

Individualised therapy for children and young people with diabetes at Copenhagen University Hospital: Herlev 10 years on

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Citation: Johannesen J, Svensson J, Mortensen HB, Olsen BS (2015) Individualised therapy for children and young people with diabetes at Copenhagen University Hospital: Herlev 10 years on. *Diabetes Care for Children & Young People* 4: 102–9

Article points

1. The clinic in Herlev, Copenhagen now has twice as many patients (aged 0–18) at it did in 2004 when it changed to individualised care for its patients.
2. The service relies on a full multidisciplinary team with a strong shared ethos and education programme so that it can support and educate patients and their families.
3. The clinic has become a research centre and has achieved positive results regarding its patients' metabolic control and the transition to adult care. There is an intention to focus on health-related quality of life in the future.

Key words

- Diabetes team
- Individualised care
- Metabolic control
- Transition to adult care

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This article looks at a diabetes clinic for children and young people at the Copenhagen University Hospital in Herlev, Denmark and how things have changed at the clinic over the past 10 years as it has doubled its number of patients and switched insulin treatment regimens. The authors document the clinic's successes, attributing them to its strong multidisciplinary team which includes social workers and psychologists, its common philosophy advocated by all team members, the use of individualised treatment schemes adjusted to the life situation of the patient, having an explicit treatment target, and being active in treatment monitoring and clinical research. The clinic has helped more than half of its patient group to achieve good metabolic control and also has a strong record in successful transition to the adult diabetes service.

Over the past 10 years, the paediatric diabetes clinic at Copenhagen University Hospital, Herlev (formerly located in Glostrup) has made major changes in order to introduce modern diabetes management in the face of a near doubling of patients from 280 in 2004 to 545 in 2014.

Before the changes, basal insulin treatment was used, with many patients having two daily injections with pre-mixed insulin rather than multiple injection therapy with long- and short-acting insulin analogues. Subsequently, insulin pump treatment and continuous glucose monitoring (CGM) was introduced.

Currently, more than half of our patients are insulin pump users, which has required higher levels of staffing and ongoing education for all staff members, as well as the introduction of advanced educational programmes for children and young people (CYP) their families. This has resulted in an improvement in overall outcomes. There have also been more opportunities to conduct clinical

research both nationally and internationally. This article reviews the progress made in our clinic following the changes that were implemented in 2000. It complements the article by Dyrloev et al (2000), which reported the major initiatives that were launched in 1995.

Changes in patient demography

The increase in incidence of type 1 diabetes has been about 3% annually over recent years (Craig et al, 2014). This has major implications for all childhood diabetes clinics as there is a year-on-year increase in the number of patients they need to treat while maintaining the quality of care. Diabetes therapies have also become more complicated, which has meant that diabetes clinics need more resources to adequately educate the patients and their families in their use.

The overall increase in newly diagnosed children and adolescents in Denmark over the past 15 years has meant an escalation in new cases at the Herlev clinic from about 30 in 2000 to 65 in 2014 (*Figure*

1a). In 2014, 25% of the newly diagnosed were aged 0–6 years, 44% were 7–12 years and 31% were over 12 years.

The overall number of individuals with diabetes attending the department has increased from 357 in 2004 to 545 in 2014 (Figure 1b). The vast majority are diagnosed with type 1 diabetes, with the proportion of monogenic or type 2 diabetes diagnoses remaining fairly constant in the range of 2–3%. Furthermore, the increase in type 1 diabetes is mostly seen in the Danish Caucasian ethnic population (Figure 2), showing an increase of about 47% from 2004, whereas no increases have been demonstrated among patients with other ethnic backgrounds.

Figure 3 shows that the group of patients over 12 years of age has expanded significantly, with no increase being seen in younger age groups. The average age of those attending Herlev is 12.4 (± 4.1) years, with 10.3% of our overall patient group being 0–6 years, 31.0% being 7–12 years and 58.7% being over 12 years. The major reason for the increase in our type 1 diabetes population is the general increase in incidence, as the way that the children are referred to the clinic and the age of transition to the adult clinic have not changed.

The diabetes team

The multidisciplinary paediatric diabetes team at Herlev University Hospital includes specialist diabetes nurses, paediatric diabetologists, dietitians, biomedical laboratory scientists, social workers and child psychologists. Furthermore, we collaborate closely with our social paediatric and youth psychiatric departments, particularly for children with psycho-social issues.

As the treatment of children and adolescents with diabetes becomes increasingly complex, diabetes clinics need more resources to educate and take proper care of their type 1 diabetes patients and their families.

The International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines recommend that for every 100 paediatric patients in a clinic there should be 1 diabetes nurse, 0.75 paediatric diabetologists, 0.5 dietitians, 0.3 social workers and 0.3 child psychologists (Pihoker et al, 2014).

The Herlev clinic has faced challenges in

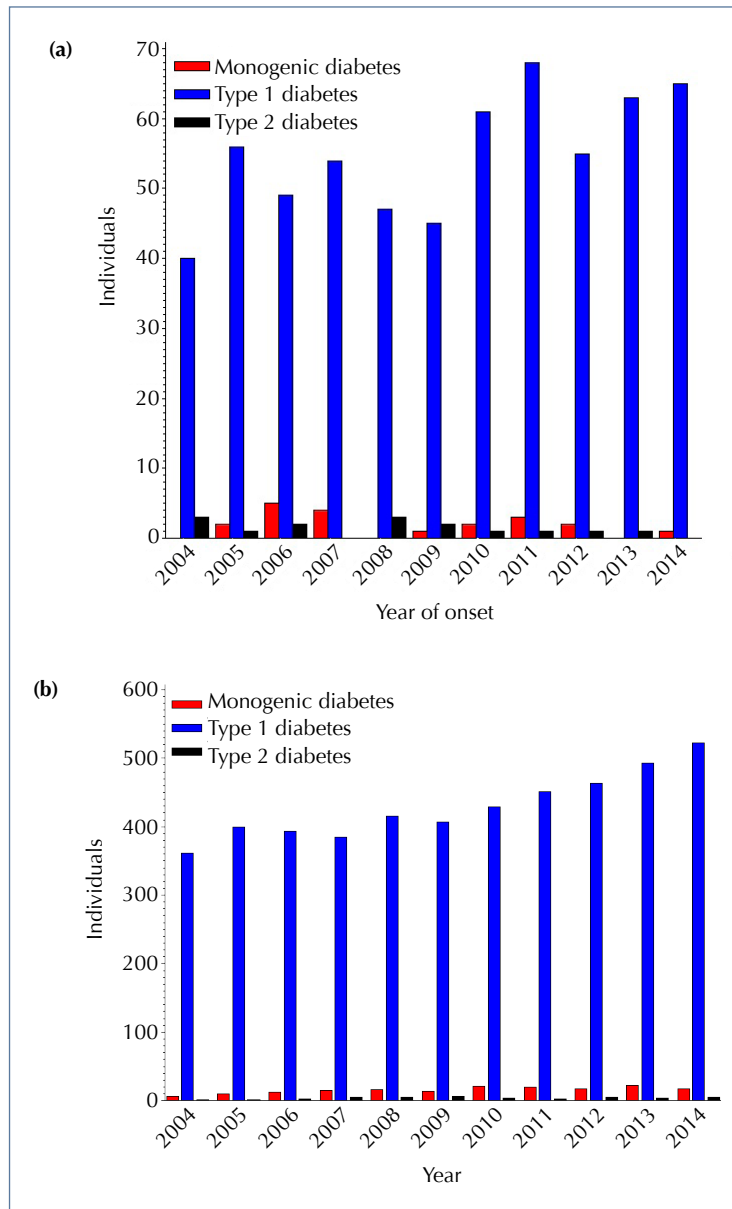


Figure 1. (a) Numbers of children and adolescents diagnosed with diabetes at the Herlev clinic each year; and (b) the overall numbers attending the clinic.

acquiring sufficient resources. Presently, for every 100 patients the clinic has 0.63 nurses, 0.4 diabetologists, 0.1 dietitians, 0.15 social workers and 0.15 child psychologists, which is significantly less than the ISPAD recommendations. Even though there has been a major increase in the number of patients, it has not been possible to increase the resources.

It has been shown that having a common philosophy and written guidelines in a diabetes team is important in improving metabolic

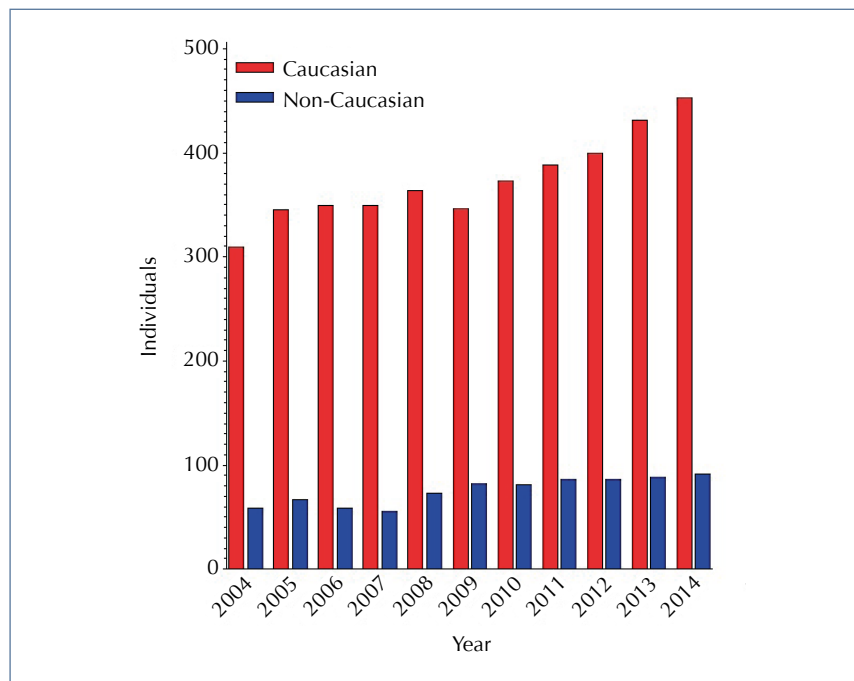


Figure 2. Numbers of children and adolescents attending the clinic each year by ethnicity.

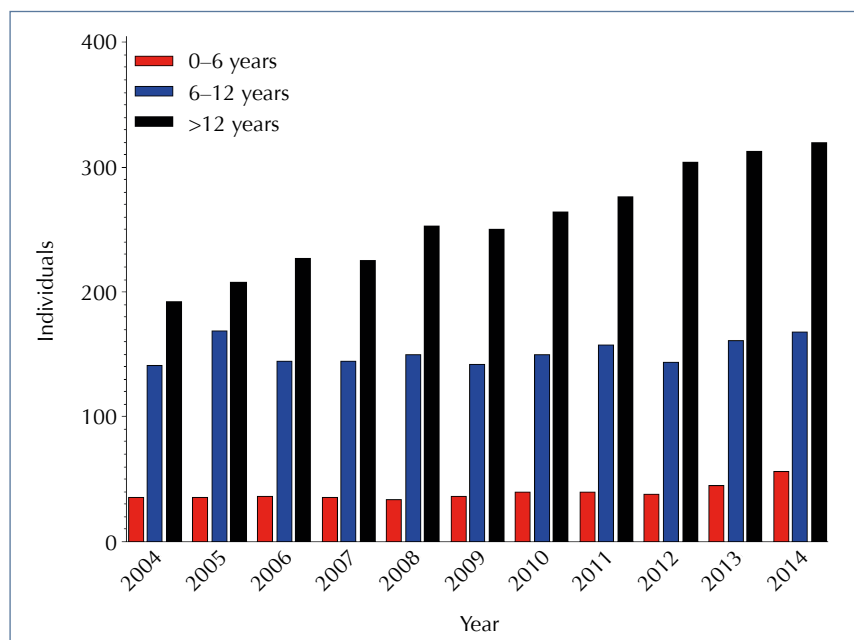


Figure 3. Numbers of patients in different age groups attending the clinic each year.

control (Swift et al, 2010). The team at Herlev tries to maintain consensus by meeting regularly, discussing challenging cases and setting treatment goals for individuals. The philosophy at the clinic is to provide an overall therapy adjusted to the patient’s ability and current need but always striving for near-normal blood glucose control. In

our team, we have two weekly meetings and have an evening dinner every second month where we discuss future strategies for our clinic and strengthen team bonding.

All team members are ensured continuous training in diabetes management by regularly attending national and international meetings and conferences. It is very important that healthcare providers have substantial experience and knowledge of individualised patient care. This includes an ongoing discussion during the outpatient visits with the patients and families regarding what aspects of their treatment and current life situation should be in focus. “One size fits all” is not an option. To improve our ability in this field, all members of the team attend the hospital’s obligatory courses in patient empowerment and communication. The fundamental approach to contact with the patient and their family is to be non-judgemental; for example, all self-monitoring of blood glucose readings measured by the patients are considered “good” as they all serve to help reach near-normal blood glucose levels. Several team members have been certified as coaches by “Camp True North” (a company providing emotional education for teens and educators), and they focus on increasing personal leadership and social competencies in patients. This, in turn, is associated with improved self-management outcomes.

The meeting in the outpatient clinic

Each patient will attend our outpatient clinic every 2–3 months, depending on their need. All have two contacts at the clinic – a nurse and a doctor – and will always meet one of them at their appointment.

Individual visits, as well as group sessions, are offered. The visit starts in the laboratory where HbA_{1c} is measured, blood tests and blood pressure taken and the glucose meter data uploaded. During the consultation the nurse or doctor will discuss daily life and family, school, friends and physical exercise. From 12–14 years of age, patients are asked whether they want to attend without their parents. In these consultations we discuss psychological issues, alcohol, smoking, drugs and sex, and make decisions with the young people on what information should be passed on to their

parents. Even in adolescence, it is very important that parents remain in the loop and take an active part in their child's diabetes care. However, the role of the parents should slowly shift into that of an active observer, with involvement when appropriate.

In Denmark, there are national indications for offering insulin pump treatment (continuous subcutaneous insulin infusion; CSII) in people with type 1 diabetes, and every month we introduce 4–6 new children to this type of therapy. The families are grouped with similarly aged children and the training lasts two days in the outpatient clinic. Selection is made after all the national indications are fulfilled, but it is equally important that the family and patient are motivated, well supported, educated and aware of the benefits and challenges of the therapy, and are able and willing to count carbohydrates.

All patients are taught to use the bolus guide and the advanced features of the pump. Initially, there is a close follow-up of the patient by phone, e-mail and in the outpatient clinic. After 2–3 months, the family is invited to a brush-up course to ensure that they understand the advanced use of the pump.

Those who benefit the most from insulin pump therapy have a starting HbA_{1c} of 59–75 mmol/mol (7.5–9.0%) and, while on the pump, self-monitor blood glucose at least seven times daily and take at least seven boluses daily at 2-year follow-up (Larsen et al, 2015).

For the past 18 months, we have also run regular, detailed courses with the families on the benefits and challenges of CGM. Patients have the opportunity to try the system for a month to see if they really want to use it. If the family and child decide to continue using the CGM system, we agree upon which parameters should improve within the next three months. If these are not met, the CGM is discontinued. Most (>70%) of our users of sensor-augmented pump therapy are very young children (under 6 years), with less than 10% of the adolescents using this therapy.

About 10–15% of our patients have serious psychological problems and need help from a social worker or psychologist. Often, we will invite the child's family, school and social worker to discuss the best way to help the family.

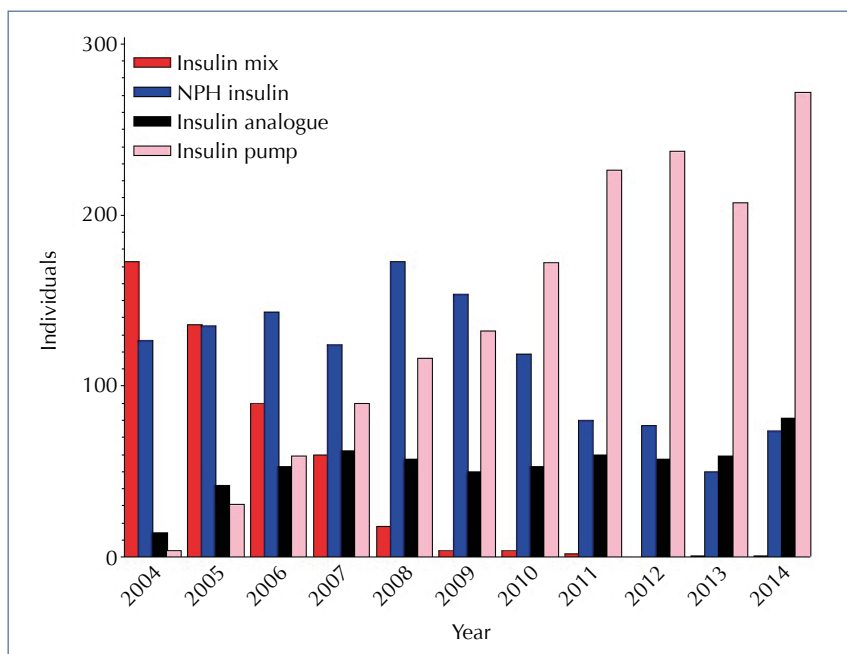


Figure 4. Changes in insulin type usage and means of administration at Herlev since 2004. NPH=neutral protamine hagedorn.

Treatment modalities

Over the past 10 years, Herlev's treatment modalities have changed dramatically. In 2004, no patients were treated with CSII and about 50% were using pre-mixed insulin twice daily. Over the next 10 years, insulin treatment was intensified and, by 2014, more than 60% of the patients were on CSII, none used pre-mixed insulin and the majority of pen-treated patients were using analogue insulin (Figure 4). Data from the Danish Registry for Diabetes in Children and Adolescents have previously shown that Danish children on CSII treatment obtain lower HbA_{1c} in all age groups compared with those on multiple daily injections (MDI; Olsen et al, 2015) and, in parallel, the incidence of severe hypoglycaemia is halved among pump users (Fredheim et al, 2014).

A requirement for optimal CSII treatment is intensive monitoring. In 2004, about 50% of our patients measured blood glucose levels 0–5 times a day, whereas in 2015 about 73% measured it 3–9 times a day and 15% measured it more than 10 times (Figure 5).

It has been shown in randomised controlled trials that the use of CGM improves metabolic control in children and adolescents (average decrease of 3.3–4.4 mmol/mol [0.3–0.4%] in

Table 1. Basis model: HbA_{1c} in type 1 diabetes patient outcomes from 2004 to 2014. Tested for the influence of gender, age, diabetes duration and ethnicity using linear regression analysis including repeated measurements.

	Groups	Estimated differences in HbA _{1c} (mmol/mol)	P value for trend
Gender	Male	0.08 (CI, -1.44 to 1.59)	P=0.92
	Female	0	
Ethnicity	Caucasian	-6.30 (CI, -8.39 to -4.22)	P<0.0001
	Non-Caucasian	0	
Age	0–6 years	-1.17 (CI, -3.10 to -0.77)	P<0.0001
	6–12 years	-3.71 (CI, -4.63 to -2.80)	
	>12 years	0	
Diabetes duration	0–1 year	-8.86 (CI, -10.16 to -7.56)	P<0.0001
	1–2 years	-4.38 (CI, -5.53 to -3.23)	
	2–4 years	-2.03 (CI, -2.92 to -1.14)	
	>4 years	0	
Visit year (see Figure 6)	–	–	P<0.0001

CI=95% confidence interval.

HbA_{1c}) if it is used frequently (more than 70% of the time; Battelino et al, 2012). Other data, however, indicate that the benefit of CGM in the daily life setting (compared to CGM trials) is modest (Wong et al, 2014). In recent years, more children in Herlev have been using CGM and, currently, 10% are permanent users.

The diabetes hotline

As the clinic expanded, it was decided to make it possible for patients to contact diabetes specialists around the clock through a diabetes telephone hotline. This is now open from 4 p.m.–8 a.m. on weekdays and 24 hours during public holidays. The hotline service is contacted an average of four times on weekdays and seven on public holidays; 71% of the calls are about insulin adjustments, 6.5% hypoglycaemia, 14.5% acute illness and high blood glucose levels, and 8% other matters. A patient satisfaction questionnaire about this service indicated that 97% of patients were aware of the hotline and 72% had used it. Of these, 98.6% were satisfied with the advice given and 100% wanted the hotline to continue. A previous Danish study showed that having access to a hotline is related to better metabolic control (Nordly et al, 2005), mainly illustrated by fewer acute hospitalisations during acute illness and fewer insulin dose adjustments made between outpatient visits.

Metabolic outcome: HbA_{1c} and severe hypoglycaemia

In accordance with the ISPAD recommendations, the clinic’s goal for HbA_{1c} has been <58 mmol/mol (7.5%) for some years, but we have now decided to reduce this goal to <55 mmol/mol (7.2%). This is to encourage the patients and their families to strive for near-normal blood glucose levels. In our data there was no correlation between a low HbA_{1c} and a higher risk for severe hypoglycaemia – this has been consistently communicated to each family by the team members. The HbA_{1c} measurements have fluctuated over the years, with a tendency to decrease in 2013 and 2014, when the mean HbA_{1c} was significantly lower than in the years before 2012 (Figure 6). We found no gender differences for HbA_{1c} levels, but age, diabetes duration, ethnicity and year of visit significantly influenced the HbA_{1c} level (Table 1). When HbA_{1c}

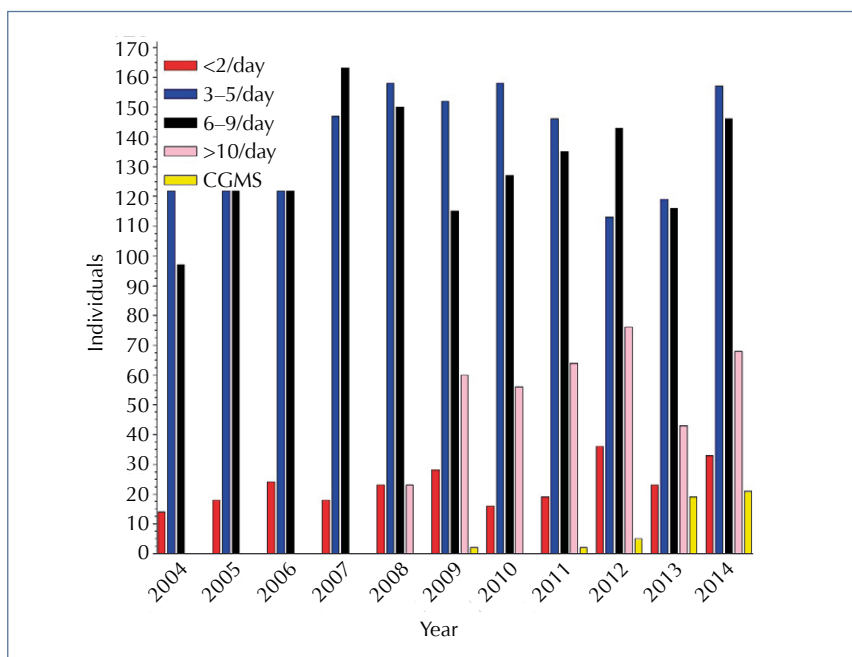


Figure 5. Number of self-monitoring of blood glucose checks recorded by children and adolescents attending the clinic each year. CGMS=continuous glucose monitoring system.

was subdivided into those below 59 mmol/mol (7.5%), those in the range 59–75 mmol/mol (7.5–9.0%) and those above 75 mmol/mol (9.0%), there was an increase in the number of individuals with values below 59 mmol/mol (7.5%), whereas the number with values above 75 mmol/mol (9.0%) was more stable (Figure 7), indicating a need to focus more on this last group to improve outcomes and prevent future complications.

The mean HbA_{1c} (mmol/mol±SD) for year 2014 was 61.8±15.2 (7.8%); for the age group 0–6 years it was 53.8±9.5 (7.0%); age 6–12 years 58.1±11.4 (7.5%) and age >12 years 64.4±16.6 (8.0%).

The number of severe hypoglycaemic events, defined as a hypoglycaemic event with unconsciousness or convulsions, fluctuated in the early years of the clinic, but within the last few years there has been a halving in the number of events per year and the level now is at its lowest ever: 2 per 100 treatment years.

Over the past 11 years, there have been 32 events of diabetic ketoacidosis leading to hospitalisation in 4043 years of observation, varying between one and six cases per year. In 2014, there were two episodes among the clinic's type 1 diabetes patients.

Patients are not currently screened for health-related quality of life (HrQoL) but this will be put in place with a translation of DISABKIDS (Simeoni et al, 2007), a European questionnaire that measures HrQoL, which is currently in the validation process. There are plans for the near future to implement annual screening with DISABKIDS to promote the issue of quality of life, which is hoped will help the young people to obtain good diabetic control (Hoey et al, 2001).

The transition to young adult clinics

Puberty is often a difficult period and it is well known that young patients, especially those who are vulnerable, may be lost in the transition process between the paediatric and adult diabetes clinics (Bryden et al, 2003).

In Herlev, patients are seen at the paediatric clinic until they are 18 (or later in specific cases). More than 90% of our young patients are transferred to the Steno Diabetes Center, Gentofte, Denmark, and there is close collaboration with the young people's clinic at this centre.

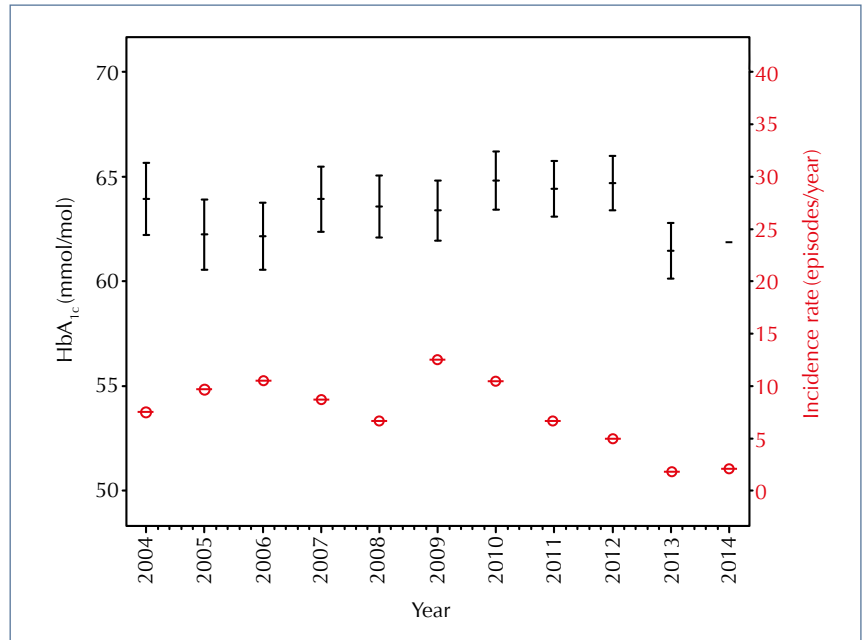


Figure 6. Average HbA_{1c} measurements and incidence rates of severe hypoglycaemia in individuals attending the clinic between 2004 and 2014. The data show no correlation between low HbA_{1c} and a higher risk of severe hypoglycaemia.

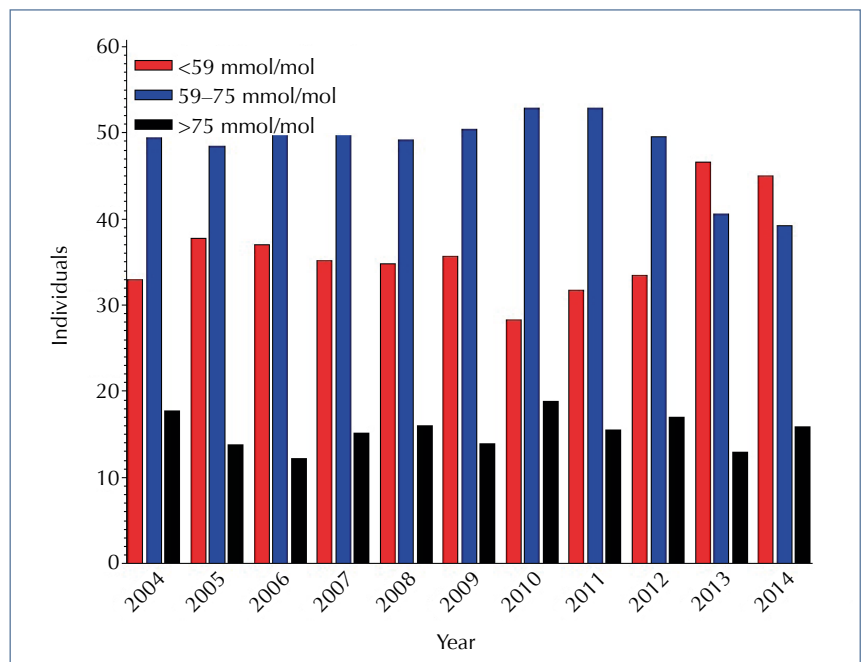


Figure 7. Grouped HbA_{1c} measurements from individuals attending the clinic. In recent years, more individuals have been recorded in the lowest HbA_{1c} group.

There is a structured programme to prepare patients for the transition. The physician the patients will see at Steno Diabetes Clinic attends the paediatric consultation to meet the young person and tell them about the new clinic. The

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two teams meet regularly to set common goals and discuss patients who have more challenges. The best time for the transferral to the Steno Diabetes Center is discussed with the individual.

A survey of the transition process from 2005–11 showed that mean age at transfer was 17.7 ± 1 years and mean HbA_{1c} at transfer was $8.4 \pm 1.3\%$ (68 mmol/mol). At follow-up after one year, mean HbA_{1c} was $8.8 \pm 1.3\%$ (73 mmol/mol). All patients were screened for late complications during the first year at the adolescent clinic and none had late complications or were lost in transition or at follow-up (according to a personal communication from BSO).

Research activities

It is of vital importance to document all the data from the clinic in order to be able to improve the delivery of diabetes care. In addition, we have established a research-oriented environment that supports good clinical research projects with the aim of improving our knowledge to benefit our patients. The research activities have been clinical with special focus upon metabolic outcome, insulin regimens and quality of life, and the development of short- and long-term diabetes-related complications, both nationally and internationally as our group was one of the founders of the international Hvidoere Study Group on Childhood Diabetes. Furthermore, we have been involved in testing insulin analogues, insulin pumps and other dosing calculators, insulin pump treatment and alternative ways of hypoglycaemia recognition, as well as extended characterisation of the remission phase in type 1 diabetes (Mortensen et al, 2009; 2010).

The basis for all these activities is careful documentation of our patient care, locally and nationally. The department was instrumental in the establishment of the Danish National Childhood Diabetes Registry (DanDiabKids) in 1996, and today this contains a variety of clinical data from more than 5500 children and adolescents. Data are recorded annually from all known diabetes patients in Denmark up to the age of 15 years, and for most cases up until the age of 18 years, when transition to adult diabetes care occurs. Since 2014, our centre has been a member of the SWEET collaboration (SWEET, 2012).

Along with the establishment of DanDiabKids, a related biobank was set up that now contains serum and DNA samples from almost all cases of type 1 diabetes from 1996 onwards, as well as from first-degree relatives from 1996 to 2010.

In 2013, The Copenhagen Diabetes Research Center (CPH DIRECT) was established, incorporating the basic beta-cell biology and type 1 diabetes genetics group of Professor Flemming Pociot, and providing the basis for translational type 1 diabetes research in children and adolescents.

These activities have resulted in ten PhD theses and, currently, we are supervising five PhD students.

Conclusion and the future

Almost half of our patient group has reached the goal of metabolic control set by international consensus. The key to achieving this has been having a full diabetes team, a common philosophy advocated by all team members, the use of individualised treatment schemes adjusted to the life situation of the patient, having an explicit treatment target, and being active in treatment monitoring and clinical research.

Clinically, there is a plan to expand Herlev's patient registration to include annual quality-of-life evaluations, as many of the patients and families find coping with diabetes stressful and challenging, despite recent progress in diabetes management and treatment. We expect that increased and specific focus on HrQoL will bring more knowledge in this area. Further, various aspects of telemedicine are being planned, with a focus on pre-school patients, with the aim of easing the lives of the children and their families. Finally, we hope to be able to establish a dedicated adolescent type 1 diabetes clinic which is staffed by paediatricians and adult diabetologists working under the same roof to ease transition.

At the educational level, the clinic will continue to have a very active role in training future diabetes educators and nurses, as well as paediatric endocrinologists. The clinic is now a partner in a European Union-funded Erasmus+ programme – Implementation of an International Advanced EU-Certified Diabetes Educator Course (Children, Young People and their Families).

In the research setting, it is hoped that the CPH DIRECT initiative will develop, and several actions have been taken to bring the process forward. A clinical diabetes research unit has been established where all clinical trials and initiatives can take place, and separate funding has been applied for. The idea is to create a variety of ongoing research projects offered to the patients in a setting that does not remove financial and human resources from the daily clinic. Furthermore, there has been an application to become an associate member of the TrialNet Center in Malmö, Sweden, with the aim of offering family members a test to measure their diabetes autoantibody status and ongoing metabolic follow-up if they are at increased risk of developing type 1 diabetes in the future.

Of course, there are always obstacles and challenges but, in the future, it will be necessary to secure sufficient funding and means to continue educating all staff members in order to maintain the high levels of knowledge and clinical flair that have been established in the clinic over the past decade. ■

Acknowledgements

We want to thank all our present and former staff members who have been dedicated to providing continuous support to all our patients and their families in order to help them strive for near-normal glucose metabolism and a good quality of life. Thanks to nurses Lene Jørgensen, Anne Marie Hertz, Line Aaberg, Nanna Lind, Jeanne Meibom, Susanne Vedersø; dietitian Mia Nielsen, lab technicians Jette Høgsmose and Sissi Polmann; social workers Niels Jacobsen and Trine Jacobsen; and psychologists Anna Larsen and Dorte From.

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