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RUNNING TITLE: Explaining Centre Differences in HbA1c

Targets and Teamwork: Understanding Differences in Paediatric Diabetes Centres Treatment Outcomes.

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Abstract

Objective: The reason for center differences in metabolic control of childhood diabetes is still unknown. We sought to determine to what extent the targets, expectations, and goals that diabetes care professionals have for their patients is a determinant of center differences in metabolic outcomes.

Research Design and Methods: Children, under the age of 11 with type 1 diabetes and their parents treated at the study centers participated. Clinical, medical, and demographic data were obtained, along with blood sample for centralized assay. Parents and all members of the diabetes care team completed questionnaires on treatment targets for HbA1c and recommended frequency of blood glucose monitoring.

Results: 1113 (53% male) children (mean age 8.0 ± 2.1 years) from 18 centers in 17 countries, along with parents and 113 health care professionals, participated. There were substantial differences in mean HbA1c between centers ranging from 7.3% ± 0.8 (53mmol/mol ± 8.7) to 8.9% ± 1.1 (74 mmol/mol ±12.0). Centers with lower mean HbA1c had 1) parents who reported lower

targets for their children, 2) health care professionals that reported lower targets and more frequent testing, and 3) teams with less disagreement about recommended targets. Multiple regression analysis indicated that teams reporting higher HbA1c targets and more target disagreement had parents reporting higher treatment targets. This seemed to partially account for center differences in Hb1Ac.

Conclusions: The diabetes care teams' cohesiveness and perspectives on treatment targets, expectations, and recommendations have an influence on parental targets, contributing to the differences in pediatric diabetes center outcomes.

The primary goal of diabetes care is to optimize the health and well-being of individuals with diabetes. This is achieved by providing evidenced based recommendations for diabetes treatment and self-management, tailored to the individual's physiological and psycho-social status. Through a range of 1:1 and group programs, the diabetes teams seek to inform, support, and enable individuals to manage their blood glucose to as near as normal levels as possible, without detrimental effects to their quality of life and acute complications of insulin treatment. However, not all diabetes care teams are equal, with several research groups demonstrating substantial differences between pediatric diabetes care teams(1-4). The Hvidoere Childhood Diabetes Study Group (HSG) was the first to report the scale of these differences between pediatric diabetes centers worldwide (4-7). The HSG has shown these center differences persist over extended periods(5-7), despite attempts to improve outcomes(6), and that these differences are not accounted for by difference in insulin treatment regimens used(4-7), differences in dietary and activity lifestyles(8), differences in family and cultural contexts(9), or differences in demographics(4-7).

To date, the only factor that has been shown to contribute to differences in center outcomes is differences in the goals or targets for HbA1c between centers (10). Differences in treatment targets, as expressed in care guidelines, was also thought to be an important factor when comparing differences between German and US pediatric diabetes care outcomes(3). Further, clarifying, renewing, and communicating treatment guidelines was also thought to be a key strategy to improving outcomes in Swedish pediatric diabetes centers (1). However, to our knowledge, there has been no published replication of the hypothesis that team treatment targets are different between pediatric diabetes centers, and that these differences are partly accountable for the differences in outcomes for children and adolescents. Thus, as part of the 2014 HSG study (7), we sought to replicate our previous findings on the role of treatment targets in determining the outcomes of care for children with type 1 diabetes.

Research Design and Methods

All children with type 1 diabetes below 11 years of age and with diabetes duration of at least 1 year, treated at the participating centers were invited to participate. In centers with more than 200 children in the age range, only those seen by the member of the Hvidoere Study Group were invited. For all children, Clinical Record Forms (CRFs), including questions on clinical characteristics, treatment, and acute complications, were collected. Questions on language difficulties with the parents or the children were included to obtain some insight into possible minority groups within the centers. Socio-economic status was estimated through use of a three item (car ownership, bedroom occupancy, holiday) Family Affluence Scale(11). A centralized HbA1c measurement was performed by the TOSOH® liquid chromatography (DCCT aligned, normal range: 4.4–6.3%; IFFC: 25–45 mmol/mmol).

The parents completed a comprehensive questionnaire that included two specific questions about goals or targets of diabetes care: 'The next questions are about the long term glucose test, HbA1c. What do you think the ideal result should be?' and 'What result would you be happy with today?'. The items both had 5 response options: 1) less than 7.0, 2) between 7.0 and 7.4, 3) between 7.5 and 8.0, 4) between 8.1 and 9.0%, and 5) don't know.

All health care professionals within each diabetes team completed a questionnaire separately and independently, which included three items about treatment targets: 'What do you consider as the most realistic and practical targets for HbA1c?'; "What do you consider the ideal target for HbA1c?", and "How often do you recommend that young people measure their blood glucose levels during the day?". For the question on HbA1c, team members were invited to give their responses for three age groups: 0–5, 6–10, and 11–18 years, with five response options available (<7.0; 7.0–7.4; 7.5–7.9; 8.0–9.0%, or no specific target). As the majority of the patient sample in this study was between 6-10 years of age, we have used the responses for this category only.

Data Analysis

Data were all double entered at a central administration center. Ambiguous data on the CRF were resolved by direct contact with participating centers. We used the target for the 6-11 age group for the whole data set, as there were insufficient numbers (n=200) distributed in the 0-5 age group to split the sample and run analysis in both groups. Analysis was run separately with the 0-5 individuals in and out of the analysis, with no meaningful differences so the whole sample analysis is reported. A measure of team congruency was generated on an item by item basis, with the number of different responses given by individuals from any one of the team recorded. The team target was generated by using the modal answer. Where the answer was bimodal or nearly bimodal

(2 items with more than 40% responses within a team), then we created a mid-point category. Two composite measures were generated, the first being the sum of the number of different answers to the questions, and the second being this sum score divided by the number of team members. We also created interaction terms for team target by team agreement for each of the three items.

All analysis was undertaken using IBM SPSS v22. All correlations were undertaken using Spearman's rho correlation coefficient, and non-parametric tests of differences were completed using chi-square and Kruskal-Wallis. Where the dependent variable was HbA1c, which was normally distributed, analysis of variance was used, controlling for demographic and clinical characteristics. Regression analysis was undertaken using stepwise entry, with criteria of inclusion at $p<.05$.

Results

Details of the children and parent sample characteristics have been previously published elsewhere (7). In summary, there were 1113 child participants from 18 centers across 17 countries. There were slightly more male children (53%) who were a mean age of 8.0 ± 2.1 years. Just under half of the children (49.7%) were on intensive insulin regimens (infusion pump or basal bolus), with a mean HbA1c of 8.0±1.0 % (±SD). As previously reported, there were substantial and significant differences, after controlling for covariates, between centers on the primary metabolic marker of HbA1c ($F = 4.04$: $df = 17$: $p < .001$; $\eta^2 = .187$), with the center mean HbA1c ranging from a mean of 7.3% ± 0.8 (53mmol/mol ± 8.7) to 8.9% ± 1.1 (74 mmol/mol ±12.0). Five centers had a mean HbA1c significantly below the sample mean, and four centers had a HbA1c mean significantly above the mean for the sample; see Figure 1.

INSERT FIGURE 1 ABOUT HERE

Parents reports of ideal target for HbA1c and what result they would be happy with were highly correlated ($r = 0.58$; $p < .001$). Responses to both ideal and happy with items were unrelated to family affluence, gender, age, or duration of diabetes. The lower parents reported the ideal result to be, and the lower the results they would be happy with, the lower the child's HbA1c ($F = 31.3$; $df = 4$; $p < .001$; $F = 82.8$; $df = 4$; $p < .001$), with and without controlling for age, duration, gender, and affluence. There was significant variation between centers for both ideal HbA1c ($Ç2 = 191.599$; $df = 17$; $p < .001$) and result they would be happy with ($Ç2 = 270.909$; $df = 17$; $p < .001$). Examination of the distribution of responses indicates that centers with higher mean HbA1c have more parents endorsing higher ideal targets and higher results that they would be happy with (see Table 1), with centre rank correlated with both ideal and happy with responses ($r = 0.37$; $r = 0.34$ $p < .001$). Parent responses to both the ideal HbA1c and HbA1c result they would be happy with items showed linear associations with HbA1c (ideal $F=6.43$; $df =4$; $p < .001$; happy with $F = 4.69$; $df = 4$; $p = .001$), with these effects remaining after controlling for age, gender, affluence, and duration of diabetes.

INSERT TABLE 1 ABOUT HERE

A total of 113 health professionals completed questionnaires from the 18 participating centers, with 49% being physicians, 27% nurses, 12% dietitians, 5% psychologist or psychiatrists, and 4% social workers. The diabetes care teams varied substantially in size from one respondent to 10 respondents, but there was no association between team size and the centers mean HbA1c

(F=8.3; df = 9, p > .95). There were significant differences between centers in how team members responded to the realistic target for HbA1c (Ç2 = 59.03; df = 17; p<.001), ideal target for HbA1c (Ç2 = 57.2; df = 17; p<.001), and number of blood glucose tests recommended (Ç2 = 67.3; df = 17; p<.001). The higher the targets for HbAc1 (realistic r = .57; ideal r = .51) and the less frequently they recommended blood glucose tests (r=.46), the higher the centers rank according to participants HbA1c (see Table 2).

INSERT TABLE 2 ABOUT HERE

Examination of Table 2 also indicates that diabetes care professionals did not always agree with one another on the targets and recommendations, and these differences were significant (Ç2 > 112; df = 17; p<.001) for all three variables. Follow-up analysis indicates that the higher the centers rank, according to their mean HbA1c, the more disagreement there was in team members' responses (realistic r = .38; ideal r = .34). The size of the team was unrelated to levels of agreement for realistic or ideal HbA1c, but larger teams reported more disagreement on the number of recommended blood glucose tests (r = .53; p <.001).

Parent reported ideal HbA1c correlated with team ideal HbA1c (r= .35, p<.001), and parent report of HbA1c result they would be happy with was correlated with team realistic HbA1c (r = .37, p <.001). In addition, the greater the number of different answers given by a team, the higher both the ideal HbA1c and that which they would be happy with was reported by parents (ideal r = .21, happy with r = .22, p<.001).

Given the association between teams' treatment targets and agreement and the center rank, these variables were examined as potential determinants of center differences in HbA1c. Using a general linear model, controlling for participant age, gender, duration, and affluence, the diabetes teams reported ideal HbA1c ($F= 28.67$, $p <.001$), reported realistic HbA1c ($F= 33.90$; $p< .001$), and team recommended number of blood tests ($F=28.54$; $p<.001$) were all associated with participant HbA1c. In addition, the number of different answers given for ideal HbA1c ($F= 26.5$, $p<.001$), number of different answers for realistic HbA1c ($F=39.36$, $p < .001$), number of different answers for recommended number of blood glucose tests ($F = 9.98$; $p<.001$), total number of different answers given to the three questions within a team ($F = 19.64$, $p<.001$), and the total number of answers divided by the number of staff ($F = 14.93$, $p<.001$) were all associated with participant HbA1c.

Therefore, we sought to determine to what extent differences in team targets and disagreement within a team accounted for center differences in HbA1c, and to what extent this relationship was mediated by parent targets. With individual HbA1c as the dependent variable, using stepwise entry, age, gender, duration of diabetes, affluence, insulin regimen, and center rank were entered in a regression analysis on step 1; the team target, disagreement measure, and interaction terms (target by agreement) were entered on step 2, and parent targets were entered on step 3 (see Table 3). This analysis indicates that after controlling for co-variates, the interaction term for the team ideal HbA1c by number of answers was significantly predictive of HbA1c, and that this had a small mediating effect on center rank as a predictor of HbA1c. However, when the parents' result they would be happy with enters the regression, the effect of the team ideal HbA1c interaction term becomes non-significant, and there is a significant reduction in the beta weight for

center rank. This suggests that parental aspirations of results they would be happy with mediates the association between team target agreement and center outcomes, and partially mediates the effect of center rank.

INSERT TABLE 3 ABOUT HERE

Conclusions

The results of this study demonstrate that pediatric diabetes care teams show substantial variability in their metabolic targets, recommendations, and expectations of parents and children with diabetes. Whilst this study largely replicates our previous exploration of centre differences, this replication has occurred with a number of different centres in this study, using a different age group, and following the development of ISPAD guidelines, which should be informing clinicians clinical practice. This may reflect differences in national guidelines, as highlighted by Maahs and colleagues (3), who concluded that differences in outcomes between the two populations of children is more likely to be a function of different treatment targets, than it is a function of insulin regimens. In addition to substantial variation between diabetes centers, some teams show substantial disagreement between the health care professionals on the targets, expectations, and recommendations they have for the parents and children they are caring for. As in previous work with adolescents, these differences between and within teams may well be a significant contributor to the differences in the outcomes of diabetes care seen between centers. Higher HbA1c targets may be related to fear of hypoglycaemia, however, in a previous Hvidoere international study it was

shown that centers with HbA1c values below the average had fewer severe hypoglaemic events, possibly as a result of better psychological support and education programmes (5).

INSERT TABLE 4 ABOUT HERE

Given many of these centers participated in the previous study that reported on disagreements within diabetes teams about treatment targets, the fact that there is still disagreement is surprising,_see Table 4. For many centres there is little to no change in their teams level of agreements, or changes in the targets they are setting out to achieve._The stability of these disagreements within teams may point to the fact that this question is acting as a marker for a wider team working issue, and that there may be a need to think of the diabetes care team as a clinical microsystem, that is a small, interdependent group of people who work together r to provide care for specific groups of patients. The research literature continues to document the importance of how a clinical microsystem works as a key determinant of outcomes for patients. The importance of examining the clinical microsystem in pediatric diabetes care has been highlighted by Peterson and colleagues (1), who reported on improvements in outcomes for pediatric centers across Sweden. In their analysis, improving communication and teamwork were identified as critical to achieving the improved outcomes between centers. So, investing time and effort into developing effective clinical microsystems may be critical to improving outcomes for children and adolescents with diabetes.

The differences in treatment targets between teams were reflected in the parent reported targets and expectations. Teams that have higher treatment targets, and evidence more disagreement about these targets, also have parents who report higher targets for HbA1c. Furthermore, these parent targets appear to mediate the relationship between team targets and

HbA1c, and partially account for the differences in center outcomes. This replicates previous work by this study group, and work by Clements(12) and Boot(13), that also show parental goals or targets are strong determinants of outcomes. Furthermore, they have shown that parental goals are often discrepant from physician goals. It is important to remember that physicians are only one member of the diabetes team, and not necessarily the one who has the most contact with parents. Clearly, communicating consistently with parents regarding the treatment goals, targets, and expectations is an important part of care and determinant of outcomes for young people with diabetes.

There are of course limitations with the cross-sectional nature of this study, and the ability to draw causal inferences from these data. However, the replication of our previous results with a different cohort of participants and their parents, ten years apart, and the consistency of results with other teams, would suggest that the results are robust. Further, the large sample size, both in terms of children and number of centers, add further weight to the importance of these findings, especially in light of the fact that no other variables have been found to explain the differences in center outcomes in this or other study groups.

This study highlights the need to pay more attention to how the diabetes care team works, in addition to considering the interactions within families with diabetes and the insulin regimens and monitoring technology used.

Contributor Statement

Prof Carine de Beaufort is the study Gurantor

TCS, CdB, HH and FC contributed to the study design, collection of data, data analysis and writing of the manuscript. All other authors researched the data, drafted, revised and edited the manuscript.

All participating researchers are named authors of the paper.

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There are no conflicts of interest to declare.

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Figure 1. Mean HbA1c ± 1 Standard Deviation for each Centre

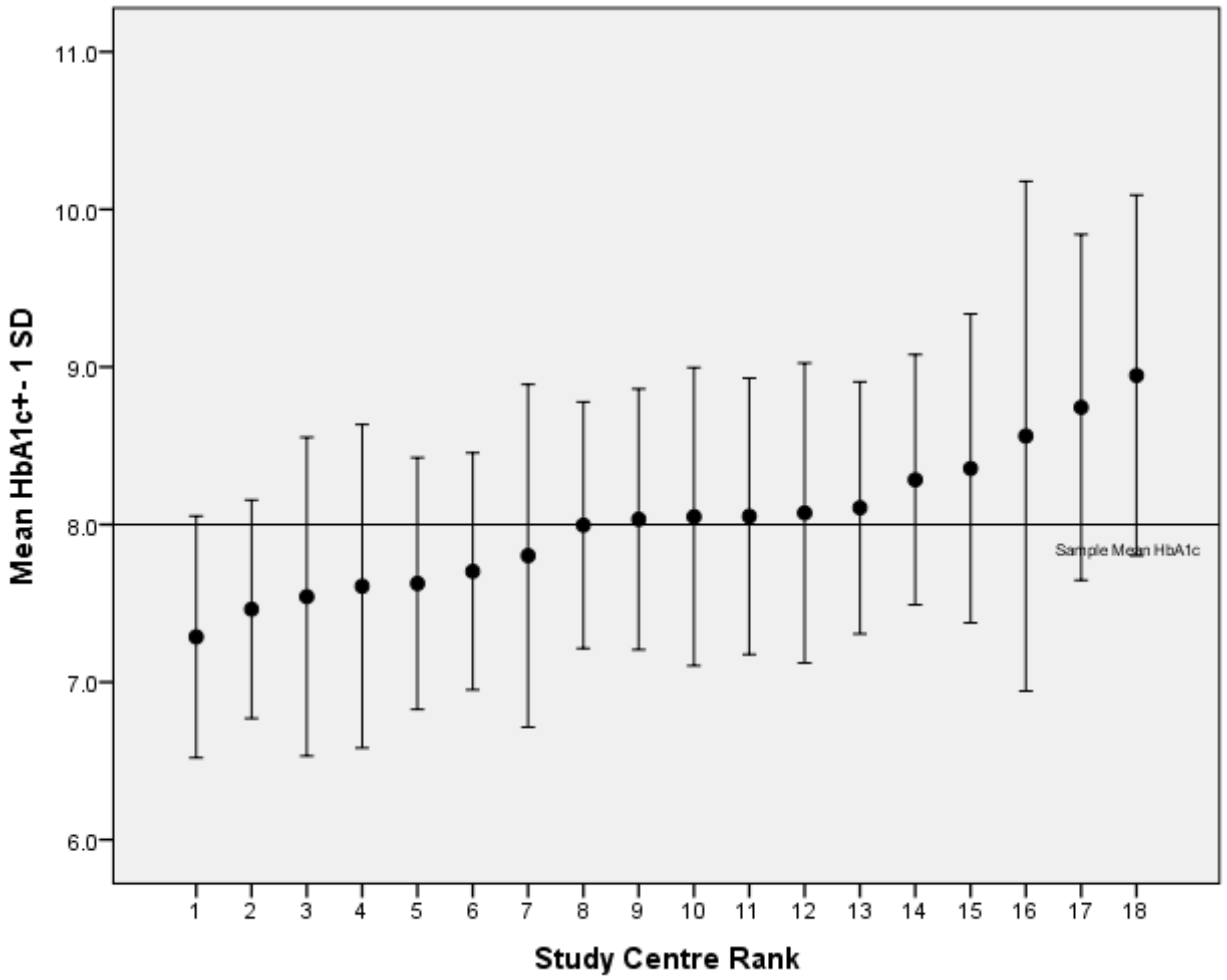

Table 1. Summary of Parents Reported Ideal Target Hab1c and HbA1c Results They Would Be Happy With by Centers According to Mean HbA1c

Centre Groups		Less Than 7.0	7.0 to 7.4	7.5 to 8.0	8.1 to 9.0	Don't Know
Lowest 6	Ideal Result	77.0%	19.6%	1.8%	0.3%	1.3%
Middle 6	Ideal Result	52.8%	34.8%	9.1%	1.9%	1.4%
Highest 6	Ideal Result	39.8%	48.1%	9.4%	0.9%	1.8%
Lowest 6	Happy With	56.5%	33.5%	9.2%	0.5%	0.3%
Middle 6	Happy With	25.8%	46.5%	23.8%	3.6%	0.3%
Highest 6	Happy With	23.0%	41.0%	30.1%	5.6%	0.3%

Table 2. Team Members' Responses to Questions about Realistic and Target HbA1c for Children 6-10 Years of Age

	Realistic HbA1c Target				Ideal HbA1c Target		
Centre Rank	<7.0	7.0-7.4	7.5-7.9		<7.0	7.0-7.4	7.5-7.9
1.00	100.0%				100.0%		
2.00	42.9%	57.1%			87.5%	12.5%	
3.00	50.0%	50.0%			75.0%	25.0%	
4.00		100.0%				100.0%	
5.00		100.0%			87.5%	12.5%	
6.00		100.0%			50.0%	50.0%	
7.00		28.6%	71.4%			100.0%	
8.00		83.3%	16.7%		16.7%	66.7%	16.7%
9.00		50.0%	50.0%		25.0%	75.0%	
10.00		40.0%	60.0%			100.0%	
11.00		55.6%	44.4%			100.0%	
12.00		100.0%				100.0%	
13.00		100.0%				100.0%	
14.00		75.0%	25.0%			100.0%	
15.00		55.6%	44.4%		22.2%	66.7%	11.1%
16.00		66.7%	33.3%		66.7%	33.3%	
17.00			100.0%			50.0%	50.0%

18.00		50.0%	50.0%		37.5%	12.5%	50.0%

Table 3. Multiple Regression Analysis to Predict HbA1c

	Beta	t	Sig.
Step 1			
Centre Rank	.424	15.315	.000
Family Affluence Score	-.115	-4.144	.000
Diabetes Duration	.063	2.268	.024
Step 2			
Centre Rank	.380	10.978	.000
Family Affluence Score	-.118	-4.255	.000
Diabetes Duration	.059	2.143	.032
Team Ideal * Disagreement	.073	2.090	.037
Step 3			
Centre Rank	.256	7.670	.000
Family Affluence Score	-.146	-5.647	.000
Diabetes Duration	.037	1.431	.153
Team Ideal * Disagreement	.057	1.758	.079
Parent HbA1c Happy With	.365	13.158	.000

Table 4. Team Reported Realistic Targets for Centers Participating in 2005 and 2009 Studies

Centre Rank 2005	Centre Rank 2009	<7	7-7.4	7.5-8	8-9	No specific Target	<7	7-7.4	7.5-8	8-9	No specific Target
1		100%					100%				
	1	100%					100%				
2		60%	40%				20%	40%	40%		
	5		100%					100%			
3			100%					100%			
	7		83%	17%				75%	25%		
4			100%					17%	83%		
	4		100%					87%	13%		
5				100%					57%	43%	
	9		40%	60%				40%	60%		
6		19%	67%	14%			52%	43%	5%		
	2	50%	50%				29%	43%	29%		
7			100%					100%			
	11		100%					100%			
8				100%				100%			
	3		100%						100%		
9			100%					60%	40%		
	8		50%	50%				25%	75%		
10			10%	50%	30%	10%		40%	40%	10%	10%
	10		56%	44%			11%	67%	22%		
11				100%				60%	20%	20%	
	6		29%	71%			17%	67%	17%		
12		100%						80%	20%		
	12		100%					100%			
13				100%						100%	
	13		75%	25%					100%		
14				100%					75%	25%	
	16		50%	50%				25%	75%		
15				80%		20%			60%	20%	20%
	14		67%	33%					67%	33%	
16			20%	80%				20%	60%	20%	
	15			100%				50%	50%		