Transition From Childhood to Adult Care in Patients with Type 1 Diabetes: 20 Years of Experience From the Tübinger Transition Study

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ABSTRACT

Aims Transition from pediatric to adult care is difficult for patients with chronic diseases. In this study, factors associated with metabolic control in childhood-onset type 1 diabetes (T1D) after transfer to adult care were analyzed.

Methods Overall, 224 persons with T1D were contacted yearly from 1998 to 2019. They voluntarily answered a questionnaire about their current hemoglobin A1c (HbA1c) levels, diabetes-associated complications, kind of care, living conditions, and family situation. Then, mixed longitudinal-cross-sectional analyses were carried out.

Results Overall, 190 patients answered at least once (mean age: 26.6 years). Diabetes complications were mentioned by 10 patients (5 microalbuminuria, 5 retinopathy). Most patients (92.6 %) were in diabetes-specific care during the first year after transfer, with a trend to leave diabetes-specific care during the observation period. Patients in diabetes-specific care displayed lower HbA1c levels (%/mmol/mol) (7.1/54 *vs.* 7.5/58). An important predictor for HbA1c after transfer was HbA1c during the year before transfer ($r = 0.67$, $p < 0.001$). Patients living alone showed no difference in HbA1c levels from those living with their parents. Married patients had lower HbA1c levels (7.0/53 *vs.* 7.3/56, $p < 0.05$) than unmarried ones. Patients with children (15.8 %) presented lower HbA1c levels (6.9/52 *vs.* 7.3/56, $p < 0.01$) than those without.

Conclusions Good metabolic results are favored in patients followed-up in specialized care, are married, and are parents. We recommend transfer to a diabetologist with experience in T1D at an individual age.

Introduction

Transition is the purposeful, planned transition of adolescents and young adults with chronic impairments from child-centered to adult-centered healthcare, with the goal of providing coordinated, uninterrupted healthcare. In contrast, a transfer is a one-time event that describes the direct handover of the patient from pediatrics to adult medicine [1]. In the German healthcare system, children and adolescents up to the age of 21 years may be cared for by pediatricians. Independent of these regulations by law, patients with chronic diseases often change their caring doctor at the age of 16 to about 21 years. For the care of children and adults with diabetes, this means that there are pediatric diabetologists (mostly associated with a hospital-associated outpatient clinic), several resident adult diabetologists, and some hospital-associated outpatient clinics for adults with diabetes. In Germany, all people with diabetes have the opportunity to be cared for by a diabetologist, regardless of their socio-economic status.

The transition from pediatric to adult care is a difficult process in patients with chronic diseases [2, 3]. This happens in a period when patients are confronted with numerous other challenges, such as the occurrence of somatic modifications. Puberty ceases, growth stops, and there are changes in the social environment,

such as the transition between high school and the beginning of job training or academic studies, often accompanied by a change in the place of residence and living conditions. For people with type 1 diabetes mellitus (T1D), a stable and structured environment contributes to satisfying metabolic control. This is why patients with chronic diseases, including those with T1D, need preparation to anticipate this process and a structured transfer to adult care [4]. The ISPAD-guidelines state that a specifically utilizing care coordinator or patient navigator, can enhance post-transition clinic attendance and engagement [5]. Disease-specific training is recommended in the German guideline on transition [1]. In our diabetes outpatient clinic, we prepare patients for transfer with targeted training (e. g., driver's license training, alcohol training, nutrition training). We transfer the adolescent by mutual agreement when life circumstances have stabilized or the patient requests it. The following criteria should be met for the patient to be transferred: adequate independent diabetes management, disease awareness, and stable metabolic control. The aim of this study was to identify factors positively associated with metabolic control after transfer to adult care. We, therefore, analyzed data of patients transferred to adult care from pediatric diabetology care. Patients were followed-up for 20 years after the transfer. We studied the kind of adult care, metabolic results, possible diabetes-associated complications, and other factors associated with the metabolic results, like family status, parenthood, or living situation.

Methods

Population

People with T1D were prepared by implementing a semi-structured program for the transfer process, as described in the introduction. A first appointment with an adult diabetologist was also mandatory. Thereafter, they had their last appointment in pediatric diabetology. All patients transferred between 1998 and 2019 were regularly contacted yearly by mail and were asked to complete a short questionnaire. The transfer was either initiated by the patient or the pediatric diabetologist or both, considering individual wishes and needs. The transfer was done by mutual agreement. The underlying procedure changed only minimally during the 20 investigated years. E.g., after 10 years, we decided to more strongly recommend further care by a specialized diabetologist.

Questionnaire assessment

The patients were asked to answer questions on a voluntary basis about their current hemoglobin A1c (HbA1c) levels, height, weight, type of care (diabetologist, hospital-associated outpatient clinic, or non-diabetes-specific care), frequency of appointments with the doctor, changes in diabetes management, eye status (diabetic retinopathy), microalbuminuria status, hospitalizations, diabetes-associated emergencies (hypoglycemia and ketoacidosis), living conditions (alone, with parents, or with family), and family status (marital status and number of children). We analyzed the data in a mixed cross-sectional-longitudinal manner. The following baseline characteristics were collected at transfer from patients records: diabetes duration, latest three HbA1c values in the year before being transferred to adult care, kind of treatment, and diabetes management (information and communication technology, ICT *vs.* continuous subcutaneous insulin infusion (CSII), or use of continuous glucose monitoring (CGM)), and the existence of a diabetes-associated complication (microalbuminuria, retinopathy, etc.). The ethics committee of our institution approved the structured analysis of the above-mentioned data (approval no. 592/2019BO2).

Data analysis

The presented data were extracted from 956 answered questionnaires sent back to us between 1998 and 2019. Mean and standard deviation (SD) were used to describe the characteristics. Linear Mixed Effect Models (LMEM) were used to analyze potential associations between HbA1c levels and other factors. For this analysis, the reported HbA1c values were winsorized to reach normal distribution without loss of data [6], and HbA1c was used as the dependent variable. We used patient ID as a random effect in the models to consider the repeated measures aspect of the data. The independent variables were therapy type (ICT or CSII) and kind of care (diabetologist or not), as well as interdependent variables, including time elapsed after transfer, age, and diabetes duration. Group or in-group differences were assessed using Student's t-test if the variables were normally distributed. Otherwise, the Kruskal-Wallis test was used. Analyses were done with the statistics program JMP 15.2.0. Sometimes, data were lacking because patients did not respond to all questions; therefore, the number of analyzed datasets is reported for each parameter. This is especially important if percentages are shown. Longitudinal analyses were performed in subgroups of patients who answered more questionnaires during a predefined time-period of 5 years. In this case, the number of analyzed patients is shown in the results section.

Results

Questionnaire response rate and population characteristics

A total of 190 out of 224 patients (84.8 %) answered the questionnaire at least once between 1998 and 2019, and the annual response rate was 40 to 50 %. Mean age when the questionnaire was completed was 26.6 ± 4.5 years (median: 25.9 years, range: from 17.0 to 42.0 years).

The maximum of completed questionnaires was 15, and the minimum was 1. The mean observation time was 7.1 ± 5.1 years with a maximum of 20.7 years after transfer in one patient. Three patients answered after 20 years. The observation period was a minimum of 5 years for 51.3 %, 10 years for 30.4 %, and 15 years for 10.3 % of patients who answered. As it was voluntary to fill out the questionnaire, some patients did not answer every year. The characteristics of the patient group who answered at least once and those of the group who did not answer at all are compared in ▶ **Table 1**.

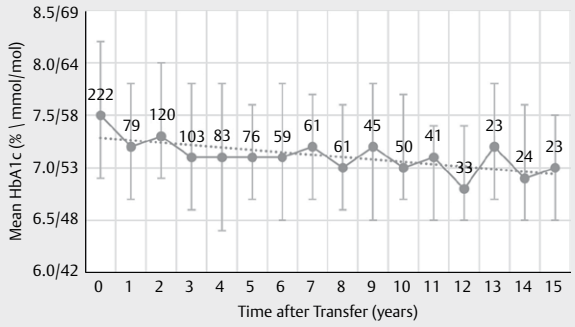
Diabetes-associated complications and HbA1c

During the 20-year observation period, 10 patients out of 163 (6.1 %) reported diabetes-associated complications (microalbuminuria (n = 5) and retinopathy (n = 5)). However, 27 patients omitted responding to this question. Patients who reported diabetes-asso-

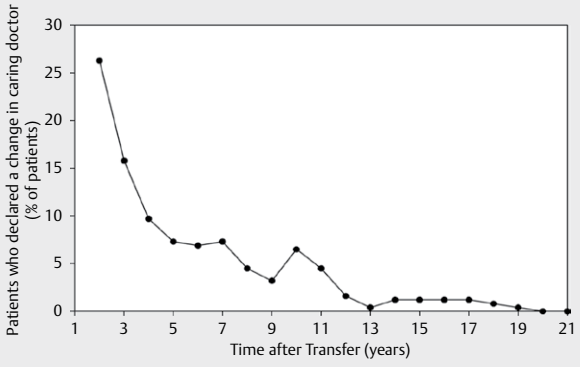
▶ **Table 1** Baseline characteristics at the time of transfer of patients who answered compared with patients who were lost to follow-up

	Patients who answered Mean ± SD (n = 190)	Patients lost to follow-up Mean ± SD (n = 34)
Gender f/m (%)	47.9/52.1	38.2/61.8
Duration since diabetes onset (years)	11.3 ± 4.3	10.7 ± 4.2
Age (years)	21.2 ± 2.5	20.5 ± 2.0
Height (cm)	173.1 ± 9.0	174.0 ± 10.6
Weight (kg)	72.7 ± 12.7	76.0 ± 12.5
BMI (kg/m^2)	24.2 ± 3.7	25.0 ± 3.3
Number of patients with diabetes-associated complications	2 out of 190	1 out of 34
Type of therapy (ICT/CSII)	62.5/37.5	97.1/2.9*
HbA1c level (%)	7.6 ± 1.1	8.4 ± 1.5*
HbA1c level (mmol/mol)	59 ± 12	69 ± 16*

BMI: body mass index, CSII: continuous subcutaneous insulin infusion, f: female, ICT: intensive conventional therapy, SD: standard deviation. m: male. *p < 0.05 significant difference compared with patients who answered.



▶ **Fig. 1** Median HbA1c levels evolution after transfer from pediatric to adult care. The year 0 represents the HbA1c at the time of transfer. The value above each dot represents the number of reported HbA1c values at the time-point after transfer. HbA1c: hemoglobin A1c.



▶ **Fig. 2** Percentage of patients who declared a change in caring doctor during 20 years after transfer from pediatric to adult care.

ciated complications presented higher HbA1c levels before transfer (8.2 ± 1.6 %, 66 ± 17 mmol/mol) compared to those who did not report diabetes complications (7.9 ± 1.2 %, 63 ± 13 mmol/mol). The difference was not statistically significant, as well as for the comparison after the transfer (8.3 ± 0.7 %, 67 ± 8 mmol/mol *vs.* 7.9 ± 1.0 %, 63 ± 11 mmol/mol). The most important predictor for HbA1c levels after transfer was HbA1c levels in the year before transfer (r = 0.67, p < 0.0001; calculated in a subgroup with values before transfer and from 2 to 6 years after transfer (n = 47)).

Evolution of HbA1c levels

With increasing time after transfer and thus increasing age, the HbA1c level decreases (LMEM for time after transfer; $R^2 = 0.68$, estimate –0.03, p < 0.0001). The effects of age and diabetes duration are not shown because these parameters depend on each other (▶ **Fig. 1**).

LMEM analysis showed that the decrease in HbA1c levels is independent of the insulin administration type (ICT *vs.* CSII), kind of care (non-diabetes-specific care *vs.* diabetologist), changes in doctor, and changes in treatment (change in type of insulin, new use of a CSII or a CGM system). The LMEMs carried out with these parameters show no associations. In addition, we found no difference in HbA1c levels between patients who used CGM or CSII and patients who did not.

Diabetes care type after the transition

Patients were transferred to 133 different healthcare institutions (diabetologists in an outpatient clinic or as residents, to a general practitioner, Internal specialist not specialised in diabetes, etc.) After the transfer, most patients were followed-up by specialized diabetologists (92.6 % during the first year after the transfer), but we observed a trend of leaving diabetes-specific care in favor of non-diabetes-specific care. After 15 years, only 78.2 % of patients indicated being in specialized care. There was no difference in HbA1c levels between patients followed-up in hospital-associated diabetes-specific outpatient clinics and those followed-up by resident diabetologists. Patients who were not in diabetes-specific care presented significantly higher HbA1c levels than the other patients (7.5 ± 1.1 %, 58 ± 12 mmol/mol *vs.* 7.1 ± 0.8 %, 54 ± 9 mmol/mol, p < 0.01).

A change of caring doctor was mentioned by 41.2 % of patients at least once, 26.3 % during the second year, 15.8 % during the third, and 9.7 % during the fourth year after the transfer (▶ **Fig. 2**). After the fifth year, only a few patients reported this change. The frequency of caring doctor change did not correlate with HbA1c levels (r = 0.0135, p = 0.8828).

Inpatient stay

Fifty-one patients (26.8 % of all patients who answered a questionnaire) reported at least one inpatient stay in the context of diabetes during the observation period. This represented a total of 80

inpatient stays during the observation period: one inpatient stay was reported by 34 patients, two stays by 9 patients, three stays by 7 patients, and seven stays by 1 patient. These patients presented significantly higher HbA1c levels in the year they were hospitalized compared with patients with no inpatient stay (7.6 ± 1.0 %, 60 ± 11 mmol/mol *vs.* 7.2 ± 0.8 %, 55 ± 9 mmol/mol, p < 0.001). In the patient group with an inpatient stay, 11 underwent an emergency hospitalization required due to severe hypoglycemia or ketoacidosis. This subgroup of patients also had higher HbA1c levels than those who did not require inpatient stay (7.7 ± 0.9 %, 61 ± 10 mmol/mol *vs.* 7.2 ± 0.8 %, 55 ± 9 mmol/mol, p < 0.05). There was no significant difference between patients hospitalized for optimization of metabolism or education and those with inpatient stays because of an emergency. Patients followed-up by a hospital-associated diabetes-specific outpatient clinic more often notified inpatient stays for education and optimization of metabolism than those followed-up by a resident diabetologist (21.8 % *vs.* 3.0 %). Those in non-diabetic specific care were in-between, with a value of 12.9 %.

Family status and living situation

Overall, during the entire observation period, 21.6 % (41/190) of patients reported they were still living at their parent's house at questionnaire completion. HbA1c levels reported by patients living alone were not significantly different compared with those still living with their parents (▶ **Table 2**).

During the observation period, 24.2 % (46/190) of patients got married. No patient was married at the time of transfer. Likewise, the HbA1c levels of married patients did not significantly differ from those who were not married at the time of transfer; however, married patients reported lower HbA1c levels during the observation period following transfer than those who were single (▶ **Table 2**). Out of 190 patients, 30 (15.8 %) reported that they became parents during the observation period. Those who became parents had lower HbA1c levels in comparison with those who had no children (▶ **Table 2**). Patients who became parents at the time of transfer presented with higher HbA1c levels compared to after becoming parents (7.5 ± 0.9 %, 58 ± 10 mmol/mol *vs.* 6.9 ± 0.7 %, 52 ± 8 mmol/mol, p < 0.05). During the observation period, 16 % (15/94) of female patients reported becoming mothers. They showed lower HbA1c levels than the other women (▶ **Table 2**). Interestingly, women reported lower HbA1c levels during the year(s) when they were pregnant compared to periods when they were not (▶ **Table 2**). The analysis with mixed linear models showed that age has only a small impact on the differences in HbA1c related to marital status and the presence of children. But the lower HbA1c value is mainly due to the women with T1D and children.

Discussion

The present study analyzed the disease course and factors associated with metabolic control in a representative cohort of young adults with childhood-onset T1D followed-up in a specialized pediatric diabetes center in Germany and then transferred to adult health service. The observation period covered 20 years. In contrast to previous studies that analyzed the outcome of structured transition programs in shorter periods of up to 3 years [7–11], we described the impact of an everyday transition process implemented by a pediatric diabetes center. With a response rate of almost 85 % (190/224 patients returning at least one questionnaire), our results offer a good overview of the evolution of people with T1D after the transfer to adult health services in Germany.

Patients who did not answer might have developed diabetes associated complications much earlier, such as retinopathy, nephropathy, neuropathy, and other micro- or macrovascular diabetes associated problems. This would also explain our finding that only 10 patients who completed the questionnaire developed diabetes associated complications. Thus, the number of diabetes complications determined in our analysis may be an underestimate; for example, some patients do not want to acknowledge their complications. However, unlike the studies of Bryden et al. [12] and Carlsen et al. [13], in which diabetes-associated complications were found in up to 37 % of the study population, our cohort displayed lower HbA1c levels at baseline and during follow-up; their baseline HbA1c levels were similar to that of our patients who did not answer. Carlsen et al. used a population-based approach with a relatively high questionnaire completion rate, while Bryden et al. had an incomplete follow-up. The rate of acute events (hypoglycemia, ketoacidosis) in the studied cohort is lower than in a published cohort of patients who underwent transfer in Germany [14]. This could be

▶ **Table 2** HbA1c levels in patients with T1D who are living with their parents, marrying, and becoming parents, at and after transfer to adult care, compared to those who are not.

HbA1c		**Yes**				**no**				
		%		**mmol/mol**		**%**		**mmol/mol**		
		mean	**SD**	**mean**	**SD**	**mean**	**SD**	**mean**	**SD**	**p**
Living at Parents	After Transfer	7.2	0.9	55	10	7.2	0.9	55	10	n.s
Married	At Transfer	7.5	1.0	58	11	7.6	1.1	60	12	n.s
	After Transfer	7.0	0.8	53	9	7.3	0.9	56	10	<0.05
With Children	At Transfer	7.5	0.9	58	10	7.6	1.1	60	12	n.s
	After Transfer	6.9	0.7	52	8	7.3	0.9	55	10	<0.05
Women with Children		6.6	0.6	49	7	7.4	0.9	57	10	<0.05
Women in the year of Pregnancy		6.4	0.7	46	8	7.3	0.9	56	10	<0.05
SD: standard deviation.										

due to incomplete reported events in the presented study and the difference in the age range of the study population.

Our results showed that good metabolic control in the years before transfer was the most important predictor for a good metabolic outcome during adult life. A reason for this association could be that patients with good diabetes control before transfer are better structured, and that those with poor diabetes control had management problems before and after the transfer. A structured preparation for the transfer is, therefore, mandatory. Guidelines state that "The patient education is an integral component of the therapy. Without appropriately coordinated medical treatment, it is not successful" [15, 16], and educational sessions should be provided by an interdisciplinary diabetes team with sufficient knowledge about age-specific needs [17–20]. This should be a continuous process that will be successful only if repeated, need-based, and offered during long-term care [21].

Interestingly, about 40 % of patients noted a change in the medical institution, sometimes up to three times, in the first 4 to 5 years after the transfer. Our results are in accordance with those from other investigators. Busse et al. [7] and Neu et al. [22] found that about 50 % of patients had changed caring institutions at least once after the transfer. We think that the trend to leave diabetes-specific care is critical and could be due, among other things, to the fact that adults with T1D are only a minority in some adult healthcare institutions. On the other hand, almost 80 % remain in specialized care after 15 years. Additional information that could be added as free text in the questionnaires indicate that the needs of adults with T1D are not always met in some diabetes-specific adult healthcare institutions. Another reason could be that patients feel that their knowledge of managing their diabetes is sufficient and that they do not need the advice of a specialist anymore. This is somehow a critical and maybe false idea because diabetes management has changed a lot in the last years, such as new CSII systems, automated insulin delivery (AID) systems, new CGM systems, new pens, etc. These developments are a challenge for specialized diabetologists; therefore, general practitioners would be less likely to know all these new developments. Auzanneau et al. [23] and Tauschmann et al. [24] concluded that the use of the new CSII and AID systems has positive effects on ketoacidosis, hypoglycemia rate, and hospitalization of T1D patients. Thus, specialized care is essential for adults with T1D, which could result in more patients staying in diabetes-specific care. We found no difference in metabolic control in patients using CSII or ICT, whereas previous studies found a superiority of CSII [25, 26]. The conflicting results between our study and previous studies could be because we present only a very selective sample of patients. But the data from the German Diabetes Patient History Documentation Registry (DPV) confirm our observation of adults in a real-life setting [27].

Married patients and patients with children displayed lower HbA1c levels compared with patients who were single and did not have children. We also found an improvement in HbA1c levels between transfer and when patients got married or became parents. Psychosocial circumstances are well-known to have a deep impact on diabetes control and metabolism. In T1D adolescents [28, 29], for instance, problems with caregivers are among the reasons for bad glycemic control [30, 31]. Moreover, family functioning and quality of life in adolescents with T1D are linked with metabolic outcomes [32, 33]. To this day, family status and its association with metabolic control have not been investigated in adults with T1D. Overall, our findings are consistent with the previous findings in adolescents [34].

Women with T1D displayed lower HbA1c levels during pregnancy. One reason could be that guidelines recommend strict diabetes control during pregnancy, with frequent check-ups and efforts to improve metabolic control [35]. These women might also be more motivated to reach good metabolic results.

The main weakness of this study is the lack of information about the patients who did not answer. These patients had poorer control of metabolism at the time of transfer. Moreover, the information (e. g., HbA1c, diabetes-related macrovascular and microvascular complications) given by the patients could not be verified independently and were sometimes incomplete, even though we believe in the honesty of our patients. Hence, the data on diabetes complications and HbA1c must be viewed with caution, as patients may not be aware of what complications they actually have and may remember the HbA1c better than it actually was.

The main strengths of the study are the long observation period and our sample size, allowing the data analysis from 190 patients with T1D transferred from one pediatric diabetes center to adult care.

Taken together, we observed that stabilization of psychosocial circumstances (marriage and parenthood) positively influenced metabolic control. To conclude, disease specific care after transfer and good preparation of patients before the transfer is the most important requirements for good diabetes control after transfer from specialized pediatric care to adult healthcare institutions. In this context, we recommend the transfer to an adult diabetologist with experience in T1D on an individual basis, at an idividual age, and when living circumstances have stabilized.

Author Contributions

Roland Schweizer: study conception, data analysis, manuscript preparation, literature study, discussion; Martina Lösch-Binder: study conception, patient recruitment, data management; Clara Hayn: data collection, conception of data analysis, data evaluation, literature study; Silas Friz: patient recruitment, data collection, concept for data analysis, data evaluation; Julia Uber: study conception, discussion; Julian Ziegler and Franziska Liebrich: study conception, discussion; Andreas Neu: study conception, manuscript preparation, discussion, supervision.

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Novelty Statement

There are several short-term studies describing the impact of a structured transition process in childhood-onset Type 1 diabetes (T1D) on metabolic control. The studies did not describe long-term outcomes. We, in our study for the first time, describe the impact of an everyday transition process in one pediatric diabetes center

on long-term (up to 20 years) metabolic control. For the first time, we could show that metabolic result (HbA1c) is positively associated with HbA1c before the transfer, specialized care, marriage, own children, and pregnancy after the transition to adult care in childhood-onset T1D.

Ethics Approval Statement

The Ethics Committee of the University Hospital, Tübingen, approved the structured analysis of the data (approval n °592/2019BO2).

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Conflict of Interest

The authors declare that they have no conflict of interest.

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