolescents got diabetes in Drammen (86). An additional reason could be that children/adolescents in Drammen are admitted to the ward whenever they start to use CSII. Also, the limit to admit patients to a pediatric ward could be lower in Drammen compared to BA, perhaps because of higher capacity in Norway at the pediatric wards. The hospitals in BA reported that the wards at the hospitals are always full, whereas Buskerud central hospital reported that the ward is practically never full. This might be an example of how the economical situations in the countries influence the health care provided to the citizens.

Diagnosis

All three hospitals use the diagnostic criteria made by ISPAD (4).

They all report the same classical symptoms such as thirst, polyuria, great appetite and impaired general condition as the main reasons for children/adolescents and their parents to seek a doctor before the diagnosis is set. The average age at diabetes onset does not differ much among the hospitals; the age is 8.8 years at Buskerud central hospital and 9.0 years both at Hospital N. Lopez and Hospital de Niños.

In Drammen the children are admitted to the pediatric ward at onset of diabetes, while the children in BA usually get their first treatment and information about diabetes at the out-patients clinic. The exception is children younger than three years and those who have DKA at time of diagnosis who will be admitted directly to the pediatric wards. As all-ready mentioned the children in Drammen stay at the hospital for 10-14 days together with their parents at onset of diabetes. This way they get treatment, close follow-up, education and time to adjust to alterations in their lives. The hospitals emphasize that both parents get equally educated, so that the child will receive the best care possible no matter family- and living situation. The children and their parents seem very content with this, it makes them feel safe and they can easily get all the information they need during this first period.

To admit all children/adolescents and their parents to a pediatric ward is expensive and requires a lot of resources. It is therefore not to be expected that Argentina would have the same opportunities as Norway to offer this due to differences in these countries economic situations and health care systems. The parents in Argentina do not get time off from work the first period after their child has been diagnosed. The child and its parents can come to the out-patients clinic every day in the first days after diagnosis to get education and the opportunity to ask questions. The doctors also give their private phone number to the patients so that they could easily be contacted if the parents have any questions. This shows the dedication the doctors in BA show for their patients and the wish to do the best out of the resources available. Whether the child and its parents get more information and better education due to the two week stay at the pediatric wards in Norway is not given, especially considering the dedication the doctors in BA show by for example giving out their private cell phone numbers and letting patients know they can be contacted any time even during their time off from work. What we do know however is that patients and their parents in Norway feel very safe during this first period of time having the possibility to be in a safe environment at all times, and start their new life at home gradually by going back and forth between the hospital and their home. According to the ISPAD guidelines the methods of delivering primary levels of education and the use of educational resources will depend on local experience and facilities (49). According to these guidelines, it seems both countries are doing their very best according to available resources.

All the hospitals use ISPAD's biochemical criteria for DKA as described in table 2 at page 21. At the hospital in Drammen 33 % has DKA at diagnosis and at Hospital de Niños the percentage is 30 %. Hospital N. Lopez is much higher with a percentage of 90 %. We did not get a good explanation for why the number is so high at Hospital N. Lopez, but we do know that some patients traveled very far to this hospital which is located approximately one hour by car outside the city center of BA, and have patients coming from areas several hours away from the hospital. This might be one of many explanations to why more patients have DKA when reaching the hospital, compared to Hospital de Niños which is centrally located in BA.

In Norway the number of patients with DKA at time of diagnosis is registered in NCDR and the hospital in Drammen register all patients electronically themselves as-well, and could therefore give us the exact number. The hospitals we visited in BA do not register the amount of children who has DKA at diagnosis. The numbers from BA is therefore based upon clinical experience of the doctors we interviewed. To estimate such a number might not be easy and could be influenced by several factors. One could imagine that there had recently been children with onset diabetes who had DKA at diagnosis at Hospital N. Lopez and that this influenced the impression the doctor we interviewed

had about how often this happened. The only way to be certain about this and to have an exact number is to somehow register all cases.

Treatment

The basal-bolus regimen has the best possibility of imitating the physiological insulin profile. According to several randomized trials, the use of MDI and pumps will give better control of blood glucose than a treatment with injections two times per day. The basal-bolus regimen is recommended by the ISPAD guidelines and is mainly followed at the hospitals. The exception is Hospital N. Lopez where 10 % of the children do not use MDI or pump (27, 28).

The use of insulin pump shows an important difference between Norway and Argentina. In Drammen they report that 80 % of the children use pumps. The hospitals we visited in BA do not offer this to the children because it is too expensive. Therefore the only children who can get pump in Argentina either have a private health insurance or are able to pay for the pump themselves.

In the only metaanalysis we could find including exclusively paediatric RCTs (Randomized controlled trials), Pankowska et al. found after short-term follow-up, that CSII is more effective than MDI regarding metabolic control (pooled weighted mean HbA1c reduction from MDI to CSII -0.24% , 95% confidence interval -0.41 to -0.07%) and allows a reduction of the daily insulin requirements. The analysis included 165 patients from six different RCTs (104).

Two larger studies have investigated treatment effect using respectively CSII and MDI. In the PedPump study (105) pump programming data from patients ages 0-18 years treated with CSII in 30 centers from 16 European countries and Israel were recorded during routine clinical visits. The average HbA1c of 1041 patients was $8.0 \pm 1.3\%$. The use of < 6.7 daily boluses was a significant predictor of an HbA1c level $>7.5\%$. The incidence of severe hypoglycemia was 6.63 events per 100 patient-years respectively. In the Hvidøre study Group twenty-one international pediatric diabetes centers from 17 countries investigated the effect of simple feedback about the grand mean HbA1c level of all centers and the average value of each center on changes in metabolic control, rate of severe hypoglycemia, and insulin therapy over a 3-year period. The average glycemic control levels in children and adolescents with MDI who participated in the Hvidøre study Group were $8.6 \pm 1.6\%$ and $8.7 \pm 1.7\%$ in 1995 (2780 patients) and 1998 (2101 patients) respectively. The overall incidence of severe hypoglycemia in the Hvidøre Study was 22 events per 100 patient-years. The incidence in pre-school children was as much as 60 events per 100 patients-years (106).

Although such a comparison should be regarded cautiously as one can assume that patients with CSII may have been biased by being motivated to carry an insulin pump, the results might indicate that the use of CSII can improve metabolic results in pediatric populations without increasing the risk of hypoglycemia (107). Also it is important to keep in mind that measurement of HbA1c varies among different laboratories. According to the ISPAD guidelines Insulin pump therapy should be available and considered in comprehensive care. ISPAD emphasize the need of more research concerning the topic and that the possibility to treat children with CSII differs due to economic issues (24).

The children/adolescents in Argentina get a BG meter free of charge from the pharmaceutical industry, but they only get a limited number of BG strips for free from the hospitals (usually 3 strips per day). It is not possible for all the children to buy more strips because of their financial situation. By personal observation at one of the hospitals in Argentina, we discovered that this was actually a problem for some of the patients; one of the mothers came with her child and they both have T1D. The child was well regulated, but the doctors soon discovered that the mother was seriously ill. The reason was that she had used all of her own BG strips to measure her daughters BG since she could not afford to buy more strips. In Norway the children have the opportunity to measure BG as often as needed.

According to the ISPAD guidelines SMBG should be prescribed at a frequency to optimize each child's diabetes control, usually 4–6 times a day, because frequency of SMBG correlates with glycemic control (18).

Treatment goals

All the hospitals use the ISPAD treatment goals; HbA1c < 7, 5 %. As listed in table 2 the hospitals in BA reported a similar achievement of treatment goals with respectively 60 % at Hospital N. Lopez and 65 % at Hospital de Niños, while Buskerud central hospital reported a percentage of 23 %.

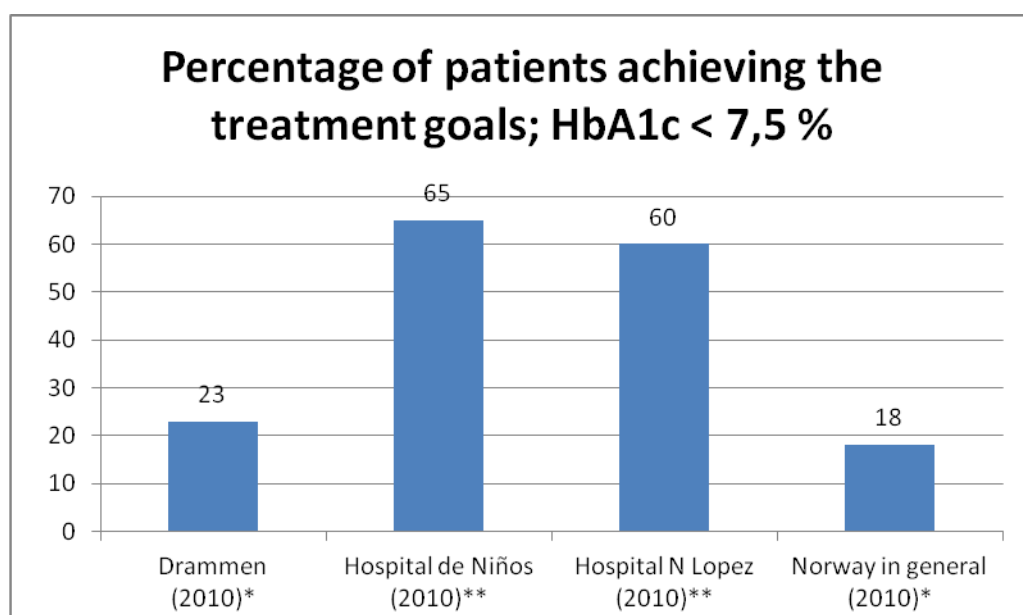


Table 9: *Percentage of patients achieving treatment goals recommended by ISPAD. The information from Argentina in general is not available. *Numbers from NCDR **Numbers based up on clinical experience.*

In Drammen they register the treatment results that the patients achieve electronically and they could therefore give us the exact number of patients achieving treatment goals; 30 out of 130, or 23%. HbA1c is always measured before every appointment. The level is written in the patients' electronic journal system and is registered among results from all the patients who are followed up at the hospital. They can therefore easily follow the patients BG over time and keep an overview over the achievement of treatment goals at the hospital in general.

In Argentina the patients measure HbA1c at the lab before the doctor's appointment and bring the result themselves to the doctor. When we participated in the consultations some of the patients had forgotten to go to the lab or had lost the note with the values written on it. The majority of the patients brought their HbA1c value to the appointment and this was written by hand in their journal. Each patient has its own folder where the doctors can go back and look at previously written HbA1c values.

In Hospital de Niños and Hospital N. Lopez they do not have a computer- based electronic system and they do not keep an overview over the patients all together. The number of patients they reported is therefore based on clinical experience. Both the hospitals in Buenos Aires reported a much higher percentage of patients achieving the treatment goals of HbA1c < 7.5 % than they did in Drammen. According to the use of insulin pump, possibility to measure BG and the differences in socioeconomic status it could be expected that Norway had a higher achievement of treatment goals. There might be several explanations for their good treatment results, none of them are based

upon clinical evidence, and more research is needed. Still, we would like to raise the question and discuss some of our theories on this matter; It is important to keep in mind that Drammen had the exact number while the hospitals in Buenos Aires did not. It is a possibility that they underestimated the number of children that did not achieve the goals. In Argentina, they have a medical specialty in diabetes and nutrition, and the doctors we met at both hospitals in Buenos Aires who worked with the children and adolescents with T1D, were all doctors specialized in diabetes and nutrition. In Norway, most of the doctors who are in charge of treating these patients are pediatricians, which means diabetes is one part of their specialization which include all childhood diseases. We got the impression that the doctors in BA confronted the children more directly with the fact that they have a serious disease than the doctors in Norway. According to Dr. Torild Skrivarhaug the seriousness of T1D are in some cases neglected by the children and their parents in Norway. The focus on the ability to live a normal life with the disease could sometimes overshadow the need to adjust satisfactory to the necessary alterations concerning treatment and lifestyle.

Nutritional management

All the hospitals use carbohydrate counting systematically when calculating the insulin bolus in relation to food. In Argentina public health service is mostly free of charge, but has its limitations. One example concerning the children with diabetes is the possibility to measure BG as often as they want to and need to. In Argentina, patients get a limited amount of strips for measuring BG and this makes carbohydrate counting even more important to obtain a satisfactory BG. The frequency of SMBG is associated with improved HbA1c, most likely because this will make the insulin adjustment for consumed food better, and the patient will be able to quickly correct glucose values that are out-of-target (108).

Children with diabetes have to adjust to the disease and take precautions in different situations, for instance in birthday parties. The children in Norway have the advantage of unlimited possibility to measure BG which makes them more flexible in such situations. We got the impression that the focus in Norway is to make the children live a life as normal as possible whereas some of the children in BA where confronted more directly with the fact that they have a disease and therefore need to take more precautions in their way of living.

The ISPAD guidelines recommend that a specialist dietitian with experience in childhood diabetes should be part of the interdisciplinary pediatric diabetes team, be available at diagnosis, and in the first year thereafter to provide a minimum of two to four follow-up sessions (35). Despite the

recommendations there are no dietitian participating in the education concerning carbohydrate counting in Drammen. The doctors in BA are specialized in diabetes and nutrition and follow the guidelines concerning nutritional management.

Education

The education is arranged differently in BA and Drammen. As mentioned above there is a difference concerning how the education at diabetes onset is organized. In Drammen the child is admitted to the pediatric ward while most of the children in BA are educated at the outpatient's clinic. Common for all hospitals is the individual education at onset diabetes and the importance of also educating parents. Norway emphasize that both parents are educated equally. Both parents get time off from work to stay at the hospital the first two weeks after diabetes onset. In BA usually one of the parents participates and none of the parents get paid time off from work.

At the hospitals in BA re-education is organized in groups containing approximately 15 children and their parents. In Drammen all the education is individual and provided at the regular check-ups. According to the ISPAD guidelines group education may be more cost effective and that the patients can benefit from meeting others in the same situation. Although there is evidence that education directed at individual needs is equally effective as group education (51).

All hospitals emphasized the importance of good education at diabetes onset and re-education whenever needed. They included both the child and its parents. According to ISPAD guidelines education is a critical element for children and adolescents with diabetes and their families. It is necessary for improving patient outcomes (48, 49). We got the impression that all hospitals provide sufficient education to the children/ adolescents. The education is organized differently, in groups or individually, but still according to the ISPAD guidelines. All hospitals emphasized the importance of good initial learning, learning of skills, behavioral modifications, family involvement and that learning is a continuous process and needs to be repeated.

Complications

All hospitals screen for the autoimmune diseases celiac disease and hypothyroidism/ hyperthyroidism annually. All hospitals also have screening programs concerning late diabetes

complications among children/adolescents with diabetes. The hospitals annually test for retinopathy, nephropathy, neuropathy and angiopathy.

The incidence of acute complications among children/adolescents under the age of 15 with T1D varies among the hospitals. In Drammen they report that 15 % of the patients have DKA annually. The percentage at Hospital N. Lopez is 20 % and at Hospital de Niños 10 %. The number of patients with severe hypoglycemia is between 0.8- 3.8 % at Buskerud Central Hospital, 10 % at Hospital N. Lopez and less than 1 % at Hospital de Niños.

In Buenos Aires the hospitals reported long term complications among children/adolescents under the age of 15. In Drammen they did not have any long-term complications among the children/adolescents.

Percentage of children with the different types of long-term complications in the hospitals of Buenos Aires compared to Drammen:

Complication	Hospital de N Lopez	Hospital de Niños	Drammen
Retinopathy	None	< 1 %	0 %
Nephropathy	3-4 %	15 %	0 %
Neuropathy, subclinical	2 %	12 %	0 %
Hypertension	1-3 %	5 %	0 %

Table 10: Percentages of patients with different long-term complications at the hospitals in Buenos Aires compared to Drammen 2010. Based on our results.

The number of complications also differs concerning registration. Drammen register the number of children with complications while the numbers reported in BA is based upon clinical experience. It is interesting that there are no children under the age of 15 in Drammen with long term complications compared to the hospitals in BA where some children have long term complications. This is hard to explain when we look at the achievement of treatment goals as discussed above. The screening programs at all three hospitals follow the ISPAD guidelines (35).

Registers

In Norway, the Norwegian Childhood Diabetes Registry is collecting data from all the Norwegian pediatric departments who treat children and adolescents with diabetes. 95 % of all the children with diabetes treated in pediatric departments in Norway are now participating in annually diabetes

examinations. The results are reported each year to the NCDR (86). In Norway there are several health registries created for different diseases and other purposes. In Argentina we did not see registration to this extent. At Hospital de Niños, they had just started to register the number of patients with diabetes and also their treatment results, and Dr. Adriana explained to us the need for more systematical registration to better monitor the incidence of T1D, treatment results, complications and so on.

Registration is a very good tool for monitoring a disease, both incidence, treatment and treatment results, complications with more. The Norwegian government and the Norwegian Institute of Public Health published the report “Good health registries – better health” in 2009, which includes a plan for improving all health registries in Norway from 2010-2020. According to this report, “One of the most important sources to new knowledge about disease, treatment effect and quality of services, is national health registries” (109). One might think that without registration of patients, it will be more challenging to follow the incidence of a disease, both locally and nationally. Also, one might not know the exact number of patients who fall out of the system, and therefore the treatment results in a group of patients might be over- or underestimated.

3.2 Conclusion

Visiting two very different countries so far apart from each other has been an interesting journey in itself. Both the economic system in the two countries as-well as the health care systems are very different. We believed that we, during our work, would find that these factors had an impact on diabetes care.

	ARGENTINA	NORWAY
GDP per capita (in US dollar)	17,700	54,200
World ranking	69	8

Table 11: *GDP per capita in Argentina and Norway, compared to the rest of the world.* CIA The World Factbook, 2011. Available at: <https://www.cia.gov/library/publications/the-world-factbook/index.html>

We would like to underline that our focus in this thesis have been the public hospitals in Argentina, as opposed to looking at both the public and the private health care system. Also as mentioned in the text we discovered through literature research that a national survey in Argentina performed in 1996-97 revealed that 18 % of the population who had recently been ill had not received any medical attention. We are not certain of the reason for this, but it should be kept in mind reading this thesis. Also, child mortality is unfortunately still high in Argentina and if some of these deaths are caused by diabetes we do not know. We would like to emphasize the importance of having these statistics available for research and for knowing exactly how well the health care system is functioning.

Some of our results were expected, for example the use of insulin pump as main insulin treatment in Norway and MDI in Argentina, and some results were more surprising; for example the very high number of children reaching treatment goals of HbA1c <7.5 % in Argentina compared to Norway. There are several theories which might explain the big difference in numbers and percentages we got from the different hospitals, and different registration routines could be one of them. Because all hospitals use the same guidelines, differences in criteria should not be a factor to be considered. There is a big difference in diabetes treatment between the two countries. In Norway, 80 % use an insulin pump, whilst in Argentina MDI is the main insulin treatment given, and 100 % of the children at Hospital de Niños and 90 % of the children at Hospital N. Lopez use MDI. According to the one meta-analysis and the two studies we found on this subject, results indicated that the use of CSII could give lower values of HbA1c, but considering our results this conclusion is difficult to make.

The children/adolescents in Argentina get a limited number of BG strips for free from the hospitals/government and it is not possible for all the children to buy more strips. In Norway the

children have the opportunity to measure BG as often as needed. According to the ISPAD guidelines frequency of SMBG correlates with good glycemic control (18). This is not shown in our result where the children in BA have better BG control although some of them have limited opportunity to measure BG. In Argentina, our impression was that carbohydrate counting was stressed a great deal with the patients as a very important part of their treatment, and the focus of diabetes being a chronic disease was explained thoroughly to both the patients and their parents. Perhaps the strict regimen of carbohydrate counting is a factor that contributes to better blood glucose levels despite less opportunity to frequent BG measurement. More research on this topic is required and much wanted.

Argentina has a much higher percentage of children and adolescents developing long term complications than in Norway, and we are not able to see the correlation between HbA1c <7.5 % and development of long-term complications.

Finally, we would like to emphasize the importance of registration of all patients, age of diabetes onset, treatment results and so on. That way both the hospitals, doctors and other involved health personnel can more easily follow each patient's process with progress and step-backs as well as the patient group as a whole. This is helpful to recognize what is working and what is not when it comes to treatment, what areas could be improved and how well each hospital are doing compared to other hospitals in the same area and the country as a whole. Registration locally at the hospital as well as a national registry is a great tool for health personnel working with a certain patient group.

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5. **Appendix:** Questionnaire – Diabetes Type 1 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 ≤ 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.

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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

- $HbA1_c < 7,5 \%$
- 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 diagnose 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 where 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?