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## The initial care when a child is diagnosed with type 1 diabetes

Tiberg, Irén

2012

[Link to publication](#)

*Citation for published version (APA):*

Tiberg, I. (2012). *The initial care when a child is diagnosed with type 1 diabetes*. [Doctoral Thesis (compilation), Department of Health Sciences]. Lund University, Faculty of Medicine, Department of Health Sciences.

*Total number of authors:*

1

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# The Initial Care when a Child is diagnosed with Type 1 Diabetes

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ISBN 978-91-87189-10-4

ISSN 1652-8220

Doctoral dissertation Series 2012:48

Printed in Sweden by Media-Tryck

*A child loves her play not because  
it's easy, but because it's hard*

-Benjamin Spock



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# Abstract

When a child is diagnosed with diabetes, the symptoms may be in its most severe form with ketoacidosis, to mild symptoms of diabetes, detected incidentally. Moderate and severe symptoms of diabetes presentation require infusion therapy and thereby necessitate hospitalisation for the first few days. The initial management is largely a preparation for family members to help them gain the practical understanding and skills needed for integrating the treatment in everyday life. Some units routinely admit the children to hospital, while others say they can be safely managed at home. There is no high-quality evidence concerning the consequences that the differences in the type of service might have for the child, family or health system. The overall aim of this thesis was to investigate the initial care for children newly diagnosed with type 1 diabetes, receiving conventional hospital-based care and hospital-based home care (HBHC), i.e. specialist care in a home-based setting. A further aim was to identify families where the child runs the risk of decreased metabolic control and to give these families increased support.

Two studies have been carried out at Skåne University Hospital Lund in Sweden. The first had a retrospective design with the aim of assessing whether temporal changes in the initial management over a ten year period affected children's metabolic control two years after diagnosis. The results showed that during the years 1997 up to 2006 all children, except one, were admitted to hospital. The duration of the hospital stay decreased from a mean of three weeks to two weeks. Seventy-five per cent of the children were not acutely ill (defined as  $\text{pH} \geq 7.30$ ) at diagnosis and 94% of the children initially received intravenous insulin treatment. Neither the length of the hospital stay nor any differences in insulin treatment were associated with children's metabolic control over time. The second study had a randomised design with the aim of comparing two different regimes for children diagnosed with type 1 diabetes: hospital-based care and HBHC. The follow-up of the study was two years. In this thesis, results one and six months from diagnosis are presented. No adverse events or severe acute diabetes complications have occurred during the trial or during the follow-up. Results one month from diagnosis showed small advantages to HBHC in the children's metabolic control with regards to plasma glucose values and numbers of episodes of hypoglycaemia. Parents were more satisfied with the service in HBHC, and healthcare costs were 30% lower in HBHC compared to the hospital-based service. The results six months from diagnosis showed that parents continued to be

more satisfied with the service in HBHC. Furthermore, the results showed that there were no differences in the children's HbA1c, in the arrangement of the parents' working hours after the child's diagnosis or in the amount of absence from work related to the child's diagnosis. The categorical risk for families' psychosocial distress, assessed by professionals at the time of diagnosis, was associated with subsequent resource use, although not HbA1c. Families that received HBHC had less use of healthcare resources, compared to families having received hospital-based care. When summarising the first month and the period from 1-6 months, the total healthcare costs were 27% lower in HBHC compared to hospital-based care.

In summary, for children diagnosed with type 1 diabetes, the length of the hospital stay has decreased significantly over a ten year period. During this time, children have usually been routinely admitted to hospital irrespective of their medical condition. The results support the suggestion that an HBHC programme is just as safe for the child as hospital-based care. The results further indicate equivalence in the efficacy of the services. These results, in combination with a high degree of acceptance by those to whom the HBHC service was offered and lower healthcare costs, could suggest that the HBHC service is more effective as compared to the conventional hospital-based care. As a whole, there are not many well-designed and controlled studies that have compared hospital services with different models of home care. This thesis, although limited in answers by power and knowledge stability, provides empirical support for the safety and effectiveness of healthcare services when a child is diagnosed with type 1 diabetes. The evaluation will continue to assess the consequences, of both HBHC and hospital-based care, for the child, family and health services over time and from different perspectives.

# Abbreviations

ADA	American Diabetes Association
BDD	Better Diabetes Diagnosis
BMI	Body Mass Index
CGMS	Continuous Glucose Monitoring System
CONSORT	Consolidated Standards of Reporting Trials
DCCT	Diabetes Control and Complications Trial
DSME	Diabetes Self-Management Education
DKA	Diabetic Ketoacidosis
EURODIAB	European Community sponsored Concerted Action on the Epidemiology and Prevention of insulin-dependent Diabetes
EQUALIS	External Quality Assurance in Laboratory Medicine in Sweden
HbA1c	Glycated haemoglobin
HBHC	Hospital-Based Home Care
HLA	Human leukocyte antigen
HQoL	Health related Quality of Life
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
ISPAD	International Society for Pediatric and Adolescent Diabetes
MRC	Medical Research Council
NGSP	National Glycohemoglobin Standardization Program
NICE	National Institute for Health and Clinical Excellence
OGTT	Oral Glucose Tolerance Test
PASIS	Patient Administrative Support in Skåne

PAT	Psychosocial Assessment Tool
PedsQL	Pediatric Quality of Life
PHC	Paediatric Home Care
POC	Point-Of-Care
RCT	Randomised Controlled Trial
RSCN	Registered Sick Children Nurse
SEK	Swedish Crown
SES	Socioeconomic Status
SF-36	Short Form – 36 Health Survey
SMBG	Self-Monitoring of Blood-Glucose
SPSS	Statistical Package for the Social Sciences
SWEDIABKIDS	Swedish Childhood Diabetes Registry
TEDDY	The Environmental Determinants of Diabetes in the Young
THU-5	Targeted Hassles and Uplifts
WHO	World Health Organisation

# Original Papers

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

- I. **Tiberg I**, Hallström I, Carlsson A. The influence of initial management and family stress on metabolic control in children with type 1 diabetes. *International Journal of Clinical Medicine*, 2010 Nov; 1, (2):41-47.
- II. **Tiberg I**, Carlsson A, Hallström I. A methodological description of a randomised controlled trial comparing hospital based care and care given in a home-like environment when a child is newly diagnosed with type 1 diabetes. *The Open Nursing Journal*, 2011, 5, 111-119.
- III. **Tiberg I**, Steen Carlsson K, Carlsson A, Hallström I. Metabolic control, healthcare satisfaction and costs one month after diagnosis of type 1 diabetes: A randomised controlled trial of hospital-based care versus hospital-based home care. (Accepted for publication in *Pediatric Diabetes*)
- IV. **Tiberg I**, Steen Carlsson K, Carlsson A, Hallström I. The effect of hospital-based home care when a child is diagnosed with type 1 diabetes: A randomised controlled trial. (Submitted)

The papers have been reprinted with the kind permission of the respective journal.



# Background

## Introduction

Type 1 diabetes is one of the most common chronic diseases in childhood. It is a serious and expensive disease with the risk of late complications where metabolic control has a significant importance.<sup>1, 2</sup> Diabetes management has the purpose of preventing, delaying and reducing the severity of acute and late complications of the diabetes disease. There is a substantial amount of evidence for the relation between family factors and metabolic control.<sup>3-7</sup> The diabetes treatment is complex and most children do not reach the recommended targets of metabolic control.<sup>8, 9</sup> There has been a gradual shift over time in the focus of diabetes management from the physician to the individual with diabetes. Concurrently with the technical progress and with the development of refined insulin, an increased responsibility for the diabetes management, and thereby for the child's future health, rests on the child and its parents. There are various arguments and disagreements as to whether in-hospital care or home management of diabetes at diagnosis is most beneficial in the support of families in their task of diabetes management. Safe care in home management also depends on the systems and the amount of time that expertise can spend with the families. Even though hospitalisation answers for a high economic burden in paediatric diabetes care,<sup>10, 11</sup> in situations where systems for adequate support are not available, reduced hospitalisation of children may be counterproductive.<sup>12</sup> The evidence is scarce and, in order to get closer towards the goals of diabetes management, evaluations of the consequences, for the child, the family and health services, of different models of home care for the initial management when a child is diagnosed with type 1 diabetes, need to be carried out.

## Type 1 Diabetes

Diabetes Mellitus was recognised in antiquity and the polyuric state resembling the disease was described as early as 1550 BC in ancient Egyptian papyrus. The term



“diabetes”, which is from Greek meaning “to pass through”, was first used by Aretaeus of Cappadocia in the second century AD as a description of conditions causing increased urine output. The term “mellitus” meaning “honey-sweet” was associated with polyuria perhaps 1000 years later by two Indian physicians, Susruta and Charuka. The urine of certain polyuric patients was described as tasting like honey.<sup>13, 14</sup> The islets of Langerhans were discovered in 1869 by a German medical student Paul Langerhans and in 1889 Joseph von Mering and Oskar Minowski found that the total removal of the pancreas in dogs resulted in diabetes mellitus.<sup>15, 16</sup> Shortly after this historic breakthrough, Moses Baron, an American vivisectionist, discovered by chance, when undertaking the autopsy of a patient with diabetes, that the islets of Langerhans were damaged and suggested this to be the cause of diabetes.<sup>14</sup>

Fredrick Banting, Charles Best, James Collip and John Macleod extracted insulin from islet of Langerhans cells in Toronto 1921. In 1922, a 12-year old boy from Canada became the first patient with diabetes to be successfully treated with insulin.<sup>17</sup> Fredrick Banting (1891-1941) and John J.R. Macleod (1876-1935) were bestowed the Nobel Prize in Physiology and Medicine in 1923 for establishing the cause of diabetes as being a lack of insulin. This was the beginning of daily insulin injections and it offered hope for survival to patients with diabetes, which had previously led to the suffering of a painful death. A decade later, in spite of insulin treatment, changes in eyes and kidneys of patients with diabetes were observed.<sup>18</sup> It became clear that the disease was still severe with late complications and with serious consequences for the patient’s life.<sup>19</sup>

## **Definition of Diabetes**

The aetiological classification of Type 1 diabetes by the World Health Organisation (WHO) and the American Diabetes Association (ADA)<sup>20</sup> is that type 1 diabetes is an idiopathic disorder, characterised by immune-mediated beta-cell destruction, usually leading to absolute insulin deficiency. Diagnostic criteria are based on plasma glucose measurements and the presence or absence of symptoms. Diabetes in children usually presents with symptoms of polyuria, polydipsia, blurring of vision and weight loss in association with glycosuria and ketonuria. The presentation may be in its most severe form with ketoacidosis, to mild symptoms of diabetes, detected incidentally.<sup>21</sup> Criteria for diagnosis are defined as casual plasma glucose concentration  $\geq 11.1$  mmol/L and symptoms of diabetes or fasting plasma glucose  $\geq 7.0$  mmol/L or 2-hours plasma glucose  $\geq 11.1$  mmol/L during oral glucose tolerance test (OGTT), performed as described by WHO.<sup>20, 21</sup>

## **Incidence**

During the past decades a rapidly increasing incidence of type 1 diabetes has been reported from many parts of the world with a shift towards a younger age of onset.<sup>22, 23</sup> Sweden has one of the highest incidences in the world.<sup>21, 22</sup> It is generally assumed that type 1 diabetes results from an interaction between genetic and environmental factors. Studies have found that human leukocyte antigen (HLA) risk genotypes have changed over time. Genotypes that were neutral twenty years ago are now significantly associated with type 1 diabetes.<sup>24</sup> Results from children and adolescents registered within the Better Diabetes Diagnosis (BDD) study in Sweden, indicated an increased incidence among children who are born in Sweden but have both parents and grandparents born outside Sweden compared to children in their parents' country of origin. This may indicate that these children are affected by non-genetic factors present in the Swedish environment.<sup>25</sup> The incidence rates in Sweden have risen from 21.6 between 1978-1980 to 43.9 between 2005 and 2007<sup>26</sup> and could indicate the impact of lifestyle-related risk factors.<sup>27, 28</sup> However, recent data suggest a break of the increasing trend of incidence in type 1 diabetes in Sweden even though these findings need to be confirmed over a longer period of time.<sup>26</sup>

## **Metabolic Control**

An important change in diabetes care occurred during the 1970s-1980s as it became possible to self-monitor blood glucose (SMBG) and to measure glycated haemoglobin (HbA1c).<sup>29</sup> The information derived from these two methods of measuring metabolic control is fundamentally different; SMBG reveals the immediate blood glucose level with a small fingerpick and 0.3 micro-liters of blood, allowing individuals to relate events in their daily life and insulin doses to glycaemic results. The introduction of SMBG caused a shift in the focus of diabetes management from the physician to the individual with diabetes. With proper understanding and communication with healthcare professionals, patients could, which was previously unimaginable, take control of their own diabetes.<sup>29</sup> More frequently SMBG is associated with better metabolic control,<sup>30</sup> and stability of plasma glucose levels has been shown to improve the child's behaviour.<sup>31, 32</sup> Studies have indicated that children with type 1 diabetes are at an increased risk of cognitive and behavioural difficulties, with early disease onset and severe hypoglycemia being risk factors.<sup>33-36</sup> Since early diabetes onset as a risk factor cannot be explained by severe hypoglycemia in early years of life,<sup>37, 38</sup> not only mean glucose levels but also glycemic variation have been suggested to be important factors.<sup>34</sup> New technologies of devices for continuous glucose monitoring systems (CGMS) are available and permit the measurement of interstitial glucose in an

ongoing fashion.<sup>39-41</sup> Advances in technology have had and probably will have a major impact on diabetes management in the future.<sup>40</sup>

Over the last 30 years, HbA1c has been the standard index of metabolic control of the preceding 8-12 weeks.<sup>29, 42-46</sup> A direct relationship exists between HbA1c and mean glycaemia because erythrocytes are continuously glycosylated during their 120-day lifespan and the rate of glycohaemoglobin formation is proportional to the ambient glucose concentration.<sup>29</sup> The nine-year Diabetes Control and Complications Trial (DCCT), completed in 1993, showed that the risk for the development and progression of the chronic complications of diabetes is closely related to the degree of glycaemic control, as measured by HbA1c.<sup>2</sup> The fact that HbA1c assay methods have not been standardised among laboratories has prevented the optimal use of the test and has resulted in several countries developing national standardisation programmes. In the USA, the National Glycohemoglobin Standardisation Program (NGSP) was created<sup>47</sup> and methods used in Sweden were standardised through External Quality Assurance in Laboratory Medicine in Sweden (EQUALIS), traceable to the Mono S method. Swedish values have been approximately 1% lower than NGSP values.<sup>48</sup> In order to achieve a uniform international standardisation, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) established a working group on HbA1c standardisation. The IFCC reference method has been widely accepted and was implemented in Sweden in January 2011. Results should be reported in IFCC units (mmol/mol) and derived Mono S units (%) using the EQUALIS equation.<sup>49</sup> There is one formula to be used to convert HbA1c in one unit to another and a separate formula to be used to convert the relative change in HbA1c from one unit to another.

Many children do not reach the recommended target of metabolic control. In England and Wales only 15% achieved the NICE (National Institute for Health and Clinical Excellence) and ISPAD (The International Society for Pediatric and Adolescent Diabetes) recommended targets in HbA1c of 58mmol/mol<sup>9, 50</sup> and 35% of the children in Sweden<sup>8</sup> achieved 63mmol/mol.<sup>50</sup> However, HbA1c is only one of the several measures of optimal metabolic control, along with frequencies of hypoglycaemia, treatment, child's age and quality of life. An important aim is to assess the level of glycaemic control achieved by each individual so that they may benefit from attaining their most realistic glycaemic targets.<sup>50</sup>

# Diabetes Care

Living with type 1 diabetes imposes extensive demands on the child's and the family's everyday life with the constant challenge of maintaining plasma glucose levels within the near-normal range. For almost a century, insulin has been refined to produce forms having both long and short durations of effect which has introduced flexibility, enabling a management and regime of insulin based on the individual patient's needs.<sup>51</sup> The concept of diabetes care includes the medical treatment and the educational process as well as the health service process. The primary foundation of diabetes care should be built around a philosophy of care and support of the patient as well as goal setting which might be even more important than different insulin types and regimens for the improvements of metabolic control.<sup>52</sup> There is a wide variation in how, for example, young people are taught to balance carbohydrate intake with insulin adjustment and the methods used for this training have been poorly evaluated.<sup>53</sup>

ISPAD is the only international society focusing specifically on all types of childhood diabetes with the aim of promoting clinical and basic science, research, education and advocacy in childhood and adolescent diabetes. The clinical practice consensus guidelines of ISPAD,<sup>54</sup> based on the current views of experts in the field, are being used to assist clinicians, and they form the basis for many national healthcare strategies for children with diabetes. Furthermore, the work is being used to improve the awareness of resources needed for optimal care and of complications that can arise due to poorly managed diabetes. The Swedish national guidelines for paediatric diabetes<sup>55</sup> have existed since the 1980s, providing consistent, high standards and important contributions to Swedish paediatric diabetes care.<sup>56</sup> Quality of care is related to safety and a guarantee of quality in healthcare must be based on a scientific process that follows and evaluates all aspects of the care.<sup>54, 55</sup> It is uncertain how well countries are able to meet national guidelines.<sup>57</sup> In spite of the high standards of Swedish diabetes care, HbA1c varies greatly between centres<sup>8</sup> and the quality is still not good enough to prevent late complications of the disease.<sup>58</sup> In a qualitative analysis of Scandinavian guidelines in childhood diabetes with the position of the parents in focus, the authors concluded that the guidelines had been expertly discoursed and suggested that, by involving different professional groups and patients in the construction of the guidelines, they might allow the everyday lives of the child and the parents to be more prominent.<sup>59</sup>

## Family and Healthcare Costs

People with type 1 diabetes have been seen to be disadvantaged in adult employment, with lower earnings and a lesser probability of attaining the highest level of education.<sup>60-62</sup> Little is known about the consequences in employment and earnings for the parents of a child with diabetes. Most parents experience work restrictions due to the child's diagnosis of diabetes,<sup>63</sup> even though children with a good metabolic control should not experience more illness or infections than children without diabetes.<sup>64</sup> No study has been identified regarding employment issues for parents of children with diabetes but a Norwegian registry-based study in childhood cancer showed no restrictions of parental employment and minor reductions in earning. This was suggested to be explained by extensive welfare options in Nordic countries with regard to the illness of children. The child's illness was associated with significant reductions in the mothers' working hours but the fathers' working hours were not affected.<sup>65</sup> In Sweden, direct medical expenses of the child's diabetes are free of charge for the family. Agreements for financial compensation concerning the parents' allowance include about 80% of the parents' salary up until the level of a predetermined salary ceiling. When a child is diagnosed with diabetes the period for this allowance includes the period when the child is admitted to hospital and another 2-3 weeks after discharge for both parents. Parents of a child with diabetes can also apply for childcare allowance which applies if the child, because of his illness or other disabilities, needs special supervision and care for at least six months, or if the child's illness or disability means that the parents' expenses increase. The childcare allowance is determined partly by the work the parents need to spend on caring for their child and partly by the family's additional costs due to the child's illness.<sup>66</sup>

Outcomes in relation to the use of resources can give the decision makers an indication of the greatest return on expenditure and thereby inform resource allocation. Among the direct medical costs of childhood diabetes post onset, the self-monitoring of blood-glucose accounted for the greater proportion thereof.<sup>67</sup> Healthcare costs have been shown to be associated with socioeconomic status, with considerably higher costs for adolescents with poor metabolic control,<sup>11, 67-69</sup> and the greatest returns may be obtained by targeting families where the child or adolescent has less than optimal glycaemic control.<sup>70</sup> Similarly, better metabolic control has been associated with lower direct medical costs and lower odds of re-admission.<sup>69</sup> Health-economic studies in paediatric diabetes are scarce and a Cochrane review only identified two studies where costs were assessed when comparing hospital-based and home-based care for children newly diagnosed with diabetes.<sup>71, 72</sup> Parental costs were found to be decreased in home-based care while healthcare costs were increased, explained by the extensive costs of setting up an out-patient system. On the other

hand, hospitalisation has been found to be the highest economic burden in paediatric diabetes care.<sup>10, 67</sup>

## Care at Diagnosis

The symptoms at presentation of type 1 diabetes are generally subdivided into a mild, a moderate and a severe form with ketoacidosis. Mild symptoms include polydipsia, polyuria, weight loss, exhaustion and problems with concentration. In the moderate form, in addition to the symptoms of mild presentation, dehydration is also present and the severe form includes mild to moderate ketoacidosis.<sup>12</sup> The moderate and severe forms of diabetes presentation require infusion therapy and thereby necessitate hospitalisation. In the EURODIAB project (European Community sponsored Concerted Action on the Epidemiology and Prevention of insulin-dependent Diabetes), the overall proportion of children with diabetic ketoacidosis (DKA) at onset (defined as pH <7.30) was 40%, varying from 26% to 67%.<sup>73</sup> In Finland, the frequency was lower with 18% and was decreasing over a 20-year period.<sup>74</sup> The Swedish National Paediatric Diabetes Registry (SWEDIABKIDS) indicates that 16% of children in Sweden, aged <18 years had DKA at diabetes onset which is the lowest published national figure reported.<sup>75</sup> In Sweden, children <5 years, participating in The Environmental Determinants of Diabetes in the Young (TEDDY) showed that 13% of the children presented with DKA.<sup>76</sup> Most often, the diabetes disease manifests itself more dramatically the younger the child is<sup>77</sup> and children aged <2 years run a high risk of having DKA at diagnosis.<sup>74</sup> Nevertheless, most children come for consultation in an earlier phase with symptoms of hyperglycaemia and polydipsia without severe dehydration or acidosis.

Routines of initial intravenous insulin treatment vary, from only including children who are acutely ill at diagnosis<sup>78, 79</sup> to including almost all children diagnosed with type 1 diabetes. Recommendations of the Swedish national guidelines for paediatric diabetes include intravenous insulin treatment for one or two days before starting with subcutaneous treatment even if the child is not acutely ill.<sup>55</sup> This is done in order to attain immediate metabolic control and, despite weak evidence, thus prolong the residual beta-cell function.<sup>80</sup> More than 80% of children and adolescents newly diagnosed with diabetes, decrease in their insulin requirement transiently after insulin treatment has been initiated.<sup>81</sup> This period, often called the “honeymoon period” is characterised by a striking fall in the exogenous insulin requirements while good metabolic control is maintained by endogenous insulin production. The fall in insulin requirements most often implies frequent episodes of hypoglycaemia for the child,

before the insulin doses have been adjusted to the lower requirement. Partial remission has been defined as when the patient requires less than 0.5 unit insulin/kg/24 hours and HbA1c level of less than 53mmol/mol (NGSP: <7%, Mono S: <6.1%).<sup>81, 82</sup> The partial remission phase commences within weeks of the start of insulin treatment and lasts for more than 12 months in approximately 40% of the children.<sup>81</sup> In Germany and Austria, children initially receiving intravenous insulin treatment had more episodes with hypoglycaemia during the first two weeks compared to children treated with subcutaneous insulin after onset of type 1 diabetes,<sup>83</sup> and this could possibly imply an association between intravenous treatment and fall in the exogenous insulin requirements. However, a recent RCT, comparing intensive subcutaneous insulin therapy and intravenous insulin infusion at onset, showed no differences after two years in HbA1c, C-peptide or insulin dose/kg/24 hours between groups.<sup>84</sup> Clinical characteristics found to be associated with less likelihood and shorter duration of partial remission, were those of younger age and DKA at onset.<sup>81, 85, 86</sup>

## Diabetes Education

Diabetes education is a cornerstone in the diabetes care and decisive to a successful practice of diabetes care. Every person with diabetes and his/her family have a right to expertly structured education so as to enable control of their own situation.<sup>87</sup> National paediatric guidelines emphasise the importance of support and education but, most often do not include more specific principals.<sup>88-90</sup> Other publications with guidelines in Diabetes Self-Management Education (DSME)<sup>91, 92</sup> report an educational process far from the mere imparting of knowledge. Diabetes management requires a practical understanding and the development of skills for integrating the treatment in everyday life. Important principles and practices of education for children are motivation, context, environment, significance, concepts, activity, reinforcement, reassessment, evaluation, auditing and continuing education.<sup>87</sup> The concept of self-management of type 1 diabetes is widely used and has been suggested to include essential attributes such as process, activity and goals.<sup>93</sup> Diabetes self-management education has been described as follows:

“The process of providing the person with the knowledge and skills needed to perform diabetes self-care, manage crisis and to make lifestyle changes to successfully manage the disease. The goal of the process is to enable the patient to become the most knowledgeable and hopefully the most active participant in his or her diabetes care”.  
(p1204)<sup>94</sup>

Increased self-management and parent involvement is associated with better metabolic control,<sup>52, 95</sup> and educational interventions have been shown to have an effect on psychosocial outcomes and a modestly beneficial effect on metabolic control.<sup>96, 97</sup> One conclusion was that interventions based on clear theoretical psycho-educational principals, involving the whole family and making use of techniques such as problem solving, goal setting, coping skills and stress management are most likely to be effective.<sup>4, 52, 87, 96, 98</sup> It is a controversial question whether or not educational interventions per se are effective.<sup>99</sup> Enthusiasm and motivation is often associated with research on new methods of providing treatment and professionals involved in the care may have potentially significant influences which could contribute to the effectiveness of the intervention.<sup>97</sup> Since diabetes education is not only a concept of knowledge transfer but also includes aspects such as enabling families to accomplish lifestyle changes, the enthusiasm and motivation of healthcare providers are likely to be important components.

## **Hospital-Based versus Home-Based Care**

The often negative impact of hospital admission on children and their families calls for alternative ways of providing care. Paediatric home care (PHC) is on the increase due to the potential psychosocial benefits of home care, on the one hand, and the costs of hospital-based healthcare, on the other hand.<sup>100</sup> There is no consensus as to the definition of PHC and the service can be based on both general and specialist schemes. General PHC services most often work from a community base in a single district. By contrast, specialist services are more likely to be hospital-based, providing service to more than one district.<sup>100-103</sup> Outpatient treatment is provided by healthcare professionals in the outpatient clinic at the hospital while PHC provides treatment by healthcare professionals in the child's home. Hospital-based home care (HBHC) refers to specialist care in a home-based setting.

A child diagnosed with diabetes should always be referred to a specialised clinic for treatment.<sup>55, 104</sup> Conventionally, children newly diagnosed with type 1 diabetes have been admitted to hospital as a part of their initial management. The duration of hospital admission has varied greatly, from a few days to several weeks,<sup>67, 105-111</sup> but over recent years there has been a trend towards shorter lengths of stay and/or exclusively outpatient management.<sup>79, 106-110</sup> Sweden has a long tradition of hospital-based care when a child is diagnosed with type 1 diabetes, as recommended by the Swedish national guidelines for paediatric diabetes.<sup>55</sup> For some children, hospital admission is necessary due to the clinical presentation. However, whether children who are not acutely ill at diagnosis, should be managed at hospital or at home, is a



strongly debated issue. Some units routinely admit to hospital, while others say the children can be safely managed at home.<sup>79, 112</sup> Hospital admission can be seen as an opportunity for intensive education which might provide benefits regarding long-term outcomes.<sup>12</sup> On the other hand home-based care has been suggested to enable parents, to a greater extent, to integrate diabetes management into the family's normal lifestyle from the time of diagnosis and by so doing to reduce the negative impact of the disease on the family.<sup>112</sup> Furthermore, it could also be argued that home-based care conveys the wrong message to families about the seriousness of the disease<sup>113</sup> even though this is not an experience communicated by parents of children managed at home from diagnosis.<sup>112</sup> Families who experienced hospital-based care at diagnosis described that the theoretical knowledge they had acquired at the hospital was no longer valid at home and the family members felt unprepared and insecure after discharge.<sup>114, 115</sup> When a child newly diagnosed with diabetes is discharged from hospital, parents need to take over the responsibility of daily decisions, previously assumed by healthcare professionals.<sup>113</sup> Parents of hospitalised children want to participate in their child's care; however, parental involvement is not always facilitated by healthcare professionals.<sup>116, 117</sup> Although a Cochrane review concluded that home-based care did not seem to lead to any disadvantages in terms of physical, psychological, social or economic outcomes compared to hospital-based care,<sup>12</sup> there is a lack of high quality evidence concerning whether hospital-based or home-based care from diagnosis of children who are not acutely ill is different in any of the named outcomes.<sup>12, 118, 119</sup>

## Family Centred Care

Our relationship with parents, partners, children, siblings and others is one of the key elements of our humanity and in many respects, these relationships shape who we are and what we become.<sup>120</sup> They can be the source of great happiness and also of tremendous distress. The family is the most central and enduring influence in a child's life and must therefore be encompassed in paediatric care.<sup>7</sup>

### **The Family**

Current theories of family development are different from those of earlier decades. Early conceptualisations viewed the family as a closed unit. During the 1970s there was a change in this view and the family was increasingly regarded as a complex, adaptive system that was ever changing and growing, selectively opening up to

transactions with other systems. This view of the family as a social system gave emphasis to familiar system theory concepts. System theory involves the notion that the parts of a system are connected such that change in one part of the system influences other parts of the system. The family is partly open to societal demands and environmental changes that require adaptation in the family. That is, the family system may exclude the external world when dealing with internal family issues and develop rules for conducting transactions with other social groups.<sup>120</sup> Research and theories of family stress were integrated into family development theory and modified the original framework.<sup>121</sup> Four factors that affect a family's adjustment to stressors were defined: the personal resources of family members, the internal resources of the family system, social support and coping strategies. When members have sufficient resources they are less likely to view a stressful situation as problematic. Basic components of personal resources are finances, education, and health and personality characteristics. The family system's internal resources are about how the family functions together for cohesion and adaptability as well as being about their problem-solving abilities. Social support is emphasised as the major protective factor against the effects of stressors and thereby the family's vulnerability. A family's strategy of coping is progressively modified over time. Because the family is a system, coping behaviour involves the management of various dimensions of family life simultaneously. Coping is a process of achieving balance in the family system which facilitates organisation and unity and promotes individual growth and development.<sup>121</sup>

Complexity is characteristic of the field of family studies and, in order to claim to understand the evolving family, clinical intervention would need to have an understanding of ethnicity, culture, religion, gender, sexual preference, family life cycle, socioeconomic status, education, physical and mental health, values and belief systems.<sup>120</sup> Cohabitation, divorce, and remarriage are quite commonplace and the limiting of the definition of a family to the nuclear family of two parents and their children, is no longer adequate. In this thesis the term family is defined by the family itself, recognising that variety and diversity is the hallmark of the family of today. The use of the term parent in this context thus refers to the parent-figure to the child.

## **The Child**

During the 1930s and 1940s, several members of the new generation of psychoanalysts observed and studied, independently of each other, the negative effects in young children's mental development if they were separated for a long time or on several occasions from the person to whom they were attached, this being at the time,

most often the mother of the child. One of them was John Bowlby (1907-1990).<sup>122</sup>,<sup>123</sup> While many of the academic psychologists looked for explanations in Freud's libido theory, Bowlby was introduced to the fields of ethology and the imprint behaviour of goslings. By the late 1950s he had accumulated a body of observational and theoretical work to indicate the fundamental importance for human development of attachment from birth. Its most important principal is that an infant's development depends on continued attachment to a responsive and responsible caregiver.<sup>123</sup>,<sup>124</sup> John Bowlby observed that the child's behaviour became more active by the end of the first year whenever certain conditions obtained and ceased when certain other conditions obtained. A child's attachment behaviour is particularly activated by pain, fatigue and anything frightening. This attachment behaviour is in no way confined to young children, it is also seen in adolescents and even adults whenever they are anxious or under stress. Parents provide a secure base from which a child or an adolescent can make sorties into the outside world and to which the child can return, knowing for sure to be welcome, nourished physically and emotionally, comforted if distressed, reassured if frightened. Children and adolescents, as they get older, venture steadily further from the secure base and for increasing spans of time.<sup>122</sup>,<sup>123</sup> Prominent psychoanalysts objected to Bowlby's view. However, when the distress and anxiety of a two-year-old in the hospital who was separated from her parents was depicted on screen in James Robertson's film, it turned out to be a powerful instrument for promoting changes in practice.<sup>122</sup>,<sup>124</sup> Margaret Mahler's separation-individuation theory which emphasises autonomy and individuation was initially also regarded as diverging from traditional views. Continued attachment permits autonomy and independence which are two sides of a complementary development. Along with self-constancy, it allows for individuation and the uniqueness of personal identity.<sup>124</sup>

## **Family Function**

One of the most consistent findings in epidemiology is that the quality of an individual's and family's health is negatively affected by lower socioeconomic status (SES).<sup>125</sup>,<sup>126</sup> In accordance with the findings, social family background factors such as a low educational level and socioeconomic situation as well as single-parenthood are associated with a greater risk of poor metabolic control and re-admissions.<sup>5</sup>,<sup>127</sup> The number of siblings may also be associated with a higher level of distress.<sup>128</sup> Self-efficacy, the belief in one's ability to successfully perform specific behaviour that will have positive health benefits, is related to better diabetes self-management behaviour.<sup>129</sup> Diabetes management requires a practical understanding and the

development of skills for integrating the treatment in everyday life<sup>87</sup> and family functioning is closely integrated with the management of diabetes in children.<sup>4, 130</sup> Higher collaborative parent involvement,<sup>130-132</sup> fathers' involvement in the diabetes management,<sup>105</sup> a warm and supportive parenting style and communication,<sup>133-135</sup> agreements about diabetes management responsibilities,<sup>136, 137</sup> supportive behaviour as well as parents' problem-solving skills<sup>138</sup> are all associated with better metabolic control. In the same way, conflicts, disagreements about responsibilities, and discrepancy concerning the diabetes-related management, are associated with worse metabolic control.<sup>130, 139</sup> Adolescents who experience lower friend support have higher life stress and the latter is associated with worse metabolic control.<sup>140</sup> Friends have been shown to provide more emotional support while family support is more instrumental which emphasises the importance of facilitating the involvement of friends in the adolescent's diabetes management.<sup>132</sup> Systematic reviews of psychological and behavioural interventions have shown a small to medium-sized beneficial effect on diabetes management.<sup>96-98, 141</sup> Interventions that were theoretically based were significantly more effective than those that were not and, also, interventions that include family relationships and communication may be more effective.

## Theoretical Framework

Guralnick<sup>142</sup> presents three family characteristics influencing the developmental outcomes of children; firstly the sensitivity of the parents' responsiveness to the child, secondly the degree of responsibility (in relation to the age of the child) that the parents take for the child's experiences, and thirdly the measure of health and safety provided by the family. Intellectual disabilities or poor health, as well as a lack of financial resources and social support affect families' levels of distress and their adjustments to stressful situations such as issues associated with the child's biological vulnerability, for example, diabetes or other chronic illnesses. These stressors are capable of perturbing even optimal family patterns of interaction.<sup>142</sup> It is presumed to be the cumulative effect that produces the greatest threat to children's physiological and mental health.<sup>143</sup> When considering risk factors regarding poor metabolic control, the greatest risk would be for children in families that are already exposed to high level of distress, over and above the stress caused by the child's diabetes. Studies indicate that the time after diagnosis is a difficult time for the whole family, characterised especially by the need for information and for resources to learn how to live with the illness as well as by difficulties in maintaining the diabetes regime.<sup>114, 115, 144, 145</sup> Theoretical information is not always easily transformed into

practical skills and experiences; a “learning by doing” approach leads, to a greater extent, to knowledge, compared to an entirely theoretical approach. This phenomenon was first described by John Dewey (1859-1952), an American philosopher, as the acquirement of knowledge being facilitated if it comes concurrently with a need for this knowledge.<sup>146, 147</sup> Experiential learning is the process of making meaning from direct experience and Dewey discussed the need to have concrete experiences in order to learn. Donald Schön<sup>148</sup> established the concept of reflection during the 1980s, and the idea that reflecting together with others may elucidate tacit knowledge. Limitations imposed on families due to the diabetes treatment might not be as severe as they initially appear, and stress related to the illness can often be avoided by practical advice and by appropriate timing within the treatment.

In this research it is assumed that what the family is taught initially and the way of living with diabetes that is first presented to them, will be experienced by them as the right way and it will be more difficult to maintain a regime the more it diverges from the family’s natural lifestyle. A home environment is presumed to move responsibility for the diabetes treatment from healthcare professionals to the family with increased family participation as a consequence. Participation is likely to raise an extended need for practical knowledge which might facilitate for the family to put theory into practice. A home environment is also presumed to make the family’s personal lifestyle more visible to health professionals, allowing for strengths and difficulties to be taken into consideration thus affording an individualised learning process and better utilisation of the resources. The social background of the family has been shown to be one of the most important factors for metabolic control and an important goal is to identify groups of families who are in particular need of increased support and to tailor this support to their needs.<sup>149</sup>

# Aims

The overall aim of this thesis was to investigate the initial care for children diagnosed with type 1 diabetes, receiving conventional hospital-based care and hospital-based home care. A further aim was to identify families in which the child runs the risk of a decreased metabolic control and to give these families increased support. The hypothesis was that of improved metabolic control after two years for children having received hospital-based home care compared to children having received hospital-based care at diagnosis.

- The aim of paper I was to assess whether temporal changes, over a ten-year period, in the initial management for children diagnosed with type 1 diabetes period affected metabolic control two years after diagnosis. A further aim was to investigate whether social factors, registered at the time for diagnosis, had an impact on metabolic control over time.
- The aim of paper II was to describe the study design and outcome measurements of a randomised controlled trial with the aim of comparing two different regimes for children diagnosed with type 1 diabetes; hospital-based care and hospital-based home care.
- The aim of paper III was to compare the two different regimens for children diagnosed with type 1 diabetes, hospital-based care and hospital-based home care in terms of child metabolic control, parents' healthcare satisfaction and healthcare costs one month after diagnosis.
- The aim of paper IV was to compare the two different regimens for children diagnosed with type 1 diabetes in terms of the child's metabolic control and healthcare resource use, as well as parents' healthcare satisfaction and degree of employment six months after diagnosis. A further aim was to evaluate healthcare resource use and child metabolic control in relation to the families' levels of risk for psychosocial distress.



# Methods

This thesis includes two studies (study A and B). Study A resulted in one paper (Paper I) and study B resulted in three papers (Paper II, III and IV). An overview of the methods is given in Table 1.

**Table 1** Overview of the study design, time period, samples and follow-up presented in the four papers

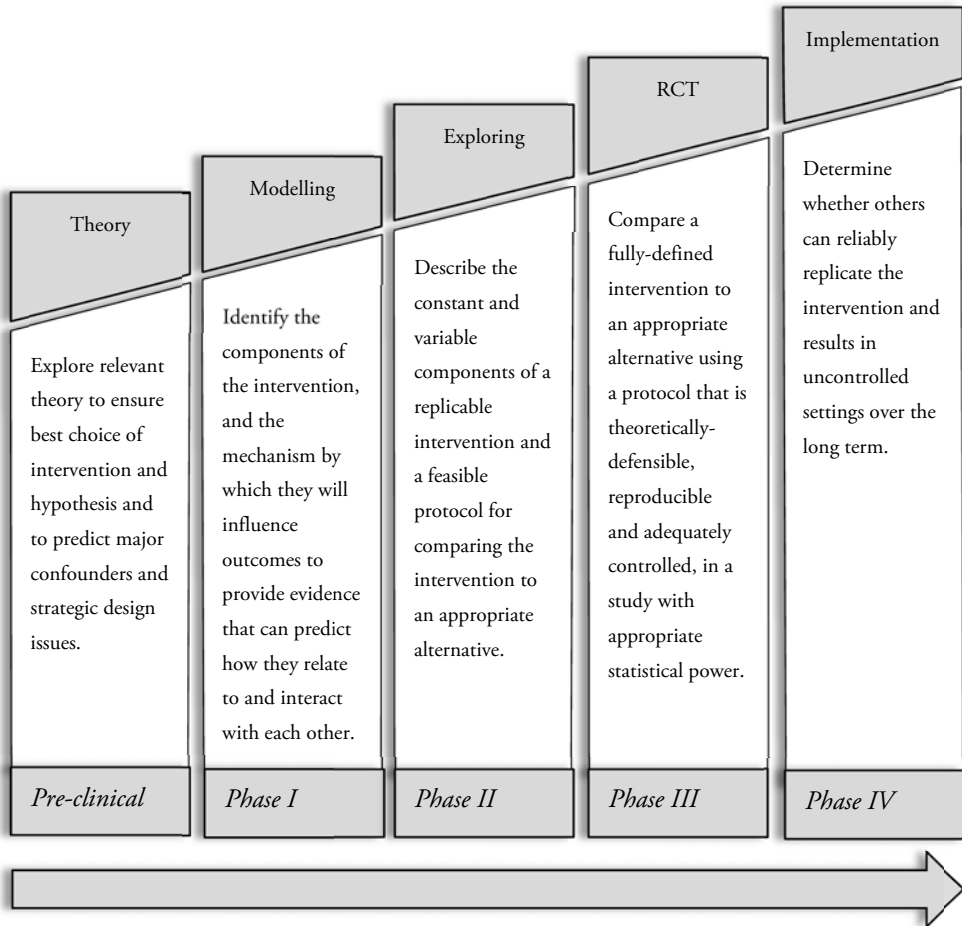
Study	Design	Time period	Sample	Follow-up	Paper
A	Retrospective	Children diagnosed from January 1997 up to December 2006	247 children, aged 0-16 years, newly diagnosed with type 1 diabetes	Two years after diagnosis	I
B	Randomised controlled trial	Children diagnosed from March 2008 up to August 2011	60 children, aged 3-15 years, newly diagnosed with type 1 diabetes	–	II
				One month after diagnosis	III
				Six months after diagnosis	IV

## Design

Study A had a retrospective design and was a historical control group to the hospital-based care, and study B was a randomised controlled trial (RCT). Interventions in healthcare are associated with several practical and methodological difficulties.<sup>96, 141, 150-154</sup> To reduce these difficulties, the design of study B was based on the Medical Research Council framework for development and evaluations of RCTs for complex interventions to improve health.<sup>155, 156</sup> The framework distinguishes five phases shown in Figure 1.



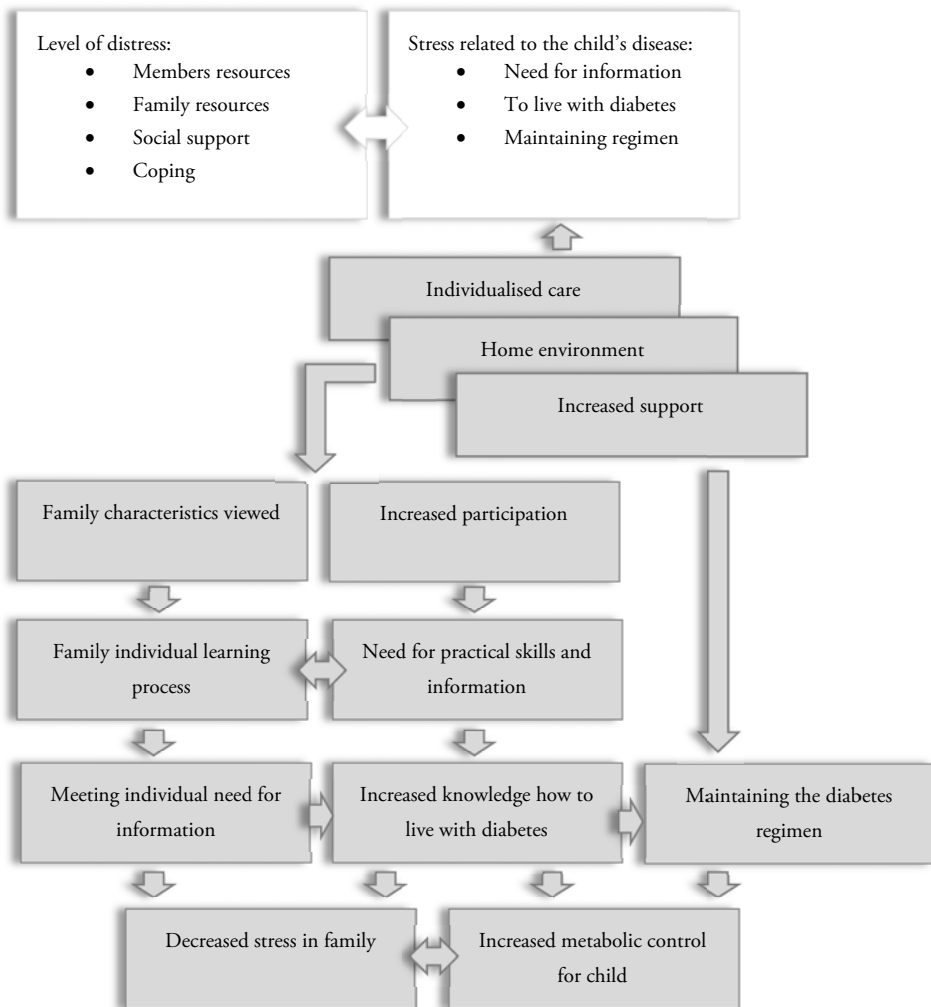
**Figure 1** Five phases of framework for trials of complex interventions (Adapted from Medical Research Council)<sup>156</sup>



In the pre-clinical or the theoretical phase the mechanism of action in the intervention was established. In the first phase and the second step in the evaluation of the complex intervention, an understanding of the components was developed as to how they may inter-relate with a modelling of the assumed directions of effects (Figure 2). In phase two the intervention was planned, including standard features such as identifying sample size, determining appropriate outcome measures, translating and testing the instruments.<sup>157</sup> The final step of phase two was to test the intervention in a pilot study, where families of two children newly diagnosed with type 1 diabetes were informed about the study and asked for consent for the pilot study. The logistics proceeded as planned and no adjustments of the design were needed. The third and central phase of the evaluation was the main RCT. The fourth

phase is a separate study. If the intervention is shown to be effective in the RCT, the question of whether the effect sustains when the intervention is implemented into routine care is still to be answered and this final step is to establish long term and real-life effectiveness of the intervention.

**Figure 2** Assumed directions of effects in the modelling of the intervention, based on the theoretical framework<sup>142</sup>



## The Context

Both studies took place at the Skåne University Hospital, in Lund, Sweden. The city Lund is situated in southern Sweden with approximately 100 000 inhabitants and the population of the city has a high educational level; 50% had at least three years of tertiary education (national average 24%), in year 2010.<sup>158</sup> The Skåne University Hospital is one of eight university hospitals in Sweden, and collaborates with other units in the region of Skåne. It is a local hospital, but since it is also a regional and university hospital service includes highly specialised care in the region as well as on a national and international level. The hospital's activities are distributed in several divisions where paediatrics is one of them, carried out at the Children's Hospital. The Children's Hospital has a local catchment area with a population of 71,684 children and adolescents (December 2010) from 0-17 years.<sup>158</sup> The diabetes department unit cares for about 250 children and adolescents, aged 0-17, and 25-35 children are diagnosed with type 1 diabetes per year.<sup>159</sup> Previous to the year 2009, the diabetes department unit cared for about 270 children. The reduction is explained by a changed age limit for adolescents' transition to the adult diabetes care setting, which was made more rigorous during the time period and the department unit's activities were only to include children and adolescents aged 0-17 years.

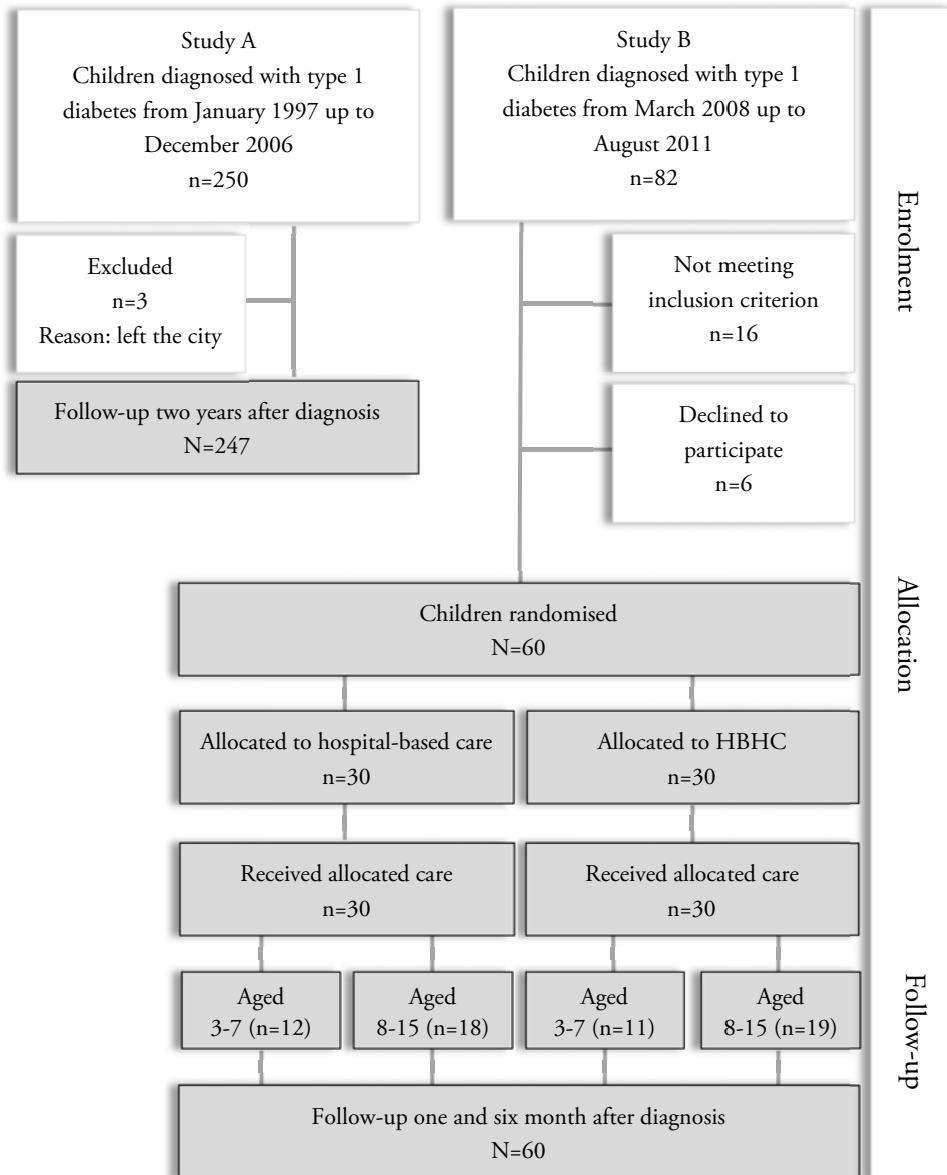
The diabetes team members included diabetes-specialised paediatric nurses (from now on called diabetes nurses), paediatricians specialised in childhood diabetes (from now on called paediatricians), a dietician and a social worker. A psychologist was available for families with special needs, consulted by the diabetes team when needed. The diabetes team was stable during the time period when both studies were carried out, in the sense that there has been a low staff turnover at the diabetes department unit. In study B, a Family House placed in the hospital area offering sick children and their families a home-like environment was chosen as a home-based form of care for the intervention group and will subsequently be referred to as hospital-based home care (HBHC).

## Study Population

A flowchart of the children in studies A and B is shown in Figure 3. Between the years 1997 and 2006, 250 children were diagnosed with type 1 diabetes at the Children's Hospital in Lund. In study A children were followed for two years and since, during this period, the transitions to the adult diabetes care setting had not

been implemented, until they had reached the age of at least 19 it allowed for the inclusion criterion of age, up to the 16<sup>th</sup> year. Data from three children were excluded as they moved from the hospital's catchment area shortly after diagnosis, meaning that 247 children were recorded within study A.

**Figure 3** Flowchart of children through the phases of study A and study B



Study B included children diagnosed with type 1 diabetes from the 1 March 2008 up to the end of August 2011. The inclusion criteria were that of children, aged from 3-15 years, newly diagnosed with type 1 diabetes at the Children's Hospital in Lund. Additional inclusion criteria were that children did not have any other difficult chronic illnesses, had no siblings with type 1 diabetes and were not in the custody of social care. Sixteen children did not meet the inclusion criteria and were therefore not asked to participate. In four cases the adolescents were more than 15 years old and in four cases the children were younger than 3 years old. Three children had another difficult chronic illness and three children had a sibling with type 1 diabetes. In one case, the family neither spoke nor understood the Swedish language and in one case the child was treated the first days after diagnosis at another hospital. Six families were informed and asked to participate but declined. The reason given was in four cases that the families preferred a hospital-based care, in one case that the family had had negative experiences of participating in studies and in one case that the family was in a difficult psychosocial situation and did not feel like they had the strength to participate. There were totally 117 parents (59 mothers and 58 fathers) of the 60 children, who participated in the initial management when their child was diagnosed with type 1 diabetes, meaning that, at the time for inclusion, three children only had contact with one parent. In several families, the parents of the newly diagnosed child were separated and the child then most often lived alternately with each parent every second week.

The children were randomised in two strata, younger than eight years or eight years and older in order to ensure that younger and older children were equally distributed between groups. An independent centre for clinical research was commissioned to perform the randomisation, and they used the software R-2.6.1.<sup>160</sup> The number of labels was unknown to the investigators and the seed of the random number generator was stored. The software had X number of labels with "Hospital based care" and X number of labels with HBHC. The software chose the labels randomly (the block size was 2\*X) and the procedure was repeated until there was a list long enough for the number of children needed for one strata. The same procedure was carried out for the next strata. The investigators received two sets of coded, sealed and opaque envelopes, one set of red coloured envelopes for older children and one set of blue coloured envelopes for younger children. In each set the envelopes were identical and contained one of two possible instruction sheets, "Hospital-based care" or "HBHC".

## **Conventional Care and Intervention**

In study B, treatment manuals were used and regularly checked, both in order to ensure that families were actually receiving treatment according to the protocol and so as to prevent treatment from sliding over time. All children received the same insulin treatment, which most often included about two days with initial intravenous insulin treatment. After the intravenous treatment, children were prescribed multiple subcutaneous injections with rapid and basal insulin analogues, with a few exceptions for the youngest children who were introduced to insulin pump therapy during the initial management. Children randomised to hospital-based care followed the conventional care at the hospital and the child as well as the child's parents had information meetings with the diabetes team members during the hospital stay. The information followed a checklist, based on the national guidelines for paediatric diabetes<sup>55</sup> where each discipline was responsible for different portions of education on the checklist. One parent could stay at the hospital with the child during the night and the other parent was encouraged to be present during the educational sessions. Towards the end of the hospital stay, when the family had received most of the planned information, they were able to leave the hospital for a couple of days before the child was actually discharged. After discharge, families followed the regular follow-up which included outpatient visits to the responsible paediatrician, more frequently during the first weeks then gradually thinning out to every third or fourth month. The diabetes nurse offered a school visit, over and above the outpatient visits to the paediatrician, with the purpose of informing teachers and school friends about the disease and the treatment with insulin. Families in the hospital-based group had accessibility to telephone support from a diabetes nurse five days a week.

Children randomised to HBHC left the Children's Hospital together with their family when the child was medically stable, and stayed at the Family House with the support of a diabetes nurse during parts of the day. The child and the child's parents had information meetings with other professionals in the diabetes team at the Children's Hospital in accordance with the conventional care. The active parts of the HBHC were defined as an individualised learning process through supportive interaction between the family and a diabetes nurse at the Family House. Another active part included the home-like environment which allowed families to practice the diabetes management with concurrent support. The final active part was an increased support after discharge in the form of three home and/or school visits by the diabetes nurse over and above the regular diabetes check visits as well as increased telephone access to the diabetes nurse, seven days a week. After discharge, there was a follow-up of the HBHC group in which they were divided into two groups based on the results of an instrument assessing the level of psychosocial distress of the families. Families

not expected to be in need for an increased support received the same follow-up as the control group, that is, the regular follow-up. Families assessed to have an increased need for support were offered one home or school visit every month by the diabetes nurse in addition to the regular diabetes check visits every third or fourth month. The design of groups in study B was diagrammed as follows:

Control group	Treatment A		Follow-up
Intervention group	Treatment B	Treatment B1 Treatment B2	Follow-up

## Data collection

In study A outcome measurements, registered prospectively, included the child's age, pH at diagnosis, HbA1c, length of initial intravenous insulin infusion, insulin type, length of hospital admissions, number of visits and social factors that might impact the family's level of distress, from now on referred to as stressors. The data was retrospectively retrieved from the Patient Administrative Support in Skåne (PASIS), patient's records and from a national quality registry, the Swedish Childhood Diabetes Registry (SWEDIABKIDS).

The primary outcome of study B was metabolic control, measured by HbA1c two years after diagnosis. Beside socio-demographic characteristics, which were based on the characteristics used in the Swedish Survey of Living Conditions information (Undersökningar av levnadsförhållanden, ULF),<sup>158</sup> the secondary outcomes of study B are shown in Table 2. The outcomes were set to evaluate consequences of the two treatments in child, family and health service and the Family was represented by the parents' answers. Outcomes included extensive data from instruments collected at the time of discharge and 6, 12 and 24 months after diagnosis. Paper III describes results of study B one month after the child's diagnosis and the data included child metabolic control measured by SMBG, severe events, parents' satisfaction with the received healthcare measured with PedsQL<sup>TM</sup> Healthcare Satisfaction Generic Module, as well as healthcare resource use and costs. Paper IV describes the results of study B six months after diagnosis and the data included child metabolic control measured by HbA1c, severe events, parents' working situation, parents' satisfaction with the received healthcare measured with PedsQL<sup>TM</sup> Healthcare Satisfaction Generic Module, healthcare resource use and the level of risk for parents' psychosocial distress in relation to subsequent resource use, measured by the Staff Psychosocial

Assessment Tool (Staff PAT), assessed by the diabetes team. A research assistant who was not involved in the care assessed the outcomes and booked appointments with the families, outside the hospital, for answering the questionnaires.

**Table 2** Secondary outcome measurements in study B, what they evaluate in relation to child, family or health services

Child	Family	Health Services
SMBG	Family costs and work situation	Healthcare resource use and costs
Hypoglycaemia and severe events	Psychosocial distress	Healthcare satisfaction
HQoL	Parent's HQoL	
Diabetes related HQoL	Mood states	
Family diabetes support	Family climate	
	Hassles and uplifts in everyday patterns	
	Disease's impact on family	
	Diabetes conflicts	

## Register

The Patient Administrative Support in Skåne (PASIS) is an administrative register for care and treatment provided by Skåne Regional Council. Every time a person is admitted to hospital, has an outpatient visit or a telephone contact within the region of Skåne, this is registered in PASIS. The register also contains information about the time and date of admission or visit, as well as which department unit and which professional category were involved. If the patient has been admitted to hospital then, at the time of discharge, the entry registration is complemented with information about the time and date of discharge.

Since the year 2000 data for each visit at the diabetes department unit, have been prospectively registered on an individual level in the Swedish Childhood Diabetes Registry (SWEDIABKIDS) and the register contains information for more than 90% of children with diabetes in Sweden. The reporting in SWEDIABKIDS includes



basic information such as height, weight, HbA1c value and type of contact as well as information about insulin regime, severe hypoglycaemia, ketoacidosis, screening for, and prevalence of, eye and kidney complications, annual control and antihypertensive treatment.<sup>159</sup>

## **Healthcare Satisfaction**

PedsQL™ Health Care Satisfaction Generic Module was developed in connection with the building of a new children's hospital in San Diego.<sup>161, 162</sup> The procedure for the development of the instruments involved literature reviews, focus groups and individual focus interviews, preparation of questions, pilot testing and subsequent field testing of the new instrument on the population group within which the instruments were intended to be used. Based on the literature reviews and focus groups, questions were constructed for the instruments. The generic instrument consists of five questions related to information, four questions regarding inclusion of family, five questions concerning communication, three questions about technical skills, four questions measuring emotional needs, and finally three questions measuring overall satisfaction; a total of 24 questions in six domains. The response scales are answered according to a 5-point Likert-scale ranging from never (0), sometimes (1), often (2), almost always (3) to always (4). In a sample of 113 parents, internal consistency reliability alpha coefficient for the whole instrument was 0.96.<sup>161</sup> A reliability of greater than 0.70 is recommended to compare groups, whereas a reliability of greater than 0.90 is recommended for comparing individuals.<sup>163, 164</sup> All subscales exceeded the minimum of 0.70 and item-scale correlation varied between 0.59-0.88 (recommended >0.40),<sup>164</sup> indicating that the instrument in relation to the tested sample showed high reliability. Factor analysis resulted in a 4-factor solution that could explain 72% of the variance. In a second sample of 40 parents, Cronbach's alpha internal consistency reliability coefficient showed an average of 0.92 (subscales ranging from 0.82-0.96).<sup>162</sup> In the current sample of study B, the Alpha coefficient for the whole instrument was 0.96 (measured at discharge) and 0.97 (measured six months from diagnosis). The authors recommended the utilization of a total scale score as the singular summary score or as the sum of the items divided by the numbers of items answered (to account for missing data) for primary analysis of parent satisfaction in randomised controlled trials. The four factor scale scores may provide the more fine-grained multi-dimensional domain scores for secondary analysis of specific satisfaction research or clinical services evaluations.<sup>161</sup>

## Families' Psychosocial Distress

In study A, based on the theoretical framework<sup>142</sup> as well as on the existing literature,<sup>4, 5, 128, 165, 166</sup> information of stressors that may put families at an increased risk of psychosocial distress when the child was diagnosed with type 1 diabetes were retrospectively retrieved from children's records and the data was therefore limited to the information available in the records. The stressors for the child that were defined were: if the child had another illness apart from type 1 diabetes, and if the child had problems in school or had no, or minimal, contact with one of the parents. Stressors that were assumed to indirectly impact the child's situation were illness in the family, parental unemployment, long term sick-leave, criminal records as well as financial problems in the family. Each stressor was registered; if it was not present (0), present for one family member (1) or present for two family members (2). The number of stressors was summarised for each family together with the parental marital status (parents living together (0), parents separated (1)).

In study B, the information of families' distress was assessed by the Staff Psychosocial Assessment Tool (Staff PAT), which is a brief psychosocial screening instrument. The instrument was originally developed for the paediatric oncology population and completed by the child's caregiver (PAT),<sup>128, 167-171</sup> based on a theoretical model recognising that families of children with illnesses represent a cross-section of the general population, with three categories of risk level. Most families are distressed but resilient (universal psychosocial risk level) at the time of diagnosis, a smaller number of families with specific constellations of individual, family, social, and economic factors, experience acute or elevated distress that puts them at greater risk for developing difficulties in the management of the disease (selected psychosocial risk level). The smallest subset of families presents multiple risk factors evident at diagnosis and warrants the most intensive and ongoing psychosocial care (targeted psychosocial risk level). The instrument has been modified to be applicable to other paediatric populations,<sup>171</sup> as well as to provide assessment of psychosocial risk from the professionals' perspective (Staff PAT).<sup>168</sup> The originally constructed PAT instrument<sup>128, 168</sup> as well as the revised version PAT2.0,<sup>170, 171</sup> completed by caregivers of children, has been tested for reliability and validity. The PAT2.0 is comprised of the following seven subscales: family structure and resources, family social support, family problems, parent stress reactions, family beliefs, child problems and sibling problems. Internal consistence reliability coefficient for the total PAT2.0 was 0.81 (subscales ranging 0.62-0.81) and the validity was supported by significant correlations between PAT2.0 and corresponding constructs.<sup>170</sup>

The Staff PAT was developed and used as a parallel assessment of healthcare professionals' perspective of the sick child and the instrument takes less than 5 minutes to complete. Consistent with the theoretical framework of the instruments,<sup>128</sup> physicians and nurses rated most families as being on the universal level (low risk), fewer families were rated as selected (moderate risk), and a small group of families were perceived to be targeted (high risk). The Staff PAT is a 17-items Likert-type rating scale as well as a three-level categorical rating. The items focus on whether a particular risk factor is an area of concern for the family and the responses range from definitely no (0) to definitely yes (3). A sum score is derived with the possible range from 0-51. The staff PAT yields two scores per family: a quantitative total score and a qualitative rating of each family in terms of the three risk levels (universal, selected and targeted). To the best of our knowledge, no clear cut-offs exist of sum scores in relation to the clinical categories. The Staff PAT subscales correspond to the subscales in PAT2.0 and have showed concordance with significant correlations between parents and professionals in the expected direction. The mothers' total scores were associated with the Staff PAT reports of both the physicians ( $r=0.45$ ,  $p<0.01$ ) and the nurses ( $r=0.38$ ,  $p<0.01$ ). The fathers' total scores were significantly correlated with the nurses' Staff PAT reports ( $r=0.36$ ,  $p<0.5$ ) but not with those of the physicians ( $r=0.17$ ,  $p>0.5$ ). Internal consistence reliability coefficient for the total Staff PAT was 0.88 for physicians and 0.82 for nurses.<sup>170</sup> In the sample of study B (measured at discharge), Cronbach's Alpha for the total Staff PAT was 0.80.

## Statistical Analysis

Analyses for Paper I and II were conducted using SPSS<sup>TM</sup> for Windows (version 14.0) and analyses for Paper III and IV were conducted using SPSS<sup>TM</sup> (version 18.0) and STATA (version 10.0). Choice of appropriate method of analysis is shown in Table 3 below.

Statistical analysis often involves comparisons such as between groups, treatments or procedures and the numerical value corresponding to the comparison of interest is the effect. Information from a sample of individuals is used to make inference about the wider population of like individuals. In statistical comparisons, a null hypothesis is one in which the effect of interest is zero and an alternative hypothesis is one in which the effect of interest is not zero. The comparison is about evaluating the probability ( $p$ ) for the observed data (or more extreme data) if the null hypothesis were true. If  $p$  is very small, then the null hypothesis appears implausible and the alternative

hypothesis appears more plausible. Conventionally a cut-off is chosen and if  $p$  is smaller than the cut-off, the null hypothesis is rejected.<sup>172</sup>

**Table 3** Statistical analyses used for Papers I-IV

Paper	I	II	III	IV
Analysis	Mann Whitney U test	Power analyses	Mann Whitney U test	Mann Whitney U test
	Students' T-test		Students' T-test	Students' T-test
	One-way ANOVA		Chi-square	Chi-square
	Repeated measures ANOVA			Spearman's rank correlation
	Bonferroni			
	Spearman's rank correlation			
	Linear regression			
	Logistic regression			

Depending upon the type of variable as well as on the distributional characteristics, parametric or non-parametric methods were chosen.<sup>172</sup> Variables are categorised in four levels of measurements as nominal, ordinal, interval or ratio and the important differences lie between nominal and ordinal on the one hand, and interval and ratio on the other.<sup>164, 173</sup> Parametric methods are based on measures of means, standard deviation, and differences among the means which can be interpreted from an interval and ratio scale. It makes no sense to calculate the average of nominal or ordinal data, they are regarded as frequencies in individual categories, and non-parametric statistics should be used. Furthermore, parametric methods make distributional assumptions and non-parametric methods make no such assumption.

The use of cut-off for  $p$  leads to treating the analysis as a process for making a decision that a statistically significant effect is a real effect and, conversely, that a non-significant result indicates that there is no effect. Two possible errors can then be made, firstly a significant result can be obtained thus rejecting the null hypothesis, when the null hypothesis is in fact true (Type I error) and alternatively, a non-significant result is obtained when the null hypothesis is not true (Type II error). The probability of Type I and Type II errors are sometimes called alpha and beta. The

value of alpha is the cut-off, usually set as 5%. The value of beta depends upon the size of effect that is of interest and the sample size or, in other words, the power of the study to detect an effect of a given size. It is common to require a power of between 80% and 90%.<sup>172</sup>

## **Power Analyses**

The main idea behind sample size calculations is to have a high chance of detecting, as statistically significant, a worthwhile effect if it exists, thus of being reasonably sure that no such benefit exists if it is not found in the trial. The greater the power of the study is, the more likely it is to find a potential difference, but greater power requires larger samples. For a study of two independent groups of individuals the following information needs to be specified: the standard deviation, a clinically relevant difference, the significant level and the power.<sup>172</sup>

In study B, the calculation of the required sample size was based on HbA1c as the primary objective two years after diagnosis when the endogenous insulin production has ceased for most children.<sup>81</sup> The analysis was first done in 2007 and again in 2009 with values of standard deviation from two different samples. Both the first and the second power analyses were performed when the reference method Mono S (%) was used in Sweden. The first sample was comprised of data from the Swedish Childhood Diabetes Registry.<sup>159</sup> As HbA1c varies as most during youth, the calculation was based on 2883 measurements from adolescents aged 10-15 years during 2004. The sample available consisted of one measurement of each individual, and the between-individual standard deviation was 7.3mmol/mol (Mono S: 0.7%). To calculate the needed sample size for a comparison of differences between groups of the individual change in HbA1c over time, information of the individual standard deviations were needed and an estimation was done so that the individual variation would not be greater than the between-individual variation. A difference between groups in HbA1c of 10.5mmol/mol (Mono S: 1%) was assessed as reasonable by clinicians. With the power 90%, at a significance level of 5%, the analysis of sample size showed that 25 children were needed in each group.

Study A gave access to another sample with repeated HbA1c measurements for each individual during the first two years after diagnosis which would offer a more precise value for the individual standard deviation. From the distribution of variations in HbA1c for children diagnosed 1997 to 2006, in the ages 3-15 years, the standard deviation for individual HbA1c measurements was 14.6mmol/L (Mono S: 1,4%). To show a mean difference of 10.5mmol/mol it then took 30 children in each group with

a power of 80%, at a significance level of 5% and 31 children in each group with a power of 83%.

## **Analyses of Variance**

The choice of appropriate method of analysis depends on the number of groups of observation, whether the groups are independent or dependent, the type of data, the distribution of data and the objective of the analysis.<sup>172</sup> To compare data from two independent groups, Students' T-test was used if the data was continuous and normally distributed and Mann Whitney U test, if the data was ordinal or not normally distributed. To compare data from three groups, One-way ANOVA was used if the data was continuous and normally distributed and Chi-square if the data was categorical or not normally distributed. Repeated measurement ANOVA is a parametric test and was used when the groups were dependent, meaning the same subjects were observed at different times. Group comparison is normally based on variance between subjects and the strength of repeated measurement ANOVA is that comparisons between the sets of observations are based on within-subject differences. Variation among the means of three or more groups increases the probability of Type I error. Each test has a 5% chance of showing a false positive result when there is no real difference. With multiple comparisons the probability of at least one false positive result is much greater than 5% and the Bonferroni correction was used to correct for the Type I error by multiplication of the  $p$ -value by three.

## **Relation between Variables**

Correlation is a method of analysis to study the possible linear association between variables and the Spearman method is a non-parametric calculation of the rank correlation coefficient. The correlation coefficient indicates the strength of the association as a single number but does not describe the relation between the variables. Correlation and regression are distinct methods which serve different purposes and regression is a method for the prediction of one variable to another. In the analysis one of the variables is considered as dependent (the outcome) and the other as independent (the predictor), and the analysis indicates the percentage of the variability of the data that is explained by the predictor variables.<sup>172</sup> To describe the linear relation between variables, linear regression was used when the dependent variable was continuous and logistic regression was used when it was categorical.



# Ethical Considerations

The necessity to apply rules of correct conduct within human experimentation was highlighted by judgments made by the war crimes tribunal in Nuremberg following World War II (Nuremberg Code). In Rome 1954, a position paper on human experimentation was adopted by the World Medical Association. Draft codes resulted in a final version of the Declaration in Helsinki 1964. The Declaration is a statement of ethical principles to provide guidance for medical research involving human subjects and has been amended six times since, most recently in October 2008.<sup>174</sup> The foundation of ethical clinical research is based upon respect for autonomy, providing beneficence and non-maleficence, and balancing benefit against risk, as well as promoting justice.<sup>175</sup> Ethical considerations in research are largely a matter of finding a reasonable balance between various interests such as our quest for knowledge, individual privacy interests as well as protection against various forms of harm or risk of harm. When research involves human participants, the researcher has a responsibility to ensure the interests of the participants. By placing some individuals in inconvenience for the good of others, ethical considerations are needed to minimise any discomfort for the participants and to ensure that individuals in the research process are being treated with respect while they contribute to the social good.<sup>176</sup> Prior to the studies each of these principles were reviewed and incorporated into the study design.<sup>153, 177-180</sup> Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject (NCT00804232) and ethical approval was formally obtained for studies A and B by The Regional Ethical Review Board in Lund (LU 305/2007).

## Autonomy

Autonomy is related to respect for the person and his/her right to know or not to know and the freedom in making decisions (to participate in or not participate in, or withdraw from, the research). Children should, whenever possible, give their own opinion in the form of written consent for a study they attend, in addition to that of the child's legal caregiver. Children, due to their age-related physical and



psychological development, may not be fully capable of understanding the research issues, benefits and risks, and have the right to be protected in line with this principle.<sup>179</sup> The ability to make an independent decision is strictly connected to the process of thinking and the ability of abstract thinking. At the age of 12 years, abstract thinking processes are developed and further built up by the age of 15 years which enables a child to give independent opinions and to perceive a situation as being multidimensional.<sup>181</sup> A free-will decision is communication-dependent and effective communication of complex concepts requires, whenever possible, terms that are used in everyday life by the majority of the population as well as being age-relevant. In study B, parents and children over the age of 12 were asked for consent and children under the age of 12 were asked for assent. Children were age-appropriately informed verbally and children 12 years or older also received age-appropriate information in writing. When seeking informed consent, the researcher should be particularly cautious if the participants are in a dependent relationship. In such situations the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.<sup>178, 180</sup> In study B, the responsible paediatrician gave the family verbal information about the study within 48 hours of diagnosis, and asked whether a researcher would be allowed to come and give further information about the study. If the family agreed, the investigator came to the hospital and informed the parents and the child about the study verbally and in writing. The family was then given time for consideration (about 12 hours) before the parent and the child were asked for consent/assent.

## Beneficence and Non-Maleficence

Every person consulting healthcare is in a vulnerable situation and a child is especially vulnerable as children are in even more dependent relationships. The principles of beneficence and non-maleficence are interwoven and imply the obligation of maximising possible benefits, protecting participants from potential/predictable harm and securing their wellbeing.<sup>179</sup> Since, in study B, the care in the control group as well as in the intervention group was based on the Swedish national guidelines for paediatric diabetes,<sup>55</sup> there was no direct threat of harmful effects due to the study. However, children younger than three years as well as children who did not live in a Swedish speaking family were not included for the sake of their safety. In medical practice and research, most interventions involve some burdens.<sup>180</sup> In the RCT, parameters concerning plasma glucose levels, HbA1c and severe acute complications were required. These parameters are registered on a regular basis for all children with

type 1 diabetes and were therefore no extra burden for children and families in the study. Children older than five years were asked to answer a few questionnaires and parents were asked to answer several questionnaires, measuring child and family quality of life, disease impact on family and healthcare satisfaction, and these might have been experienced as time-consuming. To minimise the time needed for the families to answer the questionnaires, the person who assessed the outcomes offered home visits for the filling in of forms. If the family preferred to meet at the Children's Hospital, arrangements were made to combine the meeting with the child's regular diabetes check-up visit.

Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information as well as to minimise the impact of the study on their physical, mental and social integrity. Questionnaires in study B may have raised thoughts for the child and their parents that would otherwise not exist. The first and second time the families were asked to fill in questionnaires, the person who assessed the outcomes stayed with the families when they filled in the forms, available to answer questions related to the questionnaires. Questions related to the child's diabetes were handed to the appropriate person in the diabetes team for clarification. Home visits by the diabetes nurse could have affected the integrity of the families and therefore information about the purpose with the visits was pointed out as being of a supportive nature for the everyday life of the families and that no controlling purpose existed. In some cases, families preferred to meet at the Children's Hospital and arrangement was then made to provide for those wishes.

A questionnaire for identifying psychosocial risk factors of families' resources based on the diabetes team's judgement was used and formed the basis of further support. Families in the intervention group assessed to be in need of increased support were informed about the possibility and it was emphasised that this was precisely that; an offer of increased support. To protect the confidentiality of families' personal information, questionnaires in study B were coded and no papers contained the names of family members and thereafter codes were used throughout the data collection and analysis. In studies A and B, confidentiality of each family member's personal identity and information was protected by having a single master list of enrolled subjects secured in a locked drawer. In both studies, the lists were only known to the principle investigator and to the person who collected outcomes. A potential benefit of participation in study B, was that of gaining access to an intervention to which families would otherwise not have access. Participants may also experience excitement of being part of a study as well as a sense of satisfaction that the information they provided might help others in the same situation since it added to the knowledge needed for providing improved care and initial management.<sup>182</sup>

## Justice

Justice addresses the issue of recruiting participants in a non-discriminatory fashion with regards to age, gender, and nationality.<sup>179, 180</sup> Both in study A and B, only reasons strictly related to research objectives and the children's safety defined the criteria for selection of participants. In study B, the youngest children were not included for safety reasons. Younger children cannot recognise and communicate early warning signs and symptoms of hypoglycaemia as accurately as older children or adults can.<sup>183</sup> Studies have shown an association between hypoglycaemia and an increased risk of cognitive and behavioural difficulties,<sup>33, 34, 36, 184-186</sup> particularly at a young age at onset.<sup>185, 187</sup> One family was not included due to difficulties in understanding the Swedish language. Participation required a dialogue between the diabetes team and the family where misunderstandings could have entailed a risk to the child. The upper age limit for inclusion was chosen because the transitions to the adult diabetes care setting when the adolescents have had their 18th birthday and the follow-up of two years set the upper age limit to 15 years. Since the focus of the study was type 1 diabetes, other possible major impacts on the family's situation needed to be minimised such as other difficult chronic illnesses or the child being in the custody of social care. For children who had a sibling with type 1 diabetes, the family was likely to have experiences that might differentiate them from other families and was therefore not included in the study. In environmental as well as therapeutic research, justice is directly linked to the validity of the study, and to the possibility of extrapolating research findings from the study sample to the target population, which will be thoroughly discussed in the discussion section.

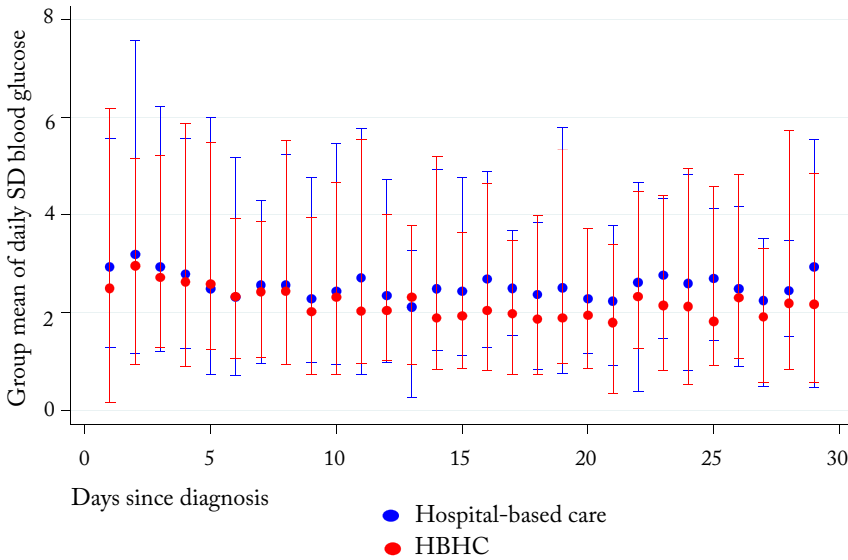
# Findings

The findings are presented in accordance with the aims of the study i.e. the investigation of the initial care for children diagnosed with type 1 diabetes in relation to different aspects of consequences of the disease: children's metabolic control including severe events, parents' healthcare satisfaction, families' levels of distress as well as the use and costs of healthcare resources.

## Children's Metabolic Control

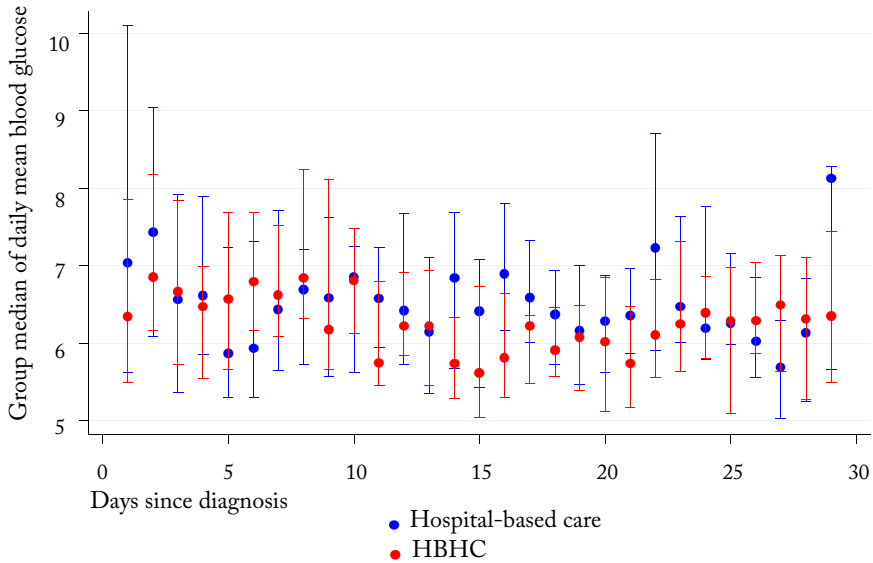
In study A there was no correlation between the duration of intravenous insulin treatment and HbA1c six months ( $r=0.065$ ,  $p=0.366$ ) or 12 months after diagnosis ( $r=0.033$ ,  $p=0.643$ ) nor any differences in subcutaneous insulin type and HbA1c  $<64$  or  $\geq 64$  mmol/mol two years after diagnosis ( $p=0.434$ ). A greater number of days of in-hospital care correlated significantly with higher HbA1c six months after diagnosis ( $r=0.162$ ,  $p=0.012$ ), which was likely to be explained by the child's age; younger children had more in-hospital care and the youngest children also had higher HbA1c (Paper I). In study B, there were no severe acute diabetes complications or other severe events reported during the trial or during the follow-up of six months. In the comparison of hospital-based and HBHC at diagnosis, the period one month after diagnosis showed significantly lower daily SMBG variability in the HBHC group compared to the hospital-based group (Figure 4) but no difference in daily mean measurements of SMBG (Figure 5).

**Figure 4** Group mean of standard deviation (minimum and maximum) in daily plasma glucose measurements in hospital-based care and HBHC, one month from diagnosis



Plasma glucose measurements of the period one month from diagnosis were divided into two periods, the period when the child received care in hospital or HBHC and the period when the child was discharged and slept in his/her own home. There was no difference in the mean glucose level or in variability when the child received care in hospital-based care or in HBHC, however when the children returned home, those who had received HBHC showed advantages in metabolic control by lower mean plasma glucose values and lower variability compared to children having received hospital-based care. Children in the hospital-based group had more episodes of hypoglycaemia compared to children in the HBHC group during the period of the first month ( $p < 0.001$ ), during the period when the child received care ( $p < 0.001$ ) and during the period when the child slept at home ( $p < 0.001$ ) (Paper III). Six months after diagnosis, there were no differences in HbA1c (mmol/mol) with a mean of 43.3 (SD 5.6) in the hospital-based care and 42.8 (7.1) in the HBHC ( $p = 0.747$ ); nor were there differences in the insulin dose/kg/24h with a mean of 0.58 (SD 0.17) in the hospital-based care and 0.59 (0.21) in the HBHC ( $p = 0.920$ ) (Paper IV).

**Figure 5** Median (interquartile range) of daily mean plasma glucose measurements in hospital-based care and HBHC, one month from diagnosis



## Parents' Healthcare Satisfaction

Fifty-eight parents in the hospital-based group and 59 parents in HBHC participated in the child's initial care. When the child was discharged from hospital-based care or HBHC, 116 parents responded to The PedsQL™ Healthcare Satisfaction Generic Module (Paper III). The mean value of parent satisfaction with the received healthcare was 76.7 (95% confidence interval 71.4-82.0) in the hospital-based group and 88.4 (85.9-91.0) in the HBHC group ( $p=0.015$ ). Six months after the child's diagnosis (Paper IV), 102 parents reported the healthcare satisfaction to a mean value of 79.1 (73.6-84.7) in the hospital-based care and 86.8 (83.0-90.6) in the HBHC ( $p=0.014$ ).

## Family's Distress

The only difference found in study A when analysing the relation of potential stressors and the child's metabolic control was that girls, with more than one stressor had a higher mean value of HbA1c compared to girls with fewer stressors or to boys ( $p=0.020$ ). To examine whether differences in parents' marital status affected children's metabolic control, a subgroup analysis was performed comparing children who lived in a family with no, or only one potential stressor, and no differences were found ( $p=0.981$ ) (Paper I). In study B there were totally 60 families and the Staff PAT was rated for 59 families. The median score in Staff PAT was 3.5 (range 0-20) in the hospital-based group and 3.0 (0-18) in HBHC ( $p=0.124$ ). The rated risk levels were in 7/30 (23.3%) cases rated as selected in hospital-based care and in 2/29 (6.9%) cases in HBHC ( $p=0.145$ ) and none were rated as targeted. Sum scores and categorical risk levels were significantly correlated ( $r=0.534$ ,  $p<0.001$ ). Staff PAT-rated categorical risk levels correlated significantly with subsequent resource use ( $r=0.285$ ,  $p=0.029$ ) and did not correlate with HbA1c at six months ( $r=-0.024$ ,  $p=0.860$ ). PAT sum scores did not correlate significantly with subsequent resource use ( $r=0.242$ ,  $p=0.064$ ) nor with HbA1c at six months ( $r=0.226$ ,  $p=0.085$ ) (Paper IV).

## Resource Use and Costs

During the years 1997 up to 2006 all children, except one, were admitted to hospital. The duration of the hospital stay decreased from a mean of 19.8 days (min-max 13-29) in 1997 to 13.6 days (7-19) in 2006 ( $p<0.001$ ). The number of hospital overnight stays decreased from a mean of 12.8 days (5-18) in 1997 to 8.4 days (4-13) in 2006 ( $p<0.001$ ). Age at diagnosis ( $p=0.004$ ) and pH at diagnosis ( $p<0.001$ ) predicted days of hospital stay (Paper I). Seventy-five per cent of the children had pH  $\geq 7.30$  at diagnosis and 94% of the children initially received intravenous insulin treatment. Duration of insulin infusion in 1997 was a median of 43 hours (min-max 15-135) and in 2006, 53 hours (24-123) ( $p=0.106$ ). After the intravenous treatment, all children were prescribed multiple subcutaneous injections. The dominant insulin type for newly diagnosed children in 1997 (24/25 children) was human insulin both for meals (regular) and for basal insulin (NPH). In 2002 most children (20/22) still started with human insulin but changed during the follow-up to insulin analogues for meals combined with NPH. In 2006 all of the children (30/30) started on insulin analogues, rapid and basal insulin, after intravenous infusion. Insulin pump therapy was introduced to 2-4 children yearly during the follow-up period. The number of

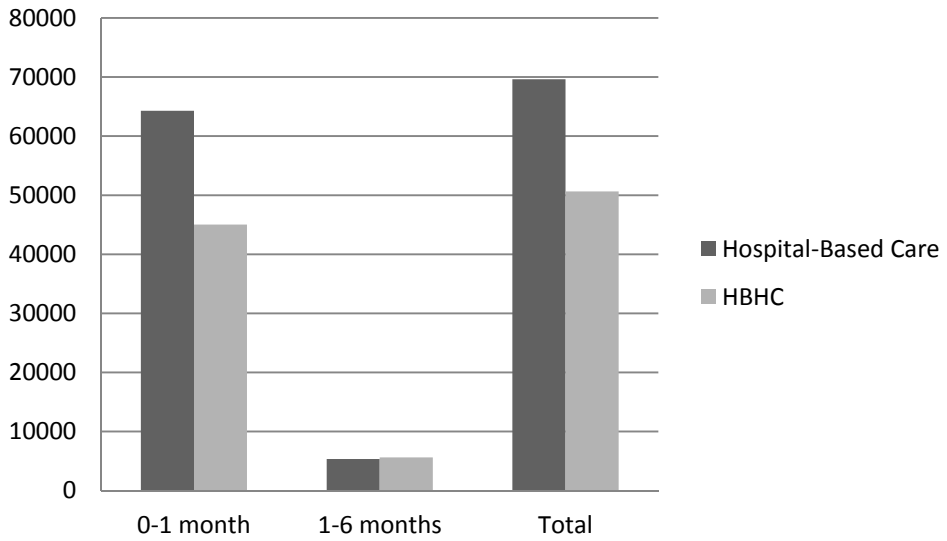
regular diabetes visits in the two-year follow-up time showed a mean of 10.7 visits (SD 1.97) in 1997 and 11.6 (SD 2.58) in 2002. Year 2006 differed from earlier years with a mean of 8.2 visits (SD 1.84). Children diagnosed during the first five year period (1997-2001) had more emergency visits during follow-up compared to children diagnosed during the last five year period (2002-2006) ( $p=0.019$ ). There were no differences between the five year periods in terms of diabetes related re-admissions ( $p=0.633$ ). The most common reason for re-admission was gastrointestinal illness associated with difficulties in maintaining the glucose levels (Paper I).

In study B, there were no differences between groups in how parents had changed their working hours after their child's diagnosis nor were there differences in parents' or significant others' absence from work related to the child's diabetes (Paper IV). The number of overnight stays in hospital amounted to a median of 8.5 (4-14) in the hospital-based care and in the HBHC the comparative number was 3.0 (1-5) of hospital overnight stays together with 6.0 (3-8) overnight stays at the Family House. The time during which the diabetes nurse interacted with the families during the initial care was significantly higher in the HBHC group compared to the hospital-based group. The paediatricians' educational time was lower in the HBHC group, while there were no differences between groups concerning other healthcare professionals' educational time use (Paper III). Healthcare resource use in hospital-based care and HBHC during the period of 1 month up to 6 months from diagnosis showed a tendency to a greater number of visits of all types for children in the hospital-based care compared to the HBHC, home/school visits excluded. For the same period, there was a significant difference in total healthcare resource use between groups with a median of 6 (min-max 3-12) visits in the hospital-based care and 5 (3-10) in HBHC ( $p=0.038$ ) (Paper IV).

Since home/school visits are more costly to the health services than visits at the hospital, total costs for the period between 1 and 6 months from diagnosis were almost equal with SEK5348 in hospital-based care and SEK5618 in HBHC. Total healthcare costs for the first month from diagnosis were 30% lower in the HBHC group compared to the hospital-based group (Paper III). When summarising the first month and the period from 1-6 months, the total healthcare costs were 27% lower in HBHC compared to hospital-based care (Figure 6).



**Figure 6** Mean healthcare costs six months from diagnosis in hospital-based care and HBHC



# Discussion

## Methodological Considerations

The view of knowledge and ethics has been described as being characterised by conceptual precision, knowledge stability and fallibility.<sup>188</sup> Conceptual vagueness increases the risk of a confused argumentation and impairs the ability to answer the research questions. The quest for a clear conceptualisation entails more than the mere ambition of defining individual concepts; the concepts must be connected to form a whole and be designed for the purpose. Furthermore, the formation of concepts, i.e. theory, says something about what we believe exists in the world. There are different levels of theory that set the limits of the answers we can expect to get.<sup>147</sup> Knowledge stability involves being aware of the quality of our knowledge and, also being aware, that it is just as important to know the limitations of knowledge as it is to have good knowledge. Finally, the approach embraces the view that the human being is fallible, and that this fallibility affects our knowledge as well as our use of the knowledge we think we have.<sup>188</sup>

Most often, the interesting questions in research are about *how*, *what* and *why*, i.e. to describe how a phenomenon is, to predict what will happen and to know why this phenomenon occurs. The method of searching for knowledge can be both inductive and deductive and the strategy chosen further determines what knowledge we can and cannot acquire - the stability of the knowledge. Francis Bacon (1561-1626), is an early philosopher of the inductive sciences.<sup>147, 189</sup> The inductive method says that scientists should observe and describe the world as it is as well as analyse and systematise the material without any guesses, hypotheses or preconceived ideas. If the conclusion made from the observations is true, then it is also applicable more generally. An inductive methodological approach does not preclude the why-question from being answered but makes deeper explanations unlikely. Francis Bacon described intervention when he claimed that it is not enough to observe the lions, we must also “twist the lion’s tail” to learn its secrets and to find causal truths.<sup>190</sup> The approach contrary to induction is deduction, where empirically testable consequences or predictions are derived from a general principle. The method asks us to formulate

hypotheses and theories from which how, what and why questions can be answered. Karl Popper (1902-1994) distinguished the validity of empirical evidence as being dependent on whether the hypothesis is verified or rejected when tested. Only the rejection or falsification of a hypothesis implies that the hypothesis is in fact false, the same logical conclusions cannot be drawn if the hypothesis is confirmed as actually being true. However, a falsification does not necessarily mean that the hypothesis needs to be abandoned, most often the hypothesis embraces a number of auxiliary assumptions, which might be false.<sup>147, 188</sup> RCTs are experiments but even though experiments are associated with inductive methods, the randomised design is not an unconditional observation. An RCT necessitates some kind of hypothesis but the research can be strongly or weakly hypothesis-driven.<sup>147</sup> The more undefined or vague the hypothesis is, the more the deductive approach passes over to become inductive as well as the more it increases its dependence on auxiliary assumptions with respect to the inference of causality.<sup>147, 190</sup> The hypothesis of this research was that of an improved metabolic control after two years for children having received HBHC compared to children having received hospital-based care at diagnosis. Based on the hypothesis, the power calculation in study B included HbA1c two years after diagnosis. However, the period of recruitment for inclusion of participants was longer than planned implying that the hypothesis of the two-year follow-up cannot be verified or rejected within this thesis.

## **Validity**

The validity refers to the approximate truth of the inferences.<sup>191</sup> To say that something is valid includes a judgment about the extent to which relevant evidence supports the inferences as being true. The evidence comes from both empirical findings and the reliability or the consistency of these findings with past findings and theories. The assessment of validity always includes the fallibility of human judgments and can never be absolute. Validity is a property of inferences and not designs or methods, it is the circumstances that contribute to more or less valid inferences and no method or design guarantees the validity of an inference. The validity typology in this thesis is based on Shadish, Cook & Campbell's<sup>191</sup> formulations.

### *Statistical Conclusion Validity*

Statistical conclusion validity concerns the validity and strength of the correlation between treatment and outcome. Potential threats to statistical conclusion validity include low statistical power, unreliability of measures, restrictions of range and unreliability of treatment implementation.

Power refers to the ability of a test to detect true relationships in the population, estimated from a single sample. The confidence interval is a range of values that we can be confident includes the true value - with a 95% confidence interval, it is expected that the true value will not be included in 5% of the times.<sup>172</sup> When a study has low power the estimation of effect size will have a wider confidence interval, it will be less precise of the true value in the population, and the risk for Type I and Type II errors increases.<sup>191</sup> Calculations of power included the primary outcome two years after the child's diagnosis and did not include any of the secondary outcomes presented in Paper III-IV. Therefore, the problems of possible errors are relevant in several comparisons in the present research, for example, in the sub-group comparisons of HbA1c in relation to stressors in the family (Paper I). Even though power calculations were performed prior to, and during study B, the defined clinical difference of effect in HbA1c might not be a likely effect size as to expect, and the power is therefore a limitation of the primary outcome as well. In a previous study, power calculations were based on a sample from the Hvidøre study group on childhood diabetes in 18 countries,<sup>192</sup> which showed that a difference in HbA1c of 5.5 mmol/mol (NGSP 0.5%) required 350 participants, a difference of 10.9mmol/mol (1.0%) required 100 participants and a difference of 16.4mmol/mol (1.5%) required a sample of 42 participants.<sup>97</sup> This means that discussions of whether or not there are differences in metabolic control between groups must always take into consideration what difference the study was powered to detect. However, there is a balance to be made between sample size and external validity over variation in settings by the period of recruitment. In 2010 results began to be reported in IFCC units (mmol/mol). In the beginning it was not clear that a separate formula was to be used to convert the relative change in HbA1c as compared to deriving one result of a measurement from the other which is the reason why the effect size is written differently in the description of the power analysis in Paper II as compared to Paper III-IV.

An additional potential threat to statistical conclusion validity is that of the unreliability of measures. New technology has become available that allows for the measurement of HbA1c in a clinical setting at the time of a consultation (point-of-care (POC) testing) which was previously solely a laboratory analysis. Even though POC testing, both concerning capillary plasma glucose measurements<sup>193</sup> and HbA1c measurements,<sup>194, 195</sup> might not be as accurate as a laboratory analysis, the advantages of clinical settings generally outweigh the disadvantages. POC testing provides the HbA1c value within 5-6 minutes and if the sample is sent to the laboratory it usually takes a few days or up to a week to receive the results. At the diabetes department unit in Lund where both of the studies were carried out, HbA1c had, up to the year 2010, either been derived from capillary blood samples in a clinical setting to then be

analysed at the laboratory or by the family using a prepared kit which was then sent to the laboratory via post. During the year 2010, the diabetes department changed its analysis method to POC for the testing of HbA1c (DCA 2000) and the laboratory at Lund University Hospital no longer performed analyses of the prepared kit. To minimise potential differences of methods, HbA1c values for children participating in study B have continued to be analysed in the laboratory by sending a prepared kit to Malmö University Hospital laboratory.

There are many types of monitors for SMBG which can yield differences in plasma glucose values and inaccuracies may arise from operator-related errors. When a child is diagnosed with type 1 diabetes, the diabetes team has chosen one type of monitor that meets certain quality standards and which all families receive at diagnosis. If the child or the parents want to change to another type of monitor, they may do so later on. Therefore, most of the children's plasma glucose values during the first month from diagnosis and included in the analyses for Paper III, were derived from the same type of plasma glucose monitor. The values were most often downloaded from the monitor by the family and e-mailed to the researchers. Only a few of the families preferred to register the plasma glucose values manually in a diary and were then asked for paper copies or, sometimes, the values were downloaded from the monitor at the diabetes surgery in connection with the diabetes check visits.

The unreliability of measures further concerns the results derived from instruments. A reliability coefficient indicates how well an instrument can distinguish between different individuals, so that the more diverse the individuals responding to the instrument are, the higher the reliability coefficient is to be. Often we talk about the instrument as having a high degree of reliability, but a high reliability coefficient of one sample is not the same as a high reliability coefficient of a different sample. However, if an instrument has been tested in many different samples and shown to demonstrate the variation between individuals, this provides more information regarding the degree of reliability.<sup>164</sup> The PedsQL™ Health Care Satisfaction Generic Module has been tested in different settings with high reliability coefficients,<sup>161, 162, 196-198</sup> which strengthens the reliability of the results presented regarding parents' satisfaction with healthcare in Paper III and Paper IV. Even though the Psychosocial Assessment Tool (PAT), completed by the child's caregiver, has been tested for reliability in different settings<sup>128, 167-169, 171</sup> with acceptable internal consistency, only one publication has been identified to test the reliability coefficient for the Staff PAT.<sup>170</sup> This makes the results of the families' levels of risk of psychosocial distress more uncertain in terms of reliability (Paper IV). Both instruments were tested for reliability in the present sample and with a high and an acceptable reliability coefficient.

Restrictions of range include ceiling effects which is when respondents cluster near the highest score. This is frequently noted in patient satisfaction surveys,<sup>199</sup> and was also seen in study B in parents' ratings of healthcare satisfaction (Paper III-IV). This has the consequence of making it difficult to distinguish between those who merely experience adequate service and those who experience superior care.<sup>200</sup>

Finally, statistical conclusion validity concerns the unreliability of treatment implementation and addresses three related problems in clinical intervention: failure to receive the full intervention, crossing over to a different treatment, and treatment diffusion.<sup>191</sup> In study B, treatment manuals were used and checked regularly. Thorough documentation of the treatment received in both the intervention and the control group was possible because the researchers worked in close collaboration with the clinical practice. Healthcare evolves continuously which was evident in the routines of a gradually increased number of outpatient visits to the diabetes nurse (Paper IV). However, healthcare is inherently complex and a potential problem occurs when results of studies that have been performed under circumstances that are not representative of the forms of treatment normally in practice, are generalised to uncontrolled circumstances.<sup>188, 201-203</sup> Since the intervention in this research is intended to be implemented within clinical practice, there needs to be a balance between the validity of inference and the implementation of treatment.<sup>188, 191</sup>

The unreliability of treatment implementation further includes how components of the intervention are related to changes in outcomes, or as philosophers would call it: the knowledge stability. In psychological research, various phenomena's associations have been systematised to build models of described causal relationships,<sup>204, 205</sup> which makes predictions possible, even though these models are not as useful in explanation.<sup>188</sup> The theoretical framework of study B identified factors that impact families' levels of distress over and above the stress caused by the child's diabetes.<sup>142</sup> The family's level of distress affects the family's health which, in turn, affects the child's health. These are consequences that are measured in the study to some extent (Table 2). The intervention was comprised of different parts with assumed directions of effect outlined in a hypothesis, meaning that the hypothesis embraced a number of auxiliary assumptions of how the interventions were assumed to alleviate families' levels of distress (Figure 2). The auxiliary assumptions, that are not measured, would have, had they been measured, afforded a much clearer identification of which parts of the outcome were the most affected by which parts of the intervention, and through which of the mediators.<sup>191</sup> If the hypothesis in this research is verified, then the causal inference will be related to all parts of the intervention, including auxiliary assumptions and mediators. If the hypothesis is falsified, then this does not necessarily

mean that the hypothesis is not true since the result can be related to auxiliary assumptions or mediators.

To sum up the treatment implementation: the strengths of study B were that the intended treatment was implemented in both hospital-based care and HBHC and not only partially implemented. Further strengths are that the study is based on a theoretical framework with well-defined active components of the intervention and an assumed direction of effects. A weakness of the study is the limitation of the answers we can expect to get in terms of the relation between intervention and outcome. Nevertheless, single studies are inevitably limited in their representation of persons, settings, treatment, and outcome. Their contribution can be to either verify or falsify the findings of many other studies conducted according to the same general causal question.<sup>191</sup>

### *Internal Validity*

Internal validity concerns the validity of inferences about whether or not the correlations resulted from a causal relationship. Study A extended over a ten year period, and there are a number of events and developments over time that could have influenced outcomes. The results of the association between differences in the initial management and insulin treatment with later metabolic control have therefore less valid inferences (Paper I). Random assignments reduce the plausibility of threats to internal validity and problems about causation arise in only two situations. The first is if attrition from the experiment differs between the groups and the second situation is if testing is different in each group. This means that groups need to be equal, not only at the time of randomisation, but also at the time of the follow-up, in all aspects other than the actual treatment.<sup>191</sup> None of these problems have occurred in study B which strengthens the inferences about descriptive causal relationships in Paper III and Paper IV. Internal validity and statistical conclusion validity are closely related and, in quantitative experiments, internal validity depends substantially on statistical conclusion validity.

### *Construct Validity*

Construct validity concerns the validity of inferences about the higher order constructs they represent.<sup>191</sup> There are most often numerous threats to construct validity in clinical research and some of the most relevant to be highlighted in the present studies concern the explication of constructs, mono-operation, novelty and disruption effects, measurement design and treatment diffusion. Retrospective tests generally refer to a design where, for example, participants are asked to recreate their use of a form of treatment retrospectively.<sup>191</sup> That design needs to be separated from

when data have been registered prospectively, though sampled retrospectively, in terms of validity of inference. This concerns a lesser threat to validity of inference in terms of the descriptions of the initial management in study A (Paper I), than if the data had been registered retrospectively. In study A, the choice of stressors identified was largely dependent on the information that was available in records based on outpatient visits at the diabetes department. It was therefore likely to be information that members of the diabetes team thought was relevant and important to the diabetes treatment. However, there are several limitations to this method resulting in a weak validity of inference. Firstly, we do not know whether the combination of the stressors chosen may represent the higher order construct of families' levels of distress compared to if other factors would have been chosen. Secondly, we do not either know to what extent these stressors are actually experienced as stressful by the family members. Furthermore, the presence of stressors was dependent on the information available in the records which was therefore what the families informed experts of, what the experts thought was relevant, and what the experts chose to make note of in the record (Paper I).

The phenomenon we wish to measure in instruments is generally either based on theory or alternatively, defined by a group of experts in the field. So, if another group of experts were asked to give their opinion, the definition might be different. Therefore, instruments are often tested in more than one way, such as, for example, by comparing the results with another scale, measuring the same construct it is supposed to represent. To strengthen the validity of results measured by instruments, the construct validity is comprised of an ongoing testing of different hypotheses in different target settings. The strength of the PAT instrument is that the construct is based on a theory that has been tested in different settings.<sup>128, 167-171</sup> Similarly, it is a weakness of the PedsQL™ Healthcare Satisfaction Generic Module that the construct is not based on theory.<sup>161, 162</sup> On the other hand, the latter instrument has been psychometrically evaluated from various aspects which strengthens the validity of the inference<sup>164</sup> (Paper III-IV).

In study B, it is a limitation that the intervention was mediated by a single diabetes nurse, precluding the possibility of separating the operationalization from the treatment construct of the HBHC programme.<sup>191</sup> When an innovation is introduced, it can give rise to excitement and enthusiasm that can contribute to success but that can also be quite disruptive. In any comparison processes in which participants and staff are aware of discrepancies between treatments, compensatory equalisation and rivalry are potential threats to construct validity. These threats are nevertheless parts of the treatment package and the potential influence cannot be separated within the construct. Treatment implementation was previously described as a strength of the



statistical conclusion validity in study B, but the extent to which treatment has been implemented as well as the extent to which nesting has been minimised between the treatment groups, are equally important to the validity of inferences in terms of treatment construct<sup>191</sup> (Paper III-IV).

### *External Validity*

External validity concerns the validity of inferences about whether the cause-effect relationship holds for targets of generalisation. Threats to external validity include the interaction of the causal relationship with units, over treatment variations, with outcomes and with settings.<sup>172, 191</sup> To be able to answer in which units the cause-effect relationships hold, one must ask how representative the participants of the research are, as well as how the diabetes department unit in Lund compares to other units. It strengthens the external validity of inference of study A to have included almost all of the children at the unit over the ten year period. The main reason for children not being asked to participate in study B was that of age and with no loss of families to follow-up, it reduced the risk of those participating in the experiment differing systematically from those who were not. The research was carried out in an area where the educational level is generally high and where parents are mainly born in Sweden. However, participants represented different socioeconomic groups and study B was designed to meet the needs of more vulnerable groups. This means that the results of study B cannot be generalised to the families with the youngest children. The results may hold for children and adolescents who are in metabolic balance and families of different socioeconomic groups but it requires a communication between professionals and families where misunderstandings can be minimised. As previously discussed, the HBHC programme was mainly performed by a single diabetes nurse and the main feature of that position in relation to the direction of the causal relationship is probably that of expert knowledge of, and experience in, childhood diabetes, which are likely to be essential features in terms of generalisation.

Interaction of causal relationships with outcomes concerns to what extent it is possible to give a fuller picture of the treatment's total impact.<sup>191</sup> From this perspective, the answers that can be obtained from study B need to be separated from what can be obtained within this thesis, limited as it is with short follow-ups and few outcomes. However, little is known of various effects of differences in the initial management of children diagnosed with diabetes and health service processes,<sup>12, 96, 97, 100, 103</sup> and every contribution makes a difference. The interaction of a causal relationship with the settings leads to the question of whether or not a Family House holds a cause-effect relationship to the families' own home. Even though the purpose of the Family House is to offer sick children and their families a home-like environment, the Family House nonetheless diverges from an

actual home in several important aspects. Firstly, the house is placed in the hospital area and families were not more than a few minutes away from assistance. Secondly, to live a family life at the Family House is different from doing so at home in terms of management of various activities of family life simultaneously, such as, for example, cleaning, washing, and bringing siblings to activities. Thirdly, there was room for 20 families to stay at the Family House at the same time which is generally quite a different situation from the one at home. The Family House was home-like in the sense that family members were the most active participants in the diabetes care and they did not have 24-hours health service as in a hospital. Families decided what to eat and they did their own shopping as well as cooking. Furthermore, the family was able to be together, including the siblings; they had a room of their own, which offered a certain amount of privacy. It is nevertheless likely that inferences about the cause-effect relationship do not hold for a generalisation to a home-situation.

## General Discussion of Results

This research was conducted to investigate the initial management when a child is diagnosed with type 1 diabetes. The main findings involve the safety and efficacy of the alternative approach of delivering care compared to the conventional care. Further important contributions were to highlight how healthcare resources are distributed and how effective funds that are available are serving health needs. The contribution can be to either confirm or falsify the inferences of many studies conducted on the same questions and to discuss the evidence for causal relationships made from the studies in the light of further research.

### Child Safety

In study B, there were no severe hyperglycaemia cases or any other type of severe events in either group up to six months from diagnosis (Paper IV). Furthermore, children in the HBHC group were found to have fewer episodes of hypoglycaemia ( $<4\text{mmol/L}$ ) compared to children in the hospital-based group during the period of the first month from diagnosis (Paper III). A Cochrane review from 2007<sup>12</sup> identified seven studies<sup>71, 72, 110, 111, 206-208</sup> comparing hospital-based and home-based care for children diagnosed with type 1 diabetes, ranging from the years 1976-2004. Additionally, two randomised controlled trials have been carried out in Scandinavia, one comparing initial management in a training apartment with traditional hospitalisation<sup>165</sup> and the other comparing short-term (about a week) with long-term

(about four weeks) initial stay at hospital.<sup>109, 209, 210</sup> One of the referred studies<sup>211</sup> reported that there were no cases of severe hypoglycaemia during the trial, and none reported if there were any other severe events during the trial. Four of the studies gave some indication of severe acute diabetes complications during the follow-up period but none reported other types of hypoglycaemia.<sup>5, 72, 206, 211</sup> One of the four studies reporting severe acute diabetes complications had a retrospective design,<sup>72</sup> one was a register-based study,<sup>206</sup> and two of the studies were randomised controlled trials.<sup>5, 211</sup> These studies found no differences between groups in severe acute diabetes complications during the follow-up period. Since there is no strong validity of inferences of safety during the interventions from previous studies, the results from the present research make a contribution to the issue. The results from study B support the causal relationship, suggested by the Cochrane review,<sup>12</sup> as to when home-care can be provided; it does not lead to any disadvantages in terms of acute diabetes complications.

## **Efficacy of Health Services**

One aim of this research was to identify families where the child runs the risk of a decreased metabolic control and to give these families increased support. The theory<sup>142</sup> says that family characteristics affect families' levels of distress and families' levels of distress affect the adjustments to stressful situations, such as the child's being diagnosed with diabetes which, in turn, affects the child's health, such as metabolic control. The intervention aimed to alleviate families' levels of distress and if the causal relationships hold, that would lead to improvements in children's metabolic control. Six months from diagnosis, the results showed no differences in children's metabolic control (Paper IV). From a philosophic point of view,<sup>147, 188</sup> if the causal inference of directions of effects in study B are confirmed during the two year follow-up, this could suggest that either the theory is not true or the intervention did not alleviate families' levels of distress. A third alternative is that the intervention did alleviate families' levels of distress and did affect other health outcomes of the child but not that of metabolic control. Other outcomes of the child's health are, to some extent, being tested within the study (Paper II), although, not within this thesis. However, clinical research has inherent complexity that bedevils inference of causal relationships.

### *Metabolic Control*

In study A, the validity of inference in terms of the causal relationship of no differences between length of in-hospital stay and length of initial insulin infusion

with metabolic control during the follow-up were weak. The RCT carried out in Finland, comparing short-term with long-term hospitalisation,<sup>109, 209, 210</sup> showed no significant differences in HbA1c values between the two groups after two years, nor did the RCT comparing intensive subcutaneous insulin therapy and intravenous insulin infusion at onset, which strengthens the validity of the suggested causal relationship. In study B, although significant, the differences of mean plasma glucose values and standard deviation during the first month from diagnosis were clinically small (Paper III) and there were no differences in HbA1c between groups, six months from diagnosis (Paper IV). Blood glucose values during the first year from diagnosis were assessed by Forsander et al.,<sup>105</sup> which showed no differences between groups, neither in comparisons of means nor in variability. Of the studies included in the Cochrane review comparing differences in the environment of the initial care i.e. home-based and hospital-based care,<sup>12</sup> there were four studies that gave information of metabolic control.<sup>72, 206, 208, 211</sup> The sample size of the studies ranged from 29 to 63 participants. One of them (63 participants) was a randomised controlled trial, carried out in Canada, and the only one that showed differences in metabolic control between groups.<sup>211</sup> The design of the RCT was in several aspects similar to study B in this research (Paper II). The children were initially hospitalised until their metabolic conditions were stabilised and education in diabetes management was mainly performed by a diabetes nurse in the family's home. Metabolic control, measured by HbA1c, was equal between groups until the two-year follow-up. Two years after diagnosis the mean HbA1c values were 7.7mmol/mol (NGSP 0.7%) lower in the home-based group compared to the hospital-based group. However, a threat to validity of causal inference was that children in the home-based care gradually increased the mean daily insulin doses compared to children in the hospital-based group.<sup>211</sup> As previously referred to, the RCT from Sweden, comparing initial management in a training apartment with traditional hospital-based care,<sup>5, 105</sup> did not either show significant differences in HbA1c values between the two groups. To sum up: there have been two RCTs<sup>5, 211</sup> besides the present RCT, with a short initial hospital stay and where the training in diabetes management has been carried out in the home or a home-like setting. One of the RCTs<sup>211</sup> resulted in improved metabolic control after two years, one RCT<sup>5</sup> showed no differences after two years and study B showed no differences after six months; there were thus no conclusive results. No study has been powered to detect differences less than 10-15mmol/mol. Since the improvements of metabolic control in the RCT from Canada<sup>211</sup> were likely to be explained by gradually increased insulin doses, the results indicate a direction of effect implying that the environment within which the training of the families is carried out does not constitute a strong indicator of great differences in children's metabolic control over time.

In Study B, groups were not only separated by differences in the environment for the initial management. Active parts of the intervention further included an approach to education with a more individualised learning process in the intervention group, and the results of children's metabolic control in our research therefore needs to be compared to other results from that perspective as well. In the RCT by Forsander et al.,<sup>5, 105, 165</sup> carried out in Sweden, families received a family-oriented crisis intervention with individualised problem-based learning, and no differences were found in children's metabolic control. This is a causal inference confirmed by two reviews of psycho-educational interventions for children and young people of type 1 diabetes.<sup>96, 97</sup> Similarly to what has previously been discussed, a possible explanation of the result is that most trials are underpowered to determine clinically significant effects on HbA1c in paediatric populations.<sup>97</sup> The review of education provided at diagnosis included the RCT by Forsander et al.,<sup>5, 105, 165</sup> and a non-randomised trial by Siminerio et al.,<sup>110</sup> which presented a short follow-up of one month. These studies were based on samples of 38 and 32 participants respectively. In sum, this means that the evidence is too weak for drawing conclusions of causal inference between psycho-educational interventions during the initial care and children's subsequent metabolic control, and emphasises that the results of study B make an important contribution to the issue.

The third active component of the present intervention was increased support to families having received HBHC by home visits during the follow-up compared to families having received hospital-based care. However, the HBHC showed less healthcare resource use compared to the hospital-based group for the period from one month up to six months (Paper IV), meaning that this part of the intervention cannot be considered as having had a great influence in terms of efficacy. In the RCT by Dougherty et al.,<sup>211</sup> more support in the home-based group was shown by the diabetes nurse during the follow-up and the only RCT comparing differences in the initial management, showed differences in metabolic control.

### *Family Impact*

In terms of the impact of the disease on the family, the results of study B showed no differences between groups in how parents had changed their working hours after the child's diagnosis, similarly to previous results.<sup>5</sup> In study A, potential stressors affecting the families' levels of distress were identified retrospectively from patient's records (Paper I), but the methodological circumstances contributed to less valid inferences of the result. In study B, families rated as being in need of increased support up to six months from diagnosis were few in numbers, and comparisons between groups were not possible (Paper IV). This means that the results from both studies A and B, in terms of families' levels of distress in relation to the initial management, hinder the inference of causal relationships. A previous screening of families' levels of distress,

based on the same theoretical framework as the PAT instrument, and completed by caregivers of the children, showed predictive validity for re-admissions but not for metabolic control.<sup>212</sup> The PAT instrument was originally developed to be completed by the child's caregivers and with the Staff PAT as a parallel assessment,<sup>128</sup> which might have been a preferable approach for emphasising the ongoing co-operation between the family and the diabetes team towards optimising the child's metabolic control based on the family's current life situation. No study was identified to have previously used the Staff PAT instrument as a freestanding measurement of families' levels of risk for psychosocial distress.

From a narrative view, parents' experiences of young children's diabetes diagnoses with diabetes described inordinate amounts of stress in relation to the diagnosis,<sup>114, 115</sup> exacerbated by the complex and intrusive nature of the diabetes management.<sup>144, 213</sup> The Cochrane review, comparing hospital-based and home-based care at diagnosis<sup>12</sup> refers to unpublished data of Hatton et al. (1994), comparing the initial management in four centres in Canada, the USA and the UK that used both out-patient/home care and hospitalisation. The data suggested that the out-patient programmes were able to reduce the stress, trauma and disruption associated with hospitalisation. The hospitalisation was associated with fear from the point of view of the child, and worry and a reduced ability to learn from the point of view of the parents. Healthcare professionals found that it was an advantage to identify problems in the families' home that would not be evident in a hospital. Of studies comparing home-based and hospital-based care, Dougherty et al.,<sup>71</sup> found no differences between groups of parents' perceived stress during the two year follow up. Similarly, Siminerio et al.,<sup>110</sup> found no differences between groups in terms of children's coping behaviour one month from diagnosis. There is a discrepancy of the results which may be partly explained by the difficulties of measuring the phenomenon of families' levels of distress. However, neither our findings nor previous research indicate that alternative approaches to hospital-based care at diagnosis would involve disadvantages in terms of the initial management and its influence on families' levels of distress. In summary, for families with a child diagnosed with type 1 diabetes the results from study B as well as previous findings, indicate equivalence in efficacy between groups, in terms of the influence of initial management on children's metabolic control, parents' working situation and families' levels of distress.

## **Quality of Health Services**

Two different quality perspectives can be perceived in terms of consequences of health services; firstly the efficacy of service, which was discussed in the previous section, and

secondly the quality of service which includes issues such as availability, communication and participation.<sup>214</sup> The interest in the patients' perceptions of service quality has been described as being mainly driven by two intellectual forces; those who pay for health service and those who provide care with perspectives on clinical practice that emphasises the need to deliver patient-centred care,<sup>199, 215, 216</sup> or as in this context; family-centred care. The call for an acquisition of families' experience and perceptions of the service has subsequently led to the development of healthcare satisfaction surveys. However, the terms perceptions and satisfaction are not interchangeable; satisfaction is an evaluation based on the fulfilment of expectations and individuals may have a complex set of important and relevant beliefs which cannot be embodied in terms of expressions of satisfaction.<sup>217</sup>

### *Healthcare Satisfaction*

In the present intervention, although parents in both groups generally stated that they were satisfied with the received healthcare, parents in the HBHC group rated greater satisfaction at discharge (Paper III) and the results six months after diagnosis confirm that parents in the intervention group continued to be more satisfied (Paper IV). Of studies comparing differences in the initial management regimen when a child is diagnosed with type 1 diabetes,<sup>72, 105, 110, 111, 206-208, 210, 211</sup> one study assessed measurements of satisfaction.<sup>211</sup> The scale was a 10-item questionnaire, developed especially for the study where parents and adolescents responded on a five-point rating scale indicating their satisfaction with various aspects of the treatment. Neither reliability nor validity of the measure was tested. The results showed no differences between groups during the two year follow-up. However, although our findings were contrary to the results presented by Dougherty et al.,<sup>211</sup> the latter were of less reliable and valid inference. Patient satisfaction surveys are frequently prone to ceiling effects and satisfactions have been said to merely be indicators of acceptable care. Thus, to measure patient's healthcare satisfaction as a method of assessing patient's perception of the quality of the healthcare service is not unproblematic and the usefulness of such measurements in generating change in health service provision can be questioned.<sup>199, 218</sup> This leads to limitations in how the results can be interpreted, yet the measurements do provide some information of the degree of acceptance by those to whom the service is being offered.

## **Effectiveness of Health Services**

Those who plan, provide, receive, or pay for health services face an incessant barrage of recurring questions about the allocation of healthcare resources.<sup>214</sup> Financing varies

from country to country, but in all OECD countries (Organisation for Economic Co-operation and Development) there is a joint responsibility of public healthcare, although distinctions can be made between countries that manage risk sharing primarily through formal insurance and those that primarily manage risk sharing through taxation. Economic evaluation is important simply because resources are scarce and choices must and will be made concerning their deployment. Methods of organised considerations of the factors involved are then preferable in a decision to commit resources to one use instead of another.<sup>214</sup> In health economy it is assumed that it is of mutual interest to society to use available resources in a way that can gain general acceptance. Therefore, the basic tasks are to identify, measure, value, and compare the costs and consequences of the alternative being considered.<sup>214</sup> It is the linkage of costs and consequences that allows for inferences of effectiveness.

### *Costs of Service*

Our findings of study B, showed 30% lower costs in HBHC during the first month from diagnosis (Paper III), and 27% lower costs six month from diagnosis compared to the conventional hospital-based care. Reduced costs for one party may sometimes imply that the costs are being transferred to another party. However, since home visit are less costly to the family than visits at the hospital, in addition to the results showing less use of health services during the follow-up, it is not likely that the findings of reduced healthcare costs of an HBHC would imply increase costs for the families in the present research. HBHC is widely applied in paediatric oncology and of five studies, four reported reduced costs in HBHC compared with inpatient care, and one study, which were the only RCT, could not demonstrate any reductions in costs in relation to HBHC.<sup>102</sup> In the literature of comparisons of differences in the initial management of childhood diabetes,<sup>12, 71, 72, 96, 103, 211, 219, 220</sup> two studies have been identified reporting costs relevant for the present discussion; Dougherty et al.,<sup>71, 211</sup> and Spaulding et al.,<sup>72</sup> a study from 1976 with a retrospective design. When comparing healthcare resource use between study B and the study by Dougherty et al., the results show several similarities. Both studies showed that home-care patients used less hospital and physician services from diagnosis to the end of the first month from diagnosis. Furthermore, both studies showed more home visits and telephone consultations in home care during the first month from diagnosis. Despite the similarities in families' use of resources, inference of costs differed considerably between the studies. Study B showed lower costs in HBHC during the first six months compared to hospital-based care and the study of Dougherty et al. suggested no overall differences in healthcare costs between home care and hospital care at diagnosis. These differences are likely to be explained by two factors. Firstly, in the study by Dougherty et al. costs of in-hospital care were calculated by counting the



specific diabetes-related services used by each child and with estimated ward nursing time. Overhead services were ignored. In study B, the price, per 24 hours, of hospital overnight stays, covered all health service expenses based on the average care costs of the specific unit with overhead included, giving a more complete picture of healthcare costs. Even though the hours the diabetes nurse interacted with families in HBHC increased compared to hospital-based care, the costs for the use of the nurse's time did still not reach the levels of the costs of overnight stays in hospital (Paper III). Secondly, our findings showed less use of healthcare resources during the follow-up (Paper IV) which was not the case in the study by Dougherty et al., where the increased support during the two year follow-up then exceeded the decreased costs in the home care group during the first month from diagnosis. In the study by Spaulding et al.,<sup>72</sup> resource use in relation to different professionals was unclear. The comparison of groups concerned patients without ketoacidosis that were either admitted to hospital for an average of 12 days or that received care at a day-unit. Standard in-hospital bed rates were used to calculate costs, and the care at the day-unit was found to be almost ten times lower than for the hospital group. No study has been identified assessing cost-effectiveness analysis in terms of costs in relation to measurements of children's and families' health. However, an on-going multi-centre RCT across eight UK paediatric diabetes centres<sup>221</sup> will be able to offer other conditions concerning power and thereby to assess the cost-effectiveness of differences in the initial health service process in relation to children's metabolic control.

In any comparison of the processes of health services, the most prominent feature is the safety of the services, especially when involving vulnerable groups such as children. Measurements of service efficacy discussed in this thesis included children's metabolic control and the impact on the family in terms of the parent's employment and working hours and levels of distress. The result indicated equivalence in efficacy of the HBHC programme and the hospital-based care. Furthermore, there was a high degree of acceptance by those to whom the HBHC service was offered and in combination with lower costs, this could suggest that the HBHC programme is a more effective process of health services. Overall, there are only few well-designed and controlled studies that compare hospital services against different models of home care. This thesis, while limited in answers by power and knowledge stability, provides empirical support for the safety and effectiveness of healthcare services when a child is diagnosed with type 1 diabetes.

# Future Perspectives

We will continue the evaluation of study B to assess the consequences of an HBHC and hospital-based care for child, family and healthcare over time and from different viewpoints. Important aspects which have not been covered by this thesis are the child's and parents' quality of life as well as the families' ability to give their child age-appropriate, diabetes-related support, so that the child may benefit from attaining their most realistic targets. The design of study B was based on the Medical Research Council framework for development and evaluations of RCTs for complex interventions to improve health,<sup>155, 156</sup> where the fourth and final phase is to establish long-term and real-life effectiveness of the intervention. If the intervention is shown to continue to be safe and effective over time, the question of whether the effect sustains when the intervention is implemented into routine care, is still to be answered.

In Sweden, there has been a long tradition of hospital-based care when a child is diagnosed with type 1 diabetes and with reliance on the national guidelines for a diabetes care with high standards. Getting new routines adopted, even when they have obvious advantages, is difficult.<sup>222</sup> That the process of implementation is carried out by known methods that are based on theory is essential to whether children, families and society will benefit from the knowledge.<sup>201, 202</sup> According to Everett Rogers,<sup>222</sup> diffusion is the process in which an innovation is communicated through certain channels over time among the members of a social system. Communication is a process in which participants create and share information with one another in order to reach a mutual understanding. An innovation is an idea, an implementation or an object that is perceived as new by an individual or a social system.<sup>223, 224</sup> Depending on how the characteristics of the innovation are experienced by the individual in a system, some innovations diffuse faster than others. The characteristics of importance for the diffusion of an innovation are its relative advantage, how compatible it is, how complex and understandable it is, how well used the innovation is and how visible the results of the use of an innovation are to others.<sup>224</sup> Based on the experiences of an HBHC, the main disadvantages of the programme were the unpredictable workloads for healthcare professionals and the need to work flexible hours, which is an important issue in terms of the adaptability of the innovation.

Most individuals evaluate innovations on the basis of friends who are already using them, not on that of scientific findings. This is likely to make an HBHC programme more compatible to the setting where the present RCT was carried out, compared to settings in which the study is more unknown. Diffusion is thus largely a social process through communication between people and, in order to enable adaptation, the innovation must be allowed to be formed by the group. The results of this research are nevertheless related to the treatment represented by the setting in the trial which do not hold for targets of generalisation when formed differently. There is once again a balance to be made between construct validity and implementation that emphasises the importance of continued evaluation of the safety and effectiveness of the health services in order to ensure diabetes care of high standards.

# Summary in Swedish

## Svensk Sammanfattning

När ett barn insjuknar i typ 1 diabetes kan symptomen vara allt från milda till måttliga eller allvarliga. Måttliga och allvarliga symptom kräver intravenös behandling och därmed är en initial sjukhusvård nödvändig. Hur barn med milda symptom ska vårdas finns däremot olika åsikter och rutiner. I vissa delar av världen blir barnen rutinmässigt inlagda på sjukhus i flera veckor medan det i andra delar anses att barnen tryggt och effektivt kan få vård i sitt eget hem och/eller med täta återbesök. Det finns få studier som har jämfört sjukhus- och hembaserad vård vid diabetes debut och resultaten är otillräckliga för att avgöra vilken vård som är bäst för dessa barn och för deras familjer. Sverige har en lång tradition med sjukhusbaserad vård i samband med att ett barn får typ 1 diabetes och vårdtiden varierar mellan olika kliniker från 1-3 veckor. Att leva med typ 1 diabetes är en komplex situation som för familjen innebär en daglig balansgång mellan insulindoser, mängd kolhydrater som barnet äter, aktivitet och infektioner såsom förkylningar, för att uppnå så nära normala blodsockervärden som möjligt. Den genomsnittliga blodsockernivån har avgörande betydelse för risken att utveckla sena komplikationer. Behandlingen tillsammans med andra krav i livet och utmaningar med att växa upp, innebär att många barn inte uppnår de rekommenderade målen för blodsockerkontroll. Studier visar att familjens funktion och psykosociala situation är starkt sammankopplad med barnets blodsockerkontroll. Sjukhusvård kan ses som en möjlighet till intensiv utbildning för att förbereda familjen i uppgiften att hantera diabetesbehandlingen hemma. Å andra sidan har föräldrar till barn som fått en sjukhusbaserad vård i samband med diagnosen, beskrivit att den teoretiska kunskap de fått på sjukhus, inte varit giltig hemma i deras vardagsmiljö. De kände sig osäkra och oförberedda i uppgiften att hantera sitt barns behandling när de kom hem från sjukhuset. Avhandlingens övergripande syfte var att undersöka den initiala vården för barn som insjuknar i typ 1 diabetes, dels med traditionell sjukhusbaserad vård och dels med vård i hemmiljö. Ett ytterligare syfte var att identifiera familjer där barnet bedöms ha en förhöjd risk att utveckla mindre god metabol kontroll och ge de familjerna ett utökat stöd.

Avhandlingen består av två delstudier vilka båda genomfördes på barnmedicinska kliniken på Skånes universitetssjukhus i Lund. Den första studien hade en retrospektiv design med syfte att utvärdera om tillfälliga förändringar i den initiala vården över en tio-års period, påverkade barnets metabola kontroll två år efter diagnos. Syftet var också att undersöka om sociala faktorer (potentiella stressfaktorer) som var registrerade vid diagnos, hade betydelse för barnets metabola kontroll två år efter diagnos. Studien inkluderade 247 barn i åldern 0-16 år som insjuknat under åren 1997-2006. Alla barn utom ett var inlagda på sjukhus i samband med diagnosen. Sjuttiofem procent av barnen hade  $pH \geq 7,30$  vid diagnos och 94 % av barnen fick intravenös behandling initialt. Vårdtiden minskade signifikant över tio-årsperioden ( $p < 0,001$ ) och varken vårdtid ( $p = 0,843$ ) eller skillnader i insulinbehandling ( $p = 0,434$ ) var associerat med barnens HbA1c värde två år efter diagnos. Det fanns inget samband mellan vårdtid och potentiella sociala stressfaktorer för familjen vid diagnos ( $p = 0,592$ ). Flickor i familjer med fler potentiella sociala stressfaktorer vid tiden för diagnos hade högre HbA1c under uppföljningen jämfört med flickor i familjer med färre potentiella stressfaktorer och jämfört med pojkar ( $p = 0,020$ ).

Den andra delstudien i avhandlingen var en randomiserad kontrollerad studie med syftet att jämföra två olika regimer för barn med nyupptäckt diabetes; sjukhusbaserad vård och vård i hemmiljö. Från mars 2008 till september 2011, inkluderades 60 barn i åldern 3-15 år, 30 blev randomiserade till sjukhusbaserad vård och 30 till vård i hemmiljö. Barn och föräldrar följdes upp vid tiden för utskrivning, efter 6, 12 och 24 månader. Sjukhusbaserad vård innebar att barnet var inskriven på sjukhus 1-2 veckor. Under denna tid hade barn och föräldrar dagliga informationsträffar med diabetesteamets olika yrkesprofessioner. När familjen fått det mesta av den planerade informationen, fick familjen nattpermission ett par dagar innan barnet blev utskriven från sjukhuset. Vård i hemmiljö innebar att barnet, efter 2-3 dagar på sjukhus, lämnade sjukhuset tillsammans med sin familj och bodde i ett familjehus med stöd av en diabetessjuksköterska. Familjehuset ligger på sjukhusområdet och erbjuder sjuka barn och deras familjer att bo i en hemlik miljö när barnet behöver vårdinsatser från sjukhuset. De aktiva delarna i hemmiljövården var definierat som individualiserat lärande utifrån familjens förutsättningar och sociala situation, en hemlik miljö som möjliggjorde praktisk tillämplig och träning av att sköta barnets behandling med samtidigt stöd. En aktiv del i behandlingen var också ett utökat stöd efter utskrivning genom tre hembesök och utökad tillgång till telefonrådgivning. Familjer som fått vård i hemmiljö och som vid utskrivningen bedömdes ha en ökad risk för större psykosocial påfrestning, erbjöds hembesök en gång i månaden.

Utvärdering för den andra delstudien och inom ramen för denna avhandling inkluderar den första månaden efter diagnos och sex månader efter diagnos. Inga

medicinska misstag eller försämrade allmäntillstånd har rapporterats under studietiden. I utvärderingen en månad efter diagnos sågs inga skillnader i barnens blodsockervärde avseende medelvärde ( $p=0,753$ ) eller variabilitet ( $p=0,276$ ) under tiden de fick vård i sjukhusvård eller vård i hemmiljö. Efter utskrivning, hade barnen som fått vård i hemmiljö lägre medelblodsockervärde ( $p=0,009$ ) och med mindre variabilitet ( $p<0,001$ ) av värdena jämfört med barnen som fått sjukhusbaserad vård. Barnen som fått vård i hemmiljö hade färre episoder med hypoglykemi ( $p<0,001$ ) jämfört med barn som fått sjukhusbaserad vård under den första månaden från diagnos. Föräldrar var mer nöjda med den vård familjen fått ( $p=0,015$ ) och hälso- och sjukvårdens kostnader var 30 % lägre för hemmiljövård jämfört med sjukhusbaserad vård. I utvärderingen sex månader efter diagnos var föräldrar fortsatt mer nöjda med den vård familjen fått i hemmiljö jämfört med sjukhusbaserad vård ( $p=0,014$ ) samt hade mindre utnyttjande av hälso- och sjukvårdsresurser ( $p=0,038$ ). Resultaten visade inga skillnader mellan grupperna avseende HbA1c ( $p=0,747$ ), förändring i föräldrars arbetstid ( $p=0,240$ ) eller föräldrars och anhörigas frånvaro från arbete på grund av barnets diabetes ( $p=0,549$ ). Grad av risk för familjens psykosociala påfrestning, bedömd vid diagnos, var associerad med den efterföljande resursanvändningen ( $p=0,029$ ) men inte HbA1c ( $p=0,860$ ).

Sammanfattningsvis visade studierna att vårdtiden har minskat över en tioårsperiod för barn med nyupptäckt typ 1 diabetes. Under denna period blev de flesta barn rutinmässigt inlagda på sjukhus och fick intravenös behandling oavsett svårighetsgrad på symptom. Vidare stödjer dessa resultat att upp till sex månader från barnets diabetesdebut, är vård i hemmiljö lika trygg och effektiv som vård på sjukhus. Föräldrar skattade en hög grad av acceptans av vården som erbjöds i hemmiljö. Dessa resultat i kombination med lägre kostnader för hälso- och sjukvård indikerar möjligen vård i hemmiljö som mer kostnadseffektiv jämfört med traditionell sjukhusbaserad vård. Uppföljningen av den randomiserade kontrollerade studien kommer att fortgå till hösten 2013, för att utvärdera konsekvenser av de olika hälso- och sjukvårdsinsatserna, för barn, familjer samt för hälso- och sjukvården över tid.



# Acknowledgements

This thesis was carried out at the Department of Health Sciences, Lund University. I would like to express my sincere gratitude to everyone who has supported me in various ways, and contributed to the completion of this thesis.

Special thanks to the many *children and their families* who have participated in the study, for your time and, although being in a difficult situation, showing willingness to contribute to the research, which may benefit others in the same situation.

It was my good fortune to have as my supervisor *Inger Hallström*, a constant source of knowledge, a professional inspiration who has provided critical and excellent supervision. Thank you for having introduced me to the scientific world.

Thank you *Annelie Carlsson*, my co-supervisor, for your unerring support and for believing in me, for having enabled opportunities and for sharing your knowledge in the field of paediatric diabetes.

I would like to express my appreciation to my co-author, *Katarina Steen Carlsson*, for your valuable contributions to my research and I hope we will have reason to work together again.

I owe a depth of gratitude to *Lisbeth Jönsson*, who is not only my co-worker in the project but who has unfailingly collected data with genuine empathy for the children and their families.

This project had not been possible without the help and the cooperation of each one of the members of the diabetes team at the Children's Hospital in Lund. *Annette Leger*, *Carina Ärlebring* and *Kristel Björkman* – thanks for all the support you have given through the years. Thanks also to *Maria Elfving*, *Peter Holmquist*, *Domniki Papadopoulou* and *Lisa Engleson* for your help in enrolling families to the research and to *Viktoria Schiöler* and *Charlotte Bengtsson* for your tireless contribution with notes of your time with families.

I would like to express my appreciation to all colleagues and friends at the Children's Hospital in Lund; it is a fortune to have you as fellow workers. Special thanks to *Anette Månsson* and *Pia Lister*.



Many thanks also to the staff at the Ronald McDonald House, for your kindly reception and for always being willing to help, with special thanks to *Carina Wittström*.

To the fellow PhD students and colleagues at the Department of Health Sciences, thank you for your support and helpful criticism during seminars - continued success to each of you, whether you are travelling first-class or inspection trolley.

Thanks to *Anna Lindgren* and *Per Nyberg* for your admirable patience and valuable help in statistics.

To all the co-workers and PhD students of the Swedish Institute of Health Sciences, *Vårdalinstitutet*, for contributing to a PhD school of top class characterised by a creative, supporting and stimulating environment. Special thanks to *Ingalill Rahm Hallberg*, for accepting me to the PhD programme and who has my deepest respect. Thanks to *Gerd Ahlström*, the Director of the Swedish Institute of Health Sciences. I would also like to thank *Anna Blomgren*, *Niklas Frost* and *Lena Gunnarsson* who have managed to help each one of us doctoral students in great and small.

To all fellow PhD students and dear friends in the “landscape” who have been a source of joy and laughter as well as supportive and fruitful discussions. Without you, this would have been a much less pleasant journey. Good luck to each of you during your own personal journey! Especially I would like to thank *Maria Lithner* and *Anna Condelius* for their supportive friendship and discussions about life, career and methodological issues. Thanks *Jimmie Kristensson* for much wise advice.

Finally, thanks to family, friends, relatives and the most important people in my life, *Bo*, *Oscar*, *Linnea* and my mother *Berit*, upon whom my life depends.

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# Paper I





# The Influence of Initial Management and Family Stress on Metabolic Control in Children with Type 1 Diabetes

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Received August 6<sup>th</sup>, 2010; revised September 11<sup>th</sup>, 2010; accepted October 11<sup>th</sup> 2010.

## Abstract

*The aim was to assess whether temporal changes in the initial management for children diagnosed with type 1 diabetes over a ten year period affected metabolic control two years after diagnosis. A further aim was to investigate if social factors, registered at diagnosis, had an impact on metabolic control two years after diagnosis. During the years 1997-2006, 247 children and adolescents were diagnosed with type 1 diabetes at a University Hospital in Sweden. The analysed data included HbA1c, pH at diagnosis, initial intravenous insulin infusion and length of hospital stay at diagnosis, subcutaneous insulin type, number of diabetes check-up visits, emergency visits, re-admissions and social factors. Length of hospital stay decreased significantly over the ten year period. Neither hospital stay nor differences in insulin treatment was significantly correlated with children's metabolic control over time. Length of hospital stay was not related with families' social stress situation. However, girls in families with more family stress at the time of diagnosis had higher HbA1c during follow-up than girls with less family stress or boys. Factors of importance for the child's long-term metabolic control need to be further investigated so the initial management can be tailored to each individual family's needs. This would imply an effective utilization of both families' and health care resources.*

**Keywords:** Type 1 Diabetes, Disease Management, Patient Admission, Life Stress, Hemoglobin A1c

## 1. Introduction

In Sweden, most children with newly diagnosed type 1 diabetes are admitted to hospital for about 1-3 weeks and receive intravenous insulin infusion the first days, in line with the Swedish national care program for pediatric and adolescent diabetes [1]. The first national care program guidelines were presented in 1982. Since then, these guidelines have become standard of care in Sweden and have led to important improvements in Swedish pediatric diabetes care. In other parts of the world, duration of hospital admission and stay after the initial diagnosis varies greatly, from several weeks to a few days or, alternatively, on an outpatient basis only [2-4]. The overall trend is for shorter lengths of stay and/or exclusively outpatient management [2-6]. A recent review, comparing hospital based and home based care, showed that studies were too limited to reach clear conclusions, but home based care did not seem to lead to any disadvan-

tages concerning metabolic control or psychological outcomes [7]. Re-admission and emergency visits rates have the potential, besides HbA1c to be utilised as an evaluation for the efficiency of treatment or education program [8].

Metabolic acidosis of clinical relevance is defined in the Swedish national program as pH < 7.30 [1]. Routines for initial intravenous insulin treatment vary between countries to only include children who are acutely ill at diagnosis [6,9], to include almost all children diagnosed with type 1 diabetes. Intravenous insulin infusion is recommended one or two days before start with subcutaneous treatment even if the child is not acutely ill. The argument for intravenous treatment is that it facilitates a stable plasma glucose level during the first days and that it might preserve beta cell function [10]. On the other hand it is argued that preserved beta cell function is likely to relate to a normal glucose level rather than to how the insulin is administered or the quantity of insulin

given [11,12].

To maintain metabolic control, major adjustments are needed by the family, requiring time and attention [13]. Family stress and social family background are most important factors concerning metabolic control [13-16]. Parental marital status, rather than socioeconomic status have been suggested to better capture family factors that impact the child's metabolic control, where biological parents who lived together were associated with lower HbA1c compared to alternative family arrangements [17]. In order to direct resources, it is of interest if social factors at the time for diagnosis can separate more vulnerable children who might be in risk to develop poor metabolic control. To guarantee quality in health care, all elements of the care need to be followed and evaluated with focus on outcomes [1,18].

The aim of our study was to assess whether temporal changes in the initial management for children diagnosed with type 1 diabetes over a ten year period affected metabolic control two years after diagnosis. A further aim was to investigate if social factors, registered at diagnosis, had an impact on metabolic control two years after diagnosis.

## 2. Methods

### 2.1. Participants

The study was carried out at the Department of Pediatrics at the University Hospital in Lund. The department's diabetes unit cares for about 270 children (in 2010) with type 1 diabetes, between the ages of 0-18 years. During the years 1997 to 2006, 250 children aged between 0-16 years were diagnosed with type 1 diabetes and were recorded. The data, for a ten year period was retrieved from the hospital's patient administrative system, patient's records and from a national quality registry, the Swedish Childhood Diabetes Registry SWEDIABKIDS [19]. Data from three children were excluded as they moved from the hospital's catchment area shortly after diagnosis. Data concerning age, pH at diagnosis, duration of initial intravenous infusion, total days for hospital stay at diagnosis, length of overnight and daytime only hospital stay, insulin type, number of regular diabetes check visits to physicians, metabolic control measured as HbA1c, number of emergency visits and re-admissions related to the diabetes, were registered prospectively.

### 2.2. Outcome measurements

Data concerning social factors, assumed to impact the child's life stress [13-16] were retrospectively retrieved from patients' records during the time of primary hospi-

tal admission in connection with the diagnosis. Social factors were if the child had a) problems at school b) illness apart from type 1 diabetes and c) no or minimal contact with one parent. Social factors assumed to have an impact on the family stress and indirectly on the child's situation were if there was a) illness in the family b) unemployed parents c) parents on long-term sick-leave d) financial problems in the family and e) parents with criminal record.

Each social factor was registered if it was not present (0), was present for one family member (1) or present for two family members (2) and summarised for each family with parental marital status (parents living together (0), parents separated (1)). The number of siblings living in the family was registered with the assumption that more siblings might have an impact on the general family stress [20]. The summarised social factors, further described as family stress, were dichotomized into children who had no or one family stress factor and children who had two or more family stress factors. The number of siblings was also dichotomized into children who had no or one sibling and children who had two or more siblings. The groups were divided from the assumption that it is a cumulative family stress that is likely to impact the child's metabolic control.

HbA1c at six, 12 and 24 months after diagnosis was recorded. For cases without recorded HbA1c at the designated time points (81 of total 730 values), values were interpolated between the two closest registrations. The interpolated value was weighted according to time interval between each anchoring registration at six, 12 and 24 months, respectively. Data were analysed both for the whole cohort and for each year. The trends are presented in a ten-year interval, year 1997 and 2006 or five-year interval, year 1997, 2002 and 2006. For some variables, groups were too small to be analysed for each year and were in those cases analysed in five year periods, 1997-2001 and 2002-2006. The study was approved by the Research Ethics Committee at Lund University (LU 305/2007).

### 2.3. Statistical methods

All analysis were conducted using SPSS<sup>TM</sup> for Windows (version 14.0) and *p*-values < 0.05 were considered statistical significant. A descriptive analysis was used to present the children's age and pH at diagnosis as well as trends concerning insulin treatment, hospital stay and out-patient visits. Continuous variables were checked for distributional characteristics and, when found not to be normally distributed, non-parametric methods were used. In those analyses HbA1c was dichotomized, a cut point at 7.1% was chosen due to Diabetes Control and Complications Trial (DCCT) mean HbA1c for the group with

This study was supported by The Swedish Institute for Health Sciences, The faculty of Medicine, University of Lund, The Swedish research council, The Swedish diabetes foundation and The Region of Skåne

intensive treatment [21]. Another argument for the cut point was that it separated 20% of the children with the highest HbA1c values. Swedish HbA1c values are ~1% lower than National Glycohemoglobin Standardization Program (NGSP) and DCCT [22].

Trends in the length of intravenous treatment and hospital stay were analyzed with Mann-Whitney test. The relationship between initial intravenous treatment and HbA1c at six and 12 months was analyzed with Spearman's rank correlation. This was not performed with values of the 24 months due to the assumption that a possible preserved beta cell function was most likely within the first year [23]. Spearman's rank correlation was also used to investigate the relation between days of hospital stay and HbA1c at six, 12 and 24 months. Since we found an association between hospital stay and metabolic control further analysis with possible predictors of time of hospital stay were analyzed using linear regression with family stress, age divided into four groups and pH at diagnosis as independent variables. Linear regression was used to analyze possible predictors of HbA1c with family stress, age groups and pH at diagnosis.

One-way ANOVA was used to compare insulin type from the time of diagnosis and HbA1c at 24 months. According to the most commonly used subcutaneous insulin types, insulin type was divided in three groups, multiple injections with a) human insulin, b) insulin analogues for meals combined with NPH and c) insulin analogues for both meals and basal insulin. Due to multiple comparisons Bonferroni correction was applied.

The influence of family stress on the development of HbA1c from six to 24 months was investigated using repeated measures ANOVA. The dichotomized variables concerning family stress and siblings were entered as between-subject factors together with age and gender. Possible predictors of HbA1c values > 7.1% at 24 months were analyzed using multivariate logistic regression (backward, likelihood ratio) with family stress and siblings as independent variables. To evaluate the influence on HbA1c of biological parents living together or not at diagnosis, a subgroup analysis was performed comparing the children with no or one family stress factor. For this group repeated measures ANOVA was used with parents' cohabitation as a between-subject factor. Trends in emergency visits and re-admission were analyzed with t-test.

### 3. Results

Of the 247 children included (130 boys and 117 girls) all except one, were admitted to hospital. The number of children included each year and age at diagnosis is presented in **Table 1**.

**Table 1. The number of children included each year and age at diagnosis**

Year	n	Age median	Min-Max	Inter quartile range
1997	25	9.94	2.63-16.50	5.43
1998	17	8.11	0.73-15.04	6.29
1999	26	10.45	1.71-15.80	6.24
2000	20	8.70	0.95-15.80	7.20
2001	28	8.86	1.71-14.79	6.47
2002	22	10.25	1.40-15.52	6.46
2003	32	8.80	0.74-14.92	6.59
2004	21	9.51	0.93-15.56	7.12
2005	26	9.85	1.26-15.66	6.13
2006	30	9.94	2.23-15.23	6.39
Total	247	9.11		

Seventy-five percent of the children had pH  $\geq 7.30$  at diagnosis. In 7% of the cases, values were missing, with each of these children with a relatively mild presentation. Ninety-four percent of the children received intravenous insulin treatment initially. Length of insulin infusion in 1997 was median 43 hours (min-max 15-135) and in 2006, 53 hours (24-123) ( $p = 0.106$ ). The time for hospital stay decreased from a mean of 19.8 days (SD 3.64) in 1997 to 13.6 days (SD 3.29) in 2006 ( $p \leq 0.000$ ). The time of hospital stay before the child left the ward daytime, e.g. a brief home visit with the parents, was mean 8.5 days (SD 2.29) in 1997 and 7.0 days in 2006 (SD 2.05) ( $p = 0.028$ ). The number of days before the child spent a night at home, while still being under care at the hospital, decreased from mean 12.8 days (SD 3.22) in 1997 to 8.4 days (SD 2.36) in 2006 ( $p \leq 0.000$ ).

After the intravenous treatment, all children were prescribed multiple subcutaneous injections. The dominant insulin type for newly diagnosed children in 1997 (24/25 children) was human insulin both for meals (regular) and basal insulin (NPH). In 2002 most children (20/22) still started with human insulin's but changed during the follow-up to insulin analogues for meals combined with NPH. In 2006 all of the children (30/30) started on insulin analogues, rapid and basal insulin, after intravenous infusion. Insulin pump therapy was introduced to 2-4 children yearly during the follow-up period. The number of regular diabetes visits in the two year follow-up time showed a mean of 10.7 visits (SD 1.97) in 1997 and 11.6 (SD 2.58) in 2002, year 2006 differed from earlier years with a mean of 8.2 visits (SD 1.84). Children diagnosed during the first five year period (1997-2001) had a mean of 0.57 emergency visits during follow-up and during the last five year period (2002-2006) 0.30 ( $p = 0.019$ ). Children diagnosed during the first five year period had a mean of 0.36 diabetes related re-admissions and 0.42 the last five year period ( $p = 0.633$ ). The most common reason for re-admission was gastrointestinal illness associ-

ated with difficulties in maintaining the glucose levels.

There was no correlation between length of intravenous insulin treatment and HbA1c at six ( $n = 198$ ) or 12 ( $n = 199$ ) months ( $r = 0.065$  and  $0.033$ ,  $p = 0.366$  and  $0.643$ ). More days of in hospital care before the child spend a night at home correlated significantly with higher HbA1c at six months (Table 2) and were likely to be explained by age at diagnosis. Younger children had more days of hospital stay and children younger than six years were also the group with highest HbA1c values at six and 12 months, but not at 24 months (Figure 1). Age and pH at diagnosis predicted days of hospital stay but not family stress (Table 3). There was no difference between groups concerning subcutaneous insulin type at diagnosis and HbA1c  $< 7.1$  or  $\geq 7.1\%$  at 24 months ( $p = 0.434$ ).

When analysing family stress and the number of siblings, the linear progression of HbA1c due to diabetes duration did not differ between the groups. However, mean HbA1c from six, 12 and 24 months differed significantly with higher HbA1c for girls with more than one family stress factor than girls with less family stress or boys (Table 4). HbA1c  $\geq 7.1\%$  at 24 months could not be explained by family stress or the number of siblings ( $p = 0.407$ ). Children's metabolic control, in the group with no or one family stress factor, where the biological parents were separated ( $n = 33$ ) did not differ from those with parents living together ( $n = 173$ ) with a mean HbA1c from the follow-up period (six, 12 and 24 months) 6.217% (SD 0.95) and 6.212% (SD 0.95) ( $p = 0.981$ ).

#### 4. Discussion

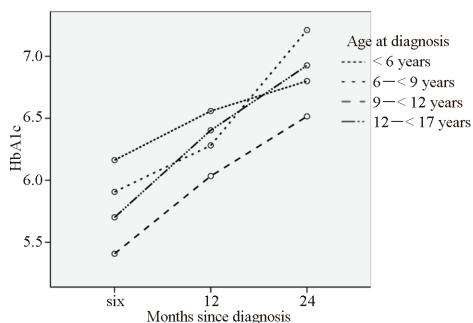
The aim of this study was to investigate the initial management and the influence on metabolic control. Length of hospital stay decreased significantly over the ten year period and resulted in similar metabolic outcomes during the two year follow-up, which is in line with earlier studies [12,24,25]. Furthermore, no changes in re-admissions and fewer emergency visits over time were found. These findings suggest that time for hospital stay is not likely to be a determining factor concerning families' possibilities to manage the diabetes treatment. However, during the analysed ten year period, insulin types have changed from human insulin to insulin analogues. This might have influenced the results as use of insulin analogues compared to human insulin was associated with reduced risk of hypoglycaemia and improved metabolic control for adults and with a diabetes duration of at least 12 months [26]. Different insulin types did not separate children with the highest HbA1c values in the present study.

Length of intravenous treatment was not shown to determine children's metabolic control over time. Earlier studies report that initial intravenous treatment was given

to children who were acutely ill or dehydrated at diagnosis [6,9,12,27]. In our study, 94% initially received in

**Table 2. Correlation between total days of hospital stay, days before the child left the ward daytime, days of overnight and HbA1c at six, 12 and 24 months.**

Groups	HbA1c % at six months	HbA1c % at 12 months	HbA1c % at 24 months
<b>Total days of hospital stay</b>			
Correlation coefficient	0.094	0.047	-0.013
Significance*	0.146	0.469	0.843
N	243	244	240
<b>Days before the child left the ward daytime</b>			
Correlation coefficient	0.098	-0.044	0.006
Significance*	0.159	0.531	0.930
N	207	208	204
<b>Days of overnight hospital stay</b>			
Correlation coefficient	0.162	0.022	0.001
Significance*	0.012*	0.740	0.985
N	238	239	235



**Figure 1. Mean HbA1c (%) at six, 12 and 24 months in relation to age at diagnosis, divided into four groups**

**Table 3. Possible predictors of days before the child could leave hospital for the night and possible predictors for HbA1c at six months.**

Model	Dependent variable	Independent variable	B-value	P-value
Adjusted R <sup>2</sup> =0.070	Days of hospital stay	Family stress		0.592
		Age at diagnosis	-0.169	0.004
		pH at diagnosis	-11.171	0.000
Adjusted R <sup>2</sup> =0.025	HbA1c at six months	pH at diagnosis		0.121
		Family stress		0.090
		Age at diagnosis	-0.043	0.008

**Table 4 Comparisons of mean HbA1c at six, 12 and 24 months after diagnosis between groups based on family stress, gender and sibling.**

Groups (n)	Mean HbA1c %	SD	Significance*	95% CI
<b>Family stress</b>				
No or one family stress factor (210)	6.208 <sup>a</sup>	1.07	<i>P</i> = 0.065	6.061-6.356
Two or more family stress factors (35)	6.579 <sup>a</sup>	1.05		6.214-6.945
<b>Gender</b>				
Girl (117)	6.585 <sup>a</sup>	1.56	<i>P</i> = 0.056	6.295-6.874
Boy (130)	6.203 <sup>a</sup>	1.50		5.938-6.468
<b>Siblings</b>				
No or one sibling (165)	6.222 <sup>a</sup>	1.51	<i>P</i> = 0.085	5.986-6.457
Two or more siblings (80)	6.566 <sup>a</sup>	1.41		6.251-6.881
<b>Family stress/gender</b>				
No or one family stress factor/Girl (100)	6.167 <sup>a</sup>	1.05	<i>P</i> = 0.020*	5.961-6.373
No or one family stress factor/Boy (112)	6.250 <sup>a</sup>	1.14		6.038-6.462
Two or more family stress factors/Girl (17)	7.003 <sup>a</sup>	1.13		6.462-7.543
Two or more family stress factors/Boy (18)	6.156 <sup>a</sup>	1.05		5.669-6.643
<b>Family stress/siblings</b>				
No or one family stress factor/no or one sibling (144)	6.230 <sup>a</sup>	1.02	<i>P</i> = 0.052	6.061-6.398
No or one family stress factor/two or more sibling (66)	6.187 <sup>a</sup>	1.01		5.943-6.430
Two or more family stress factors/no or one sibling (21)	6.213 <sup>a</sup>	1.03		5.772-6.655
Two or more family stress factors/two or more siblings (14)	6.945 <sup>a</sup>	1.10		6.366-7.524

a. Covariates appearing in the model are evaluated for age at diagnosis=8.9876.

travenous treatment, in line with the Swedish national care program [1]. This is well above the reported 37.5% of children receiving insulin in Germany and Austria, where the majority of children receive intravenous insulin for management of diabetic ketoacidosis [27]. Acidosis at diagnosis is associated with low beta cell function and high HbA1c [28]. Thus, children initially receiving intravenous insulin treatment had more episodes with hypoglycaemia during the first two weeks compared to children treated with subcutaneous insulin after onset of type 1 diabetes [27].

A further aim was to investigate if social factors, recorded at diagnosis influenced metabolic control. We found a significant difference for girls, living in families with more family stress, when looking at mean HbA1c over the two year period. Parental support has been shown to be an independent factor for adolescent girls and parental relationships was suggested to be more strongly associated with the mental health of adolescent females than males [29,30]. Family stress factors in the present study were limited to the information available from patient's records. Each family saw a social worker during the initial hospital stay who recorded details of home environment. The validity of social factors was however limited as it was not possible to weight the factors in relation to families' experiences and should therefore be interpreted carefully. Social supports, educational level and socio-economic statuses was not available but are known to be important factors when

considering the child's risk to develop poor metabolic control [14,16,31].

When factors related to family stress were dichotomized, a breakpoint with no family stress factor and one or more family stress factors were considered to obtain more equal groups. In the group with one family stress factor, the single stress factor was mainly separated parents. A subgroup analysis was chosen instead to evaluate the influence of parents' cohabitation on HbA1c. Interestingly, when family stress, that sometimes follows a separation was excluded, there was no difference in the child's mean HbA1c for children where the parents lived together or were separated. These findings might not be in contrast to Swift's results that found children living with their biological parents had lower HbA1c compared to alternative family arrangements [17] since the results were explained by less social stress and more cohesive family environment [32]. In spite of the fact that groups were small when factors related to family stress were analysed, they were close to significant and may have led to false conclusions concerning non-significant differences. An interesting finding was that family stress did not predict hospital stay which is recommended by the Swedish care program [1] in order to support family out of their needs and possibilities to handle the new situation.

In conclusion, factors of importance for the child's long-term metabolic control need to be further investigated so the initial management can be tailored to each

individual family's needs. This would imply an effective utilization of both families' and health care resources.

## 5. Acknowledgment

We would like to thank Per Nyberg for statistic counseling and Elisabeth Crang-Svalenius for reviewing the English language.

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# Paper II



# A Methodological Description of a Randomised Controlled Trial Comparing Hospital-Based Care and Hospital-Based Home Care when a Child is Newly Diagnosed with Type 1 Diabetes

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**Abstract:** *Aim and objective:* To describe the study design of a randomised controlled trial with the aim of comparing two different regimes for children with newly diagnosed type 1 diabetes; hospital-based care and hospital-based home care.

*Background:* Procedures for hospital admission and sojourn in connection with diagnose vary greatly worldwide and the existing evidence is insufficient to allow for any conclusive determination of whether hospital-based or home-based care is the best alternative for most families. Comparative studies with adequate power and outcome measurements, as well as measurements of cost-effectiveness are needed.

*Design:* The study design was based on the Medical Research Council framework for complex interventions. After two to three days with hospital-based care, children between the ages of 3 and 16 were randomised to receive either continued hospital-based care for a total of 1-2 weeks or hospital-based home care, which refers to specialist care in a home-based setting. The trial started in March 2008 at a University Hospital in Sweden and was closed in September 2011 when a sufficient number of children according to power calculation, were included. The primary outcome was the child's metabolic control during the following two years. Secondary outcomes were set to evaluate the family and child situation as well as the organisation of care.

*Discussion:* Childhood diabetes requires families and children to learn to perform multiple daily tasks. Even though intervention in health care is complex with several interacting components entailing practical and methodological difficulties, there is nonetheless, a need for randomised controlled trials in order to evaluate and develop better systems for the learning processes of families that can lead to long-term improvement in adherence and outcome.

*Trial Registration:* Trial Register NCT00804232.

**Keywords:** Type 1 diabetes, disease management, family, research design, randomised controlled trial, haemoglobin A1c.

## INTRODUCTION

Type 1 diabetes is one of the most common chronic diseases in children and adolescents. It is a serious and expensive disease with a risk for late complications [1, 2]. Research during the last decade has provided a substantial amount of evidence for the relation between family factors and metabolic control [3-7]. The Swedish national guidelines for paediatric diabetes [8] have existed since the 1980s, providing consistent, high standards and important contributions to Swedish paediatric diabetes care. Recommendations of the Swedish national guidelines for paediatric diabetes include hospital-based care at the time of diagnosis and intravenous insulin treatment for the first days even if the child is not acutely ill. There are few recent studies that describe hospital admission procedures for children with newly diagnosed type 1 diabetes. However, previous descriptions show that hospital admission and sojourn at the

time of diagnosis varies greatly worldwide, from several weeks to a few days or completely on an outpatient basis [9-14].

The often negative impact of hospital admission on children and their families calls for alternative ways of providing care [15, 16]. Paediatric home care (PHC) facilitates the continuation of normal life for children and their families and is on the increase due to the potential psychosocial benefits of home care and the costs of hospital-based health care [17]. There is no consensus on the definition of PHC and the service can be based on both general and specialist schemes. General PHC services most often work from a community base in a single district. By contrast, specialist services are more likely to be hospital-based, providing service to more than one district [17-20]. Outpatient treatment is provided by health care professionals in the outpatient clinic at the hospital while PHC provides treatment by health care professionals in the child's home. Hospital-based home care (HBHC) refers to specialist care in a home-based setting. The existing evidence is insufficient to allow for any conclusive determination as to which process, hospital-based or home-based care, is best for most children

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when diagnosed with type 1 diabetes. Comparative studies with adequate power and outcome measurements, with cost-effectiveness measurements and with a follow-up of at least two years, are needed [18, 21].

## BACKGROUND

The goals of initial treatment and management are for the child to attain metabolic balance and for the families to understand the illness and learn how to manage the treatment. Clinical practice consensus guidelines of the International Society for Pediatric and Adolescent Diabetes (ISPAD), with the current views of experts in the field [22] are being used to assist clinicians in managing childhood diabetes. ISPAD's guidelines state that health professionals should deliver structured education using behavioural learner-centred approaches rather than didactic approaches [23]. Both ISPAD's and national paediatric guidelines emphasise the importance of individualised support and education by a diabetes specialised team [8, 24-26]. Educational interventions have shown an effect on psychosocial outcomes and a modestly beneficial effect on metabolic control [27, 28]. Interventions based on clear theoretical psycho-educational principals, involving the whole family and making use of techniques such as problem solving, goal setting, coping skills and stress management are most likely to be effective [4, 23, 27, 29].

An optimal research situation would be for scientists to be able to introduce an intervention under circumstances in which no other variables could be confounded with the introduction. However, full control and full isolation of the intended treatment is seldom possible. Complex intervention in health care often comprises a number of components, which may act both independently and interdependently. The number of components, including behaviour both of those delivering and receiving the intervention, the flexibility of the intervention and the variability of outcomes are dimensions of the complexity of the intervention [30, 31]. With a random assignment the plausibility of alternative explanations for observed effects is reduced. This is presuming that the procedure of randomisation has been carried out correctly, and that the groups are equal, not only at the time of randomisation, but also at the time of the follow-up, in all aspects other than the actual treatment. A further condition for the evaluation of the effectiveness of an intervention is that the treatment that was intended becomes the treatment actually received, not only partially received. There is always a risk for interventions to slide such as, for example, if the participants in the intervention group and the control group respectively, converse and thereby receive partial access to both treatments, so-called "nesting" [32].

There are promising results from interventions with the aim of empowering individuals to manage their own health. However, it is often not clear which are the active ingredients of many successful interventions [27, 33, 34]. Furthermore, in order to comprehend and assess the validity of a randomised controlled trial (RCT), readers must understand the design, conduct, analysis and interpretation of the study [35-37], which requires a comprehensive description for complex interventions, based on a clear theoretical framework [30, 31].

## Theoretical Framework

A number of family patterns of interaction that can substantially impact on the intellectual development of young children are identified. Guralnick [38] presents three family patterns influencing the developmental outcomes of children:

- The quality of parent-child transactions, described as a sensitive responsiveness. The parents see, listen to and encourage the child in a discourse-based and non-intrusive way.
- Family-orchestrated child experiences: The parents take responsibility for organising home and community experiences; the home environment contains stimulating toys and experiences adequate for the child's age.
- Health and safety is provided by the family; providing proper nutrition and ensuring the child's safety is also essential for the child's development.

Family characteristics, such as intellectual disabilities or poor health, as well as a lack of financial resources and social support can create stressors. As can the child's characteristics associated with his/her biological vulnerability, such as, for example, diabetes or other chronic illnesses. These stressors are capable of perturbing even optimal family patterns of interaction. Potential stressors for families created by the child's disability or illness are the parents' need for information, interpersonal and family distress, as well as the parents' lack of confidence and resources [38]. It is presumed to be the cumulative effect that produces the greatest threat to children's physiological and mental health [39]. When considering risk factors regarding poor metabolic control, the greatest risk would be for children in families that are already exposed to general stressors, besides the stressor caused by the child's diabetes.

This article describes the study design and outcome measurements of a randomised controlled trial with the aim of comparing two different regimes for children with newly diagnosed type 1 diabetes; hospital-based care and hospital-based home care.

## MATERIALS AND METHODOLOGY

The study design is based on the Medical Research Council framework for development and evaluations of RCTs for complex interventions to improve health [30, 31]. The framework distinguishes five phases; the first phase is theoretical and the second is about developing an understanding of the components in the intervention. In the third phase, the intervention can be explored or tested. The fourth phase includes an RCT with adequate power and appropriate outcome measurements. The fifth and final step in the evaluation of a complex intervention is long term surveillance in order to study the real-life effectiveness of the intervention.

Qualitative research is helpful for identifying critical components of importance for the intervention [30, 31]. In the first pre-clinical phase, we elaborated the theoretical framework with a literature review of the results of families' experiences of living with childhood diabetes from the time

of diagnosis and through the following three years [15, 16, 40, 41]. The studies indicated that the time after diagnosis is a difficult time for the whole family, characterised especially by the need for information and for resources to learn how to live with the illness as well as by difficulties in maintaining the diabetes regime [16, 40, 41]. Theoretical information is not always easily transformed into practical skills and experiences; a “learning by doing” approach is more likely to lead to knowledge acquisition than an entirely theoretical approach. This phenomenon was first described by John Dewey [42, 43], but Donald Schön [44] established the concept during the 1980s. Reflection together with others may elucidate tacit knowledge. Limitations imposed on families due to the diabetes treatment might not be as severe as they initially appear, and stressors created by the illness can often be avoided by practical advice and by appropriate timing within the treatment. What the family is initially taught and the way of living with diabetes that is first presented to them, will be experienced by them as the right way and it will be more difficult to maintain a regime the more it diverges from the family’s natural lifestyle.

In the second phase, the components of the intervention were identified and explored from a second literature review and from interviews with the parents of children with type 1 diabetes as well as with professionals working in the diabetes team, in order to develop an understanding of the components in the intervention and how they may interrelate. A home-based environment was presumed to move the responsibility for the diabetes treatment from health care professionals to the family with increased family participation as a consequence. Participation was likely to raise an extended need for practical knowledge that might facilitate for the family to put theory into practice [42, 44]. A home-based environment was also presumed to make the family’s personal lifestyle visible to health professionals, allowing for strengths and difficulties to be taken into consideration in creating an individualised learning process and for making good use of available resources. The study and the randomised design were planned and instruments

were translated and tested [45].

In the third phase, the intervention was explored with a pilot study where study design and logistics were tested. Parents of two children, newly diagnosed with type 1 diabetes, were informed about the study and asked for consent for the pilot study. Parents and children in both families consented and received hospital-based home care according to the study design. No adjustments of the study design were needed. However, some clarifications for the procedure were made concerning which person would be best suited to inform the families about the study and to ask for informed consent. The fourth phase included the main randomised controlled trial, with adequate power calculation, randomisation, treatment protocol and informed consent of the participants. The main trial started in March 2008 and was closed in September 2011 when a sufficient number of children, according to power calculation, were included. A flow diagram of the progress through the phases of the main trial is shown in Fig. (1).

The study was registered at clinicaltrials.gov with the identity number NCT00804232 and follows the CONSORT (Consolidated Standards of Reporting Trials) recommendations, a statement issued in order to improve the reporting of RCTs [35-37]. The study was approved by the Research Ethics Committee at Lund University (LU 305/2007).

**Setting**

The trial took place at a University Hospital in Sweden. The Hospital has a catchment area with a population of 71 684 (December 2010) children and adolescents from 0-18 years [46]. The diabetes department unit cares for about 250 children and adolescents; aged 0-18 (in 2010), and approximately 25-30 children are diagnosed with type 1 diabetes per year [47]. The diabetes team members included diabetes specialised paediatric nurses (from now on called diabetes nurses), paediatricians specialised in paediatric diabetes (from now on called paediatricians), a dietician and a social worker. A psychologist was available for families with special needs and was consulted by the diabetes team

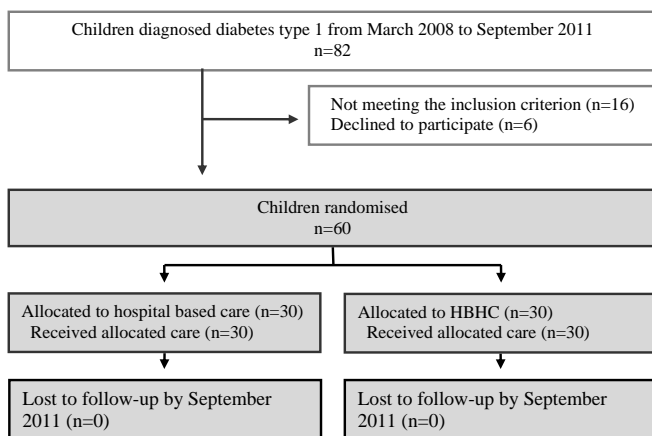
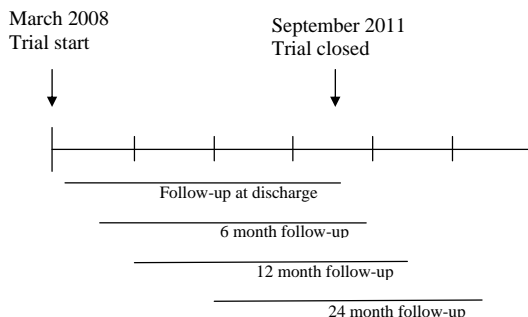


Fig. (1). Flow diagram of the progress through the phases of the trial until September 2011, when the trial was closed.



**Fig. (2).** Time axis of the trial and follow-up.

when relevant. According to Swedish law, parents of children who are ill have the possibility of receiving a parents' allowance during the child's care. When a child is diagnosed with diabetes the period for this allowance also includes another 2-3 weeks after discharge for both parents. Agreements for financial compensation concerning the parents' allowance include about 80 % of the parents' salary up until the level of a predetermined salary ceiling.

Due to organisational factors, and in order to facilitate for the family, a form of care was chosen for the HBHC intervention group that would be familiar both to health professionals at the Children's Hospital and to the families, namely The Family House. The Family House offers sick children and their families a home-like environment and is placed in the hospital area. There is room for 20 families and each family has one room where the whole family, including siblings, can stay together. Parents make their own meals and there are spaces for children to be physically active.

### Participants

Children from 3-16 years of age, who are newly diagnosed with type 1 diabetes at the University Hospital, without any other difficult chronic illnesses or siblings with type 1 diabetes, living in a Swedish speaking home and not in custody of social care, were candidates for inclusion in the study. The age span of 3-16 years was chosen because it was not considered safe to include the youngest children and there was a transition to the adult diabetes care setting when the adolescent was 18 years. A follow-up of two years set the limit at a maximum of 16 years of age for inclusion. Children in both groups received, as inpatients, intravenous treatment to attain metabolic balance, and followed the Swedish national guidelines for children newly diagnosed with diabetes [8] during the first two or three days. When the child was medically stable, families received subsequent care according to their randomisation. At the time of discharge and irrespective of randomisation, the paediatrician completed the Psychosocial Assessment Tool (PAT) [48], an instrument for identifying psychosocial risk factors at diagnosis to predict the subsequent use of psychosocial resources, based on the judgement of the diabetes team. After discharge, all families followed the regular diabetes check-ups with visits at the outpatient department unit after about 1, 3 and 6 weeks. Gradually the visits thinned out to

every third or fourth month, which was the frequency of the continued visits.

Members of the diabetes team asked the parents if a researcher could come and inform about the study. If the parent consented, one of the investigators provided verbal and written information about the study within 48 hours of the diagnosis. Children were age-appropriately informed verbally and children who were 12 years or older also received age-appropriate information in writing. The families were then given time for consideration (12 hours) before the parents and children over the age of 12 were asked for consent. Children under the age of 12 were asked for assent. If the parents and child consented/assented, the child was randomised to either hospital-based care or HBHC.

### Randomisation

The children were randomised in two strata, younger than eight years or eight years and older. The randomisation was performed by an independent centre for clinical research using the software R-2.6.1 [49]. Within each stratum children were assigned to the two different treatments by sampling without replacement from a block consisting of, to the investigators, unknown number of labels from each treatment group. The seed of the random number generator was stored. According to the routine procedure for RCT in clinical settings the investigators received two sets of coded, sealed and opaque envelopes, one set for older children and one for younger children. The envelopes were identical and contained one of two possible instruction sheets, "Hospital-based care" or "HBHC".

### Sample Size

HbA1c was the primary objective two years after diagnosis, when the endogenous insulin production had ceased for most children. A difference in HbA1c of 10mmol/mol was estimated as clinically relevant and statistical power was calculated on a known variation in HbA1c during the first two years after diagnosis. During 1997-2006, 247 children who were 3-16 years old at the time of diagnosis showed a standard deviation of 14mmol/mol in individual HbA1c measurements. To show a mean difference of 10mmol/mol between two groups, it took 30 children in each group with a power of 0.79, and a significance level of 5%.

### Hospital-Based Care

Children randomised to hospital-based care followed the routine care at the hospital which involved a total of 1-2 weeks of hospital-based care. The child with diabetes and the child's parents' were called to information meetings with the diabetes team members during the hospital stay. The paediatrician, the dietician and the social worker usually had 3-4 meetings with each family and the diabetes nurse had 4-8 meetings. Each meeting lasted for about 30-60 minutes. The information followed a checklist, based on Swedish national guidelines for paediatric diabetes, where each discipline was responsible for different portions of education on the checklist. One parent could stay at the hospital with the child during the night. The other parent was encouraged to be present during the educational sessions. The child could leave the ward in the daytime between meetings when parents felt secure in their management of hypoglycaemia and if they had an agreement with the responsible paediatrician. Towards the end of the hospital stay, the family returned to their home for two-three days until discharge. During these days, the family reported, by phone, the child's glucose levels for the previous 24 hours and received prescribed insulin doses for the following 24 hours. After discharge, families could contact a diabetes nurse for counselling by phone during the daytime, five days a week, which was the routine procedure. During evenings, nights and week-ends they could receive assistance from the general hospital staff. The diabetes nurse offered a school visit with the purpose of informing teachers and school friends about the disease of diabetes and the treatment with insulin.

### Hospital-Based Home Care

The active ingredients in the HBHC were defined as:

1. a home-like environment, which allowed families to learn management tasks in a "hands on" fashion such as selecting food, trying to anticipate the effect of food and activity on plasma glucose, understanding how the components relate to each other and evaluating the results;
2. individualised learning based on the need for knowledge, the family's resources, and the home, school and work situations;
3. increased support after discharge by
  - a. increased access to a diabetes nurse - by telephone seven days/week and three home/school visits for all families in the intervention group, and
  - b. visits to school/home once a month during the follow-up for families with special concerns

Children randomised to HBHC left the Children's Hospital after the first initial days with their parents and lived in a home-like environment, the Family House, until families felt confident to return home. The staff members at the Family House worked daytime and were not trained in nursing. A diabetes nurse was available for the family during parts of the day at the Family House and had daily structured conversations starting by identifying the families' needs. The family's learning process was based on reflective discussions of problems and thoughts as they came up [42, 44]. The

family could reach the diabetes nurse on a mobile phone between 08 am and 10 pm during the stay at the Family House. If families needed to contact health care staff during the night, they could receive advice by phoning the general hospital staff. The child and the child's parents had information meetings with the paediatrician, the dietician and the social worker, according to the Swedish national guidelines for paediatric diabetes [8], at the Children's Hospital.

After discharge, the diabetes nurse made three home or school visits besides the regular diabetes check-up visits. Follow-up for the intervention group was then divided into two groups based on the results of the instrument for identifying psychosocial risk factors. Families with an expected good prognosis received the same follow-up as the control group, that is, the regular follow-up. Families assessed to have an increased need for support were offered one home or school visit every month by the diabetes nurse over and above the regular diabetes check-up visits every third or fourth month. All families in the intervention group had accessibility to telephone support during the follow-up by mobile phone to the diabetes nurse, seven days a week.

### Outcome Measurements

The hypothesis was improved metabolic control for children in families having received hospital-based home care, compared to children in families having received traditional hospital-based care. The primary outcome was metabolic control measured by HbA1c 6, 12 and 24 months after diagnosis, self-monitoring of blood-glucose (SMBG) and acute complications during the 24-month follow-up. Secondary outcomes were set to evaluate general stressors and specific stressors for the child and for the family caused by the child's illness. A time axis of the trial and the follow-up is shown in Fig. (2). Outcomes included extensive data from valid and reliable instruments, collected at the time of discharge and at 6, 12 and 24 months after inclusion for assessing the effectiveness, cost-effectiveness and understanding of the change process. Children filled in the forms when they were relevant for their age and were assisted by a research assistant if needed. The instruments used in the trial are shown in Table I. Child general outcome included background variables and PedsQL™ Generic Core Scales Child self-report [50-53], measuring generic health related quality of life together with The PedsQL™ 4.0 Generic Core Scales Parent proxy-report scales [51, 53], where parents estimated their child's generic health-related quality of life. The generic core scales were designed to be integrated with disease-specific instruments. Child diabetes specific outcomes included PedsQL™ Diabetes Module [54], measuring diabetes-specific health-related quality of life, both in the form of child self-reports and parent proxy-reports. The child diabetes-specific outcome also included the Diabetes Family Behaviour Scale [55], measuring diabetes-specific family support.

Family outcomes were represented by the parents' answers, and parents filled in the forms independently of each other. It generally took 35-45 minutes to complete the instruments at each follow-up. The family general outcome included background variables, SF 36 Health Utility Index [56-61], measuring parents' health-related quality of life and



**Table 1. Instruments Used in the Trial, what they Measure, who Fills in the Forms and When**

Instrument	Measuring	Child	Parent	Diabetes Team	Follow-Up at
Diabetes Family Behaviour Scale	Diabetes specific family support (Child and Adolescent 8-18 years)	X			After 6, 12 and 24 months
PedsQL Generic Core Scales Child self-report	Generic health related quality of life (Adolescent 13-18 year)	X			After 6, and 24 months
PedsQL Diabetes Module	Diabetes specific health related quality of life (Child 5-7 years and 8-12 years, Adolescent 13-18 years)	X			After 6, 12 and 24 months
Background variables	Include child gender, age and siblings and parental gender, age, education, income, family situation.	X	X		Discharge, after 6, 12 and 24 months
PedsQL Family impact	The disease's impact on family		X		Discharge, after 6, 12 and 24 months
Parents' nearest absence	Parents' and those nearest, absence from work due to the child's diabetes		X		Discharge, after 6, 12 and 24 months
Family climate	A list with 85 adjectives where parents' mark at least 15 that best describe their situation		X		Discharge, after 6, 12 and 24 months
PedsQL Health Care Satisfaction Generic Module	Parents' satisfaction with health care		X		Discharge, after 6, 12 and 24 months
SF 36 Health Utility Index	Parents' health related quality of life		X		Discharge, after 12 and 24 months
Mood Adjective Checklist	38 adjective measuring mood states		X		Discharge, after 12 and 24 months
Diabetes Family Conflict	Diabetes related family conflict		X		After 6, 12 and 24 months
THU-5	Hassles and uplifts in everyday patterns		X		After 6, 12 and 24 months
The PedsQL 4.0 Generic Core Scales	Parent estimate their child's generic health related quality of life (Child 3-12 and Adolescent 13-18 years)		X		After 6 months
PedsQL Diabetes Module	Parent estimate their child's diabetes specific health related quality of life (Child 2-4, 5-7 or 8-12 years, Adolescent 13-18 years)		X		After 6 and 12 and 24 months
Psychosocial Assessment Tool (PAT)	Identifying psychosocial risk			X	Discharge, after 6, 12 and 24 months

Mood Adjective Checklist [62], measuring parents' mood states. The family general outcome also included THU-5 [63], measuring parents' experiences of problems and progress in everyday patterns as well as Family climate [64-66]. Diabetes-specific family outcome was measured by PedsQL™ Family impact [45, 67] and Diabetes Family Conflict [68].

The structure of the organisation was evaluated according to the level of parent's satisfaction with health care using PedsQL™ Health Care Satisfaction Generic Module [53, 69, 70] as well as according to the health care costs. Costs for the use of hospital services were obtained from the hospital's patient administrative system, hospital records and questionnaires. Costs of professionals' time were determined by telephone logging and additional documentation of time spent by team members. Furthermore, information concerning

children's and parents' absenteeism from work and school was collected. Parents' experiences in both control and intervention groups were described in qualitative interviews 8-10 months after diagnosis.

### Blinding

A research assistant who was not involved in the care assessed the outcomes and booked appointments with families outside the hospital to fill in the instruments. It was not possible to do the intervention blinded to either participants or to health care providers, as it was obvious whether the care had been the regular hospital-based care or the hospital-based home care. Families in hospital-based care and in HBHC had, for the most part, contact with different diabetes nurses, while the rest of the diabetes team included the same persons for both groups. The first author was also

the diabetes nurse in the HBHC intervention group. There were four paediatricians at the department unit working with children diagnosed with diabetes. They alternated in taking on new patients and were responsible for the same children from the time of diagnosis onwards. There was one dietician and one social worker in the diabetes team who had contact with all of the families irrespective of the randomisation.

#### Data Analysis Plan

Data will be analysed by using appropriate statistical methods (dependent upon type and variable) for descriptive data as well as multivariate analysis [71]. The relationship between child and family outcomes, and parents' education, income, and family situation will be analysed using descriptive statistics, rang sum test and logistic regression. The HBHC was comprised of different parts and we will not be able to explain a possible effect from a specific part in the programme. However, with the solid theoretical base as to how the intervention might bring about change we can build a cumulative understanding of causal mechanisms. The objective of the cost-effectiveness (CE) analysis is to relate the marginal value of alternative medical interventions in improving health care to the cost of the intervention. Effects on costs will be calculated from both the health sector perspective, where health and quality of life gains will be compared to health sector costs and from a broader societal perspective where parents' days loss of working days are added to the cost [72].

#### DISCUSSION

Even well-defined interventions in health care have inherent complexities that can bedevil the research. With a detailed description of what was intended to be included in the treatment before the trial was carried out and a protocol of what the families actually received during the trial, analysis of which the intended treatment was to be after the close of the trial, is possible [32]. An optimal scientific situation would be to have a sufficient flow of participants to minimise external influences by recruiting children over a long period of time. A protocol of what was intended to be included in the treatment also became important in order to control for the trial not sliding in treatment over time. The treatment protocol was checked regularly by the first author, who was also responsible for the implementation of the survey, as well as two persons responsible for the medical and nursing care in the study. To reduce the risk for nesting in treatment, there were different diabetes nurses in the intervention group and in the control group. Both diabetes nurses had long professional experience with families and children with diabetes. Avoiding nesting between families was facilitated by a limited flow of participants. Most often only one family at a time with a newly diagnosed child was receiving care at the department unit. Furthermore, groups were separated after randomisation by the environment in the hospital-based care and the HBHC. To minimise drop-outs during the follow-up, the person assessing the outcomes offered home visits to families so they could fill in the forms. If the family preferred to meet at the Children's Hospital, arrangement was made to combine the meeting with the child's diabetes check-up visit.

Limitations to this study included sample size and the relatively long period of recruitment. Medical therapies, including nursing, evolve continuously and may affect the routine care given to families during a trial and, at the same time, the trial may affect the procedures of the routine care [35-37]. Even though multi-centre studies would offer other conditions concerning power, a well-conducted one-centre randomised controlled trial is graded to have a high level of evidence by the American Diabetes Association [73].

Which information is shared and how it is received by the families from the point of view of their unique family situation could be important factors affecting the ways in which families manage to achieve the goals for diabetes treatment. The social background of the family has been shown to be one of the most important factors for metabolic control [3, 5-7, 12] and an important goal for research is to identify groups of families who are in particular need of increased support and to tailor this support to their needs [74]. By identifying important ingredients for the child's long-term metabolic control, the intervention can be put into operation in other contexts [30, 31]. In Sweden, there has been a long tradition with hospital-based care when a child is diagnosed with type 1 diabetes and of a diabetes care with high standards [75, 76]. The choice of the Family House rather than actual home-based care was made in order to smoothen the transition to home, as families had indicated that the time after diagnosis was a difficult time for the whole family [16]. The HBHC was still within the recommendations of the Swedish national guidelines for paediatric diabetes [8]. The intervention was designed to be a structured learning process and may in the future be used as home-based care if found to be efficient.

#### CONCLUSION

This study has been designed by using a clear theoretical framework to describe how an intervention might bring about change; it is designed to minimise any threats to validity and provide adequate reporting, which is decisive in order to be able to determine the validity of the results of complex interventions. Childhood diabetes is a chronic condition in which it has been shown that intensive management leads to better outcomes. This intensive management requires families and children to learn to perform multiple daily tasks when the child is diagnosed with type 1 diabetes. Even though intervention in health care is complex with several interacting components with practical and methodological difficulties, there is a need for randomised controlled trials to evaluate and develop better systems for the learning processes of families, leading to long-term improvement in adherence and outcome.

#### ACKNOWLEDGEMENTS

This study was supported by The Swedish Institute for Health Sciences at Lund University, The Faculty of Medicine, Lund University, The Swedish Research Council, The Swedish Diabetes Foundation and The Region of Skåne. The authors are most grateful to Lisbeth Jönsson, RN, RSCN, for the collecting of outcomes. We wish to thank the diabetes team and health care professionals at the paediatric department. Thanks also to Carina Wittström and the staff at the Family House for their support and for always finding

room for the families. We are also very much obliged to the families who participated in the study.

### CONFLICT OF INTEREST

None declared.

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Received: July 18, 2011

Revised: September 23, 2011

Accepted: September 28, 2011

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**Avhandlingar i ämnet vårdvetenskap med inriktning omvårdnad vid forskargruppen; Barns och familjers hälsa & reproduktiv hälsa, Institutionen för hälsa, vård och samhälle, Medicinska fakulteten, Lunds universitet.**

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Ovanstående kan rekvireras från:

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