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DIABETIC Medicine

RESEARCH: EDUCATIONAL AND PSYCHOLOGICAL ASPECTS

Identifying HbA1c trajectories and modifiable risk factors of trajectories in 5- to 9-year-olds with recent-onset type 1 diabetes from the United States

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Abstract

Objective: To explore glycated haemoglobin (HbA1c) patterns in 5- to 9-year-olds in the recent-onset period of type 1 diabetes and identify parent psychosocial factors that may predict children's HbA1c trajectory using a prospective, longitudinal design.

Research design and methods: We measured family demographics and parent psychosocial factors at baseline. We collected HbA1c levels from children every 3 months for up to 30 months. Deriving several features around HbA1c trends, we used k-means clustering to group trajectories and linear and logistic regressions to identify parent psychosocial predictors of children's HbA1c trajectories.

Results: The final cohort included 106 families (48 boys, mean child age 7.50 ± 1.35 years and mean diabetes duration 4.71 ± 3.19 months). We identified four unique HbA1c trajectories in children: high increasing, high stable, intermediate increasing and low stable. Compared to a low stable trajectory, increasing parent-reported hypoglycaemia fear total score was associated with decreased odds of having a high stable or intermediate increasing trajectory. Increasing parent-reported diabetes-specific family conflict total score was associated with increased odds of having a high stable or intermediate increasing trajectory.

Conclusions: We are the first to identify distinct HbA1c trajectories in 5- to 9-year-olds with recent-onset type 1 diabetes as well as parent psychosocial factors that may predict high stable or increasing trajectories and could represent future treatment targets.

KEYWORDS
children and adolescents, education, psychological aspects, self-management

1 | INTRODUCTION

The recent-onset period of type 1 diabetes is a challenging time for families of young school-age children because parents must quickly learn multiple self-care behaviours to help regulate their child's blood glucose levels.[1] Further challenging families, current international[2] guidelines recommend that children <18 years-old maintain a haemoglobin A1c (HbA1c) of <53 mmol/mol (<7.0%) or as low as safely possible to protect against risk of future diabetes-related complications.[3,4] We know that older youth and youth who are not in the recent-onset period have a difficult time attaining

an optimal HbA1c level and that youth and parent depressive symptoms, hypoglycaemia fear, diabetes distress and conflict relate to suboptimal HbA1c levels.[1,5–7] Several recent studies also suggest that socio-demographic and treatment engagement may relate to HbA1c trajectories in youth beyond the recent-onset period.[8–10] However, there is limited research examining HbA1c trajectories in children <8-years-old[11] or studies exclusively focused on children with recent-onset type 1 diabetes.[12,13] Children with recent-onset type 1 diabetes can have unique physiological (i.e. honeymoon period)[14] and behavioural characteristics (i.e. families learning new diabetes self-care) that may render it inappropriate to generalize to them the existing HbA1c trajectories found in older youth and youth beyond the recent-onset period. Additionally, it is possible that associating children's HbA1c trajectories in the recent-onset period to parent psychosocial factors could help to identify potential modifiable targets to inform new interventions. Thus, in a sample of 5- to 9-year-olds, we sought to examine two hypotheses. First, we hypothesized that children with recent-onset type 1 diabetes would exhibit distinct HbA1c trajectories that differed quantitatively by several characteristics. Second, we hypothesized that parent psychosocial factors measured early in their child's diabetes would predict children's HbA1c trajectory and trajectory characteristics in this period.

Novelty Statement

- This study presents novel data exploring haemoglobin A1c (HbA1c) trajectories in children with recent-onset type 1 diabetes and prospective associations between children's HbA1c trajectories and parent-reported psychosocial variables.
- The results reveal four unique trajectories: low and high stable and intermediate and high increasing HbA1c trajectories.
- Compared to a low stable trajectory, researchers observed associations between higher parent-reported diabetes-specific family conflict total and higher odds of children having a high stable or intermediate increasing trajectory.
- The study provides evidence for tailoring behavioural interventions to families of young school-age children at the highest risk for an increasing or high stable HbA1c trajectory soon after diagnosis.

2 | METHODS

We used data from a prospective, longitudinal project completed at two regional paediatric diabetes centres in the Midwestern and Rocky Mountain regions of the USA (US; TACKLE-T1, Treatment Adherence and Control in Kids: a Longitudinal Evaluation in T1; R01 DK100779). Children were eligible for the larger project if they were between 5- and 9-years-old and within 12 months of their diabetes diagnosis. All children used multiple daily injections or an insulin pump. Parents/primary caregivers (parents) who participated reported having primary responsibility for their child's diabetes self-care and were English speaking.

We recruited eligible families by telephone and in clinic. Participating parents provided written informed consent and children ≥7-years-old provided assent. Researchers attained assent to continue with the project from all children who turned 7-years-old after study enrolment. Data collection occurred every 3 months or during routine diabetes clinic visits for up to 30 months post-study enrolment. At the first study visit, parents completed psychosocial surveys and a family demographic form, while children provided a small blood sample to measure their HbA1c. Children repeated the procedures for measuring their HbA1c at subsequent study visits. Children received a toy valued at up to 10 US dollars for each HbA1c measure. We obtained Institutional Review Board approval for all study procedures at both participating institutions prior to family enrolment.

2.1 | Measures

2.1.1 | Demographic form

Parents reported on child age and sex, parent age and relationship to the child and parent–child dyad's race and ethnicity. Additionally, we measured time since the child's diabetes diagnosis in months.

2.1.2 | Diabetes distress

Parents completed the Problem Areas in Diabetes–Parent Revised (PAID-PR).[15] Higher scores on the PAID-PR reflect greater perceptions of diabetes distress. We calculated a total score (PAID-PR Total) and subscale scores reflecting parents' immediate (PAID-PR Immediate) and long-term (PAID-PR Theory) distress.

2.1.3 | Fear of hypoglycaemia

Parents completed the Hypoglycaemia Fear Survey for Parents (HFS-P). Higher scores on the HFS-P reflect greater perceptions of symptoms. We calculated a total score (HFS-P Total) and subscales score reflecting hypoglycaemia

avoidance behaviours (HFS-P Behaviour) and worry (HFS-P Worry).[16]

2.1.4 | Depressive symptoms

Parents completed the Center for Epidemiological Studies Diabetes Scale (CES-D).[17] We calculated a Total score with higher scores reflecting greater depressive symptoms.

2.1.5 | Family conflict

Parents completed the Diabetes Family Conflict Scale–Revised (DFCS-R). Higher scores on the DFCS-R reflect greater perceptions of conflict. We calculated total score (DFCS-R Total) and subscale scores reflecting conflict over daily diabetes self-care tasks (DFCS-R Direct) and conflict over less frequent diabetes self-care tasks or non-diabetes tasks (DFCS-R Indirect).[18]

2.1.6 | Child HbA1c

We measured children's HbA1c using a validated finger stick blood sample and laboratory kit in a central laboratory. We analysed blood samples using automated high-performance liquid chromatography (reference range 20–42 mmol/mol [4.0%–6.0%]; Tosoh Corporation).[19] In the few cases of missing or diluted laboratory samples, we used children's most recent point-of-care values (reliability >0.90 with available laboratory-based values).

2.1.7 | HbA1c trajectory-derived features

Although HbA1c offers a standardized measure of glucose levels, the raw magnitude of these data represents only one aspect of what it means to have near-normal HbA1c. Therefore, we sought to transform children's HbA1c trajectories into a set of clinically meaningful derived features to capture various descriptors of temporal trends. These included slope, variability, variability ratio, percentage above 58 mmol/mol (>7.5%) and density, which we define in Table 1. We selected percentage above 58 mmol/mol (>7.5%) because, during the TACKLE-T1 study, this was the target for US youth,[20] which suggests suboptimal levels.

3 | ANALYSES

To minimize sources of potential bias, we added two exclusion criteria to the complete cohort of 130 families. These included removing families with missing baseline parent psychosocial surveys (n = 6) and removing families if children have fewer than 5 HbA1c levels in 15 months, equating to <50% of follow-up visits (n = 18); resulting in a final cohort of 106 families. Next, we characterized children's HbA1c trajectories by computing descriptive statistics for slope, variability, variability ratio, percentage above 58 mmol/mol (>7.5%) and density, as well as for parents' baseline psychosocial variables. To identify subgroups of children based on our HbA1c trajectory characteristics, we used an unsupervised K-means clustering approach. Specifically, we created a vector comprised of derived HbA1c features for each child and we min-max normalized the distributions for each derived feature to calculate the vector-defined distance between a pair of instances (children) while minimizing the risk that scale differences could artificially inflate the importance of any single attribute. Then, with each feature rescaled, we used the gap statistic to determine an optimal number of clusters, (k) = 4, and with 20 random initializations to establish stability and reproducibility, we grouped children by their HbA1c cluster and recomputed descriptive statistics for each cluster. For completeness, we also implemented a standard bootstrapped cluster stability metric[21] and found the clusters to be highly robust.

Finally, using a series of robust linear regressions with a HuberT weight function,[22] we explored associations for each HbA1c trajectory-derived feature (dependent variable) with parent psychosocial variables (independent variables), while multinominal logistic regression was used to evaluate the associated odds of children belonging to a specific HbA1c trajectory-derived cluster as a function of parents' psychosocial variables using the low stable cluster as a reference. We adjusted regressions for child age, time since diagnosis, sex, race and clinic site, and we mean-centred parent psychosocial variables to aid interpretation.

Consistent with contemporary recommendations,[23] we quantify our associations between child HbA1c trajectory characteristics and parent psychosocial variables by evaluating their effect size, directionality and confidence intervals. To obtain confidence intervals, we implemented a 10,000-sample bootstrap analysis for each regression. Sampling with replacement, to estimate expected (average) effect sizes along with their corresponding 95% conference intervals. We performed our primary analyses using python 3.7.6, pandas 1.0.1,[24] numpy 1.18, scipy 1.4.1[25] and statsmodels 0.11.[26]

4 | RESULTS

Table 2 summarizes all sample demographics, children's HbA1c-derived features and parents' baseline psychosocial survey results for the entire cohort (n = 106) and by HbA1c

TABLE 1 Descriptions of derived HbA1c features

Slope	This describes the global trend in children's HbA1c levels. To compute this value, we fit children's HbA1c level against a temporal covariate representing absolute time since baseline for each HbA1c level and we used a robust linear model with HuberT weight[22] to account for potential measurement error and noise when obtaining the line of best fit. We report slope based on mmol/mol change in year.
Variability	This describes the relative amount of visit-to-visit change in children's HbA1c levels. For this feature, we calculated the standard deviation of collected HbA1c levels for each child.
Variability ratio	Because monotonically increasing trends can have artificially large standard deviations, we created a secondary measure of variability representing the ratio of variability (standard deviation) between the first and second half of study visits. Because to remain in our sample, all children had to have HbA1c data from ≥6 study visits, each ratio represents a minimum of 6 months and 3 HbA1c levels. Here, a value of 1 suggest identical variability across the study, >1 suggests higher variability during the first half of study visits and <1 suggests higher variability during the second half of study visits.
Percentage >58 mmol/mol (>7.5%)	This reflects the percentage of all visits for which children's HbA1c level was >58 mmol/mol (>7.5%), which was the target HbA1c level in place for children during the larger study.[20]
Density	This reflects how rapidly changes occurred in children's HbA1c levels over the course of the study. We added this derived feature as all children were in the recent-onset period of T1D and potentially experiencing a honeymoon period during the study, which could impact their HbA1c levels. To derive this metric, we computed the area under the trajectory curves for each child over the study period. We then identified the point in time at which a child's trajectory reached an area under the curve of 25% of their eventual total. We reported this time as percentage from total time. In this way, those children with a rapid increase after onset have a lower value than those with a slower increase. For reference, a child with a completely flat trajectory over the study would reach this value at exactly 25% of their total time.

trajectory subgroups. Overall, the slope and density of children's HbA1c trajectory curves suggest their HbA1c levels were, on average, increasing over time. Children's longitudinal HbA1c levels evidenced variability, especially in the first versus second half of the study visits. Moreover, for the entire cohort, children's HbA1c was, on average, above 58 mmol/mol (>7.5%) at 71% of their visits. Parental psychosocial outcomes demonstrated scores in the mild-to-moderate range across surveys.

Figure 1 presents the median trend for subgroups of children in the recent-onset period who exhibited HbA1c trajectories with similar characteristics. Applying labels used previously,[9,10] our four HbA1c trajectories were as follows: (1) high increasing, (2) high stable, (3) intermediate increasing and (4) low stable. The smallest cluster was the high increasing trajectory. Eight children comprised this subgroup, demonstrating longitudinal HbA1c values with the largest positive slope, high variability and an average of 71% of HbA1c values above target. In contrast, the largest cluster was the high stable trajectory. Forty-one children comprised this subgroup and averaged 90% of HbA1c values above 58 mmol/mol (>7.5%) with minimal temporal change and variability in overall HbA1c level. Children who clustered in the intermediate increasing trajectory (n = 30) demonstrated modest positive slope and variability in their overall HbA1c level and averaged 81% of HbA1c values above target. Finally, children who clustered in the low stable trajectory (n = 27) averaged 32% of HbA1c levels above target and evidenced low variability in their HbA1c level. In follow-up sensitivity analyses, characterizing trajectories based on child age (dichotomized <8- or ≥8-years-old), there was a comparable proportion of children ≥8-years-old included in the high and low stable trajectory subgroups (51% and 52% respectively). In contrast, there were seven children in the high increasing (87.5%) and twelve children in the intermediate increasing (40%) trajectory sub-groups ≥8-years-old at baseline.

Relating parents' baseline psychosocial survey results to children's HbA1c-derived features (Figure 2), we found a negative association between parent-reported HFS-P Behaviour scores and the percentage of visits with an HbA1c

TABLE 2 Derived HbA1c features and parent psychosocial variables for the entire cohort and each HbA1c trajectory

Variable	Entire Cohort (n = 106)	High Increasing (n = 8)	High Stable (n = 41)	Intermediate Increasing (n = 30)	Low Stable (n = 27)
Demographics (M ± SD or %)					
Child age (y)	7.50 ± 1.3	9.13 ± 0.83	7.86 ± 1.42	7.74 ± 1.34	7.87 ± 1.26
Child time since diagnosis (mo)	4.71 ± 3.19	4.12 ± 2.47	5.76 ± 3.76	3.80 ± 2.52	4.33 ± 2.76
Parent age (y)	37.05 ± 6.13	39.86 ± 9.51	35.95 ± 6.02	36.65 ± 5.27	38.30 ± 6.04
Child sex n (%)					
Boy	48 (45)	4 (50)	15 (37)	13 (43)	16 (59)
Girl	58 (55)	4 (50)	26 (63)	17 (57)	11 (41)
Parent–child Race n (%)					
White	90 (85)	5 (63)	34 (83)	26 (86)	25 (92)
Black/African American	10 (9)	2 (25)	5 (12)	2 (7)	1 (4)
Preferred not to report	6 (6)	1 (12)	2 (5)	2 (7)	1 (4)
Parent–child Ethnicity n (%)					
Hispanic/Latinx	14 (13)	1 (12)	6 (15)	3 (10)	4 (15)
Parental role n (%)					
Mother	92 (87)	8 (100)	40 (97)	25 (83)	22 (81)
Parent marital status n (%)					
Married	87 (82)	5 (63)	34 (83)	23 (77)	22 (81)
HbA1c-Derived Feature (M ± SD)					
HbA1c slope (mmol/mol per year)	4.40 ± 7.40	23.51 ± 6.78	1.08 ± 4.50	7.27 ± 3.70	0.39 ± 3.31
Variability (mmol/mol)	8.50 ± 5.40	23.56 ± 4.29	6.11 ± 2.31	10.03 ± 3.21	5.97 ± 2.14
Variability ratio	1.63 ± 1.21	1.82 ± 1.72	1.15 ± 0.64	1.76 ± 0.99	2.17 ± 1.63
Percentage >58 mmol/mol (>7.5%) (%)	71.27 ± 27.65	71.34 ± 18.54	89.89 ± 12.41	81.08 ± 14.99	32.06 ± 15.93
Density (%)	30.52 ± 4.93	42.32 ± 5.70	28.36 ± 1.59	36.17 ± 2.48	30.07 ± 3.74
Parent Psychosocial Variables (M ± SD)					
PAID-PR Total	1.41 ± 0.86	1.20 ± 0.73	1.44 ± 0.87	1.37 ± 0.88	1.48 ± 0.90
PAID-PR Immediate	0.86 ± 0.73	0.45 ± 0.31	0.93 ± 0.75	0.83 ± 0.78	0.91 ± 0.72
PAID-PR Theory	1.90 ± 1.09	1.87 ± 1.25	1.90 ± 1.07	1.85 ± 1.04	1.99 ± 1.19
HFS-P Total	66.02 ± 13.84	70.00 ± 12.85	64.05 ± 11.54	62.53 ± 12.47	71.70 ± 17.09
HFS-P Behaviour	32.74 ± 5.65	35.50 ± 7.13	32.22 ± 4.50	31.57 ± 4.79	34.04 ± 7.23
HFS-P Worry	33.27 ± 12.46	34.50 ± 16.24	31.83 ± 10.00	30.97 ± 10.73	37.67 ± 15.62
CES-D	11.24 ± 8.92	8.75 ± 3.10	12.44 ± 9.62	9.27 ± 8.09	12.37 ± 9.66

(Continues)

TABLE 2 (Continued)

Variable	Entire Cohort (n = 106)	High Increasing (n = 8)	High Stable (n = 41)	Intermediate Increasing (n = 30)	Low Stable (n = 27)
DFCS-R Total	22.99 ± 5.89	23.00 ± 4.28	23.32 ± 6.65	24.13 ± 7.08	21.22 ± 2.50
DFCS-R Direct	11.71 ± 3.52	11.12 ± 2.36	11.95 ± 3.99	12.33 ± 4.05	10.81 ± 2.09
DFCS-R Indirect	11.28 ± 2.84	11.87 ± 2.29	11.36 ± 3.09	11.80 ± 3.60	10.41 ± 0.89

Note: The Problem Areas in Diabetes–Parent Revised scores range 0–4 (PAID-PR Total, PAID-PR Immediate and PAID-PR Theory). The Hypoglycaemia Fear Survey–Parent Total score ranges 25–125 (HFS-P Total), Behaviour score ranges 10–50 (HFS-P Behaviour) and Worry score ranges 15–75 (HFS-P Worry). The Center for Epidemiological Studies Depression Scale score ranges 0–60 (CES-D). The Diabetes Family Conflict Scale–Revised Total score ranges 19–57 (DFCS-R Total), Direct score ranges 9–27 (DFCS-R Direct) and Indirect score ranges 10–30 (DFCS-R Indirect).

above 58 mmol/mol (β = −6.60) and negative associations between PAID-PR Immediate scores and children's HbA1c slope (β = −1.83) and density (β = −1.23). In contrast, we saw a strong positive association between parent-reported DFCS-R Total scores and the per cent of visits with an HbA1c above 58 mmol/mol (β = 5.47), and positive associations between parent-reported PAID-PR Theory scores with children's HbA1c slope (β = 1.74) and children's HbA1c density (β = 1.21).

In multinomial regressions using the low stable trajectory as our comparator (Figure 3), we found increased odds of children following a high increasing versus low stable HbA1c trajectory for parents reporting higher HFS-P Behaviour (β = 2.45) and DFCS-R Indirect scores (β = 3.83). In contrast, we found decreased odds of children following a high increasing versus low stable HbA1c trajectory for parents' reporting higher DFCS-R Direct (β = −2.56) and PAID-PR Immediate (β = −6.65) scores. We found increased odds of children following a high stable versus low stable HbA1c trajectory for parents reporting higher DFCS-R Total (β = 0.81) and DFCS-R Indirect (β = 1.56) scores, while we found decreased odds of children following a high stable versus low stable trajectory for parents reporting higher HFS-P Total (β = −0.81), HFS-P Behaviour (β = −0.51) and HFS-P Worry (β = −0.66) scores. Finally, we found increased odds of children following an intermediate increasing versus low stable trajectory for parents reporting higher DFCS-R Total (β = 1.10) and DFCS-R Indirect (β = 1.39) scores, while we found decreased odds of children following an intermediate increasing versus low stable trajectory for parents reporting higher HFS-P Total (β = −0.86), HFS-P Behaviour (β = −0.58) and HFS-P Worry (β = −0.68) scores.

5 | DISCUSSION

In a discovery data set, we examined for HbA1c trajectories in young school-age children with recent-onset type 1 diabetes. Based on our derived HbA1c trajectory-based features, we observed that, on average, children's HbA1c levels exhibited a positive slope, with variability at nearly 8% of the total available range (20–129 mmol/mol [4%–14%]), and levels exceeding the appropriate US target at nearly three-quarters of study visits. Our results also suggested HbA1c trajectories that were similar to trajectories published for older youth with longer duration of type 1 diabetes.[9,10] Specifically, we found two subgroups following stable trajectories at either a high (i.e. above the clinical target) or low (i.e. at or below the clinical target) level and two subgroups following increasing trajectories, with the main difference being the per cent of HbA1c levels above the target.

We further observed that greater parental hypoglycaemia fear (HFS-P Behaviour, Worry and Total scores) predicted

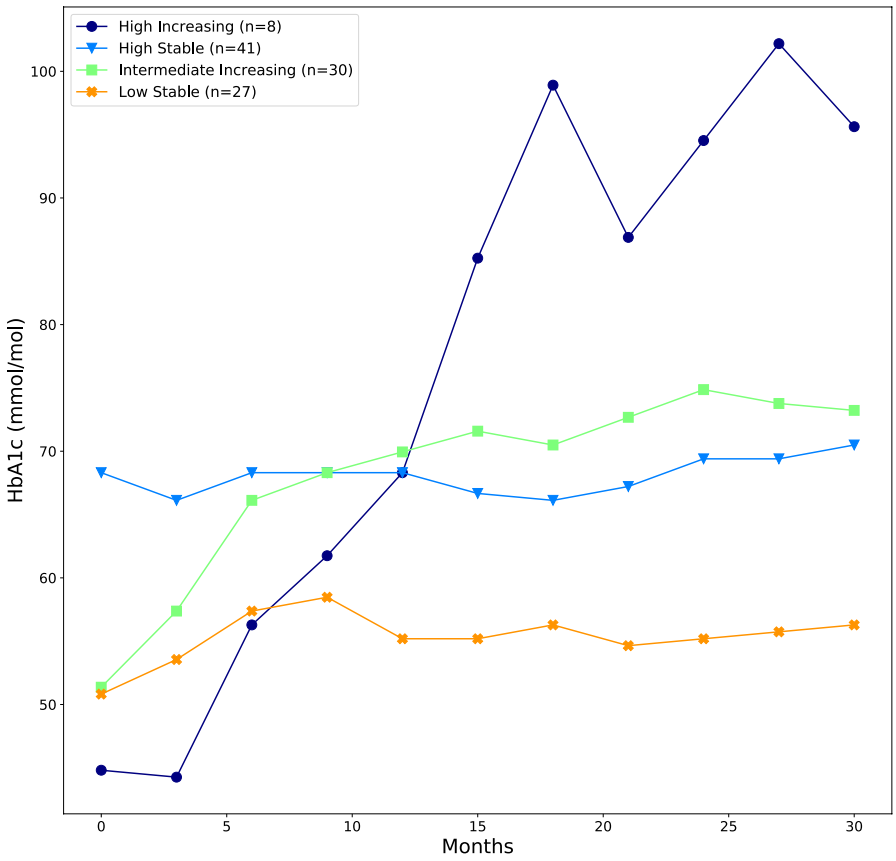

FIGURE 1 Median HbA1c trajectory clusters for 5–9 year-olds with recent-onset type 1 diabetes and living in the US [Colour figure can be viewed at wileyonlinelibrary.com]

decreased odds of children following a high stable and intermediate increasing HbA1c trajectory versus a low stable trajectory in the recent-onset period. It is possible that these associations emerged because parents perceived heightened vulnerability to child hypoglycaemia and, therefore, were working exceptionally hard to manage their child's glucose leading to more stable and optimal levels. Yet, we also saw greater parental HFS-P Behaviour scores predicted increased odds of children following a high increasing versus low stable HbA1c trajectory, suggesting that, for some families, practicing hypoglycaemia avoidance behaviours predicted suboptimal HbA1c levels in the recent-onset period. We saw that greater parental diabetes distress related to daily self-care (PAID-PR Immediate) predicted a smaller and slower rise in child HbA1c among those with increasing trajectories and associated with decreased odds of children following a high increasing versus low stable HbA1c trajectory. Finally, we saw associations between increasing parent-reported diabetes-specific family conflict (DSFC-R Total) and a greater percentage of visits with child HbA1c levels above 58 mmol/mol (>7.5%) as well as increased odds of children following a high stable or intermediate increasing versus low stable trajectory, perhaps identifying conflict as early treatable risk factor for less optimal child HbA1c levels.

These results suggest that young school-age children are likely to experience variable and increasing HbA1c levels in the recent-onset period of type 1 diabetes. Additionally, our trajectory-based subgroups identify several patterns of HbA1c change over time, but still suggest that most children (74%) may follow an HbA1c trajectory that is predominantly above target. These findings are clinically noteworthy as, based on the theory of metabolic memory,[4,27] we might expect children who are able to achieve and maintain optimal HbA1c levels closer to diabetes onset to be at lower risk of developing long-term diabetes-related complications. Thus, our results may suggest a need for greater support and/or new interventions to help young school-age children to maintain optimal HbA1c levels closer to the onset of their diabetes.

Our results associating children's HbA1c-based trajectories to parents' psychosocial variables may also inform new interventions. For example, the associations we found between early parent-reported diabetes-specific family conflict total scores and future suboptimal child HbA1c levels and HbA1c trajectories suggest that families of young school-age children in the recent-onset period might benefit from education and adjunctive treatments targeting conflict.[28] Interestingly, even though our results suggest that parental hypoglycaemia fear (all scales) and diabetes-specific family conflict direct scores early in type 1 diabetes may associate with a low stable HbA1c trajectory in children, the available literature in families of youth with longer duration type 1 diabetes does not support fear or conflict as helpful long term.[1,6,7] Thus, contrary to our results, we would propose that these findings also support a need for adjunctive

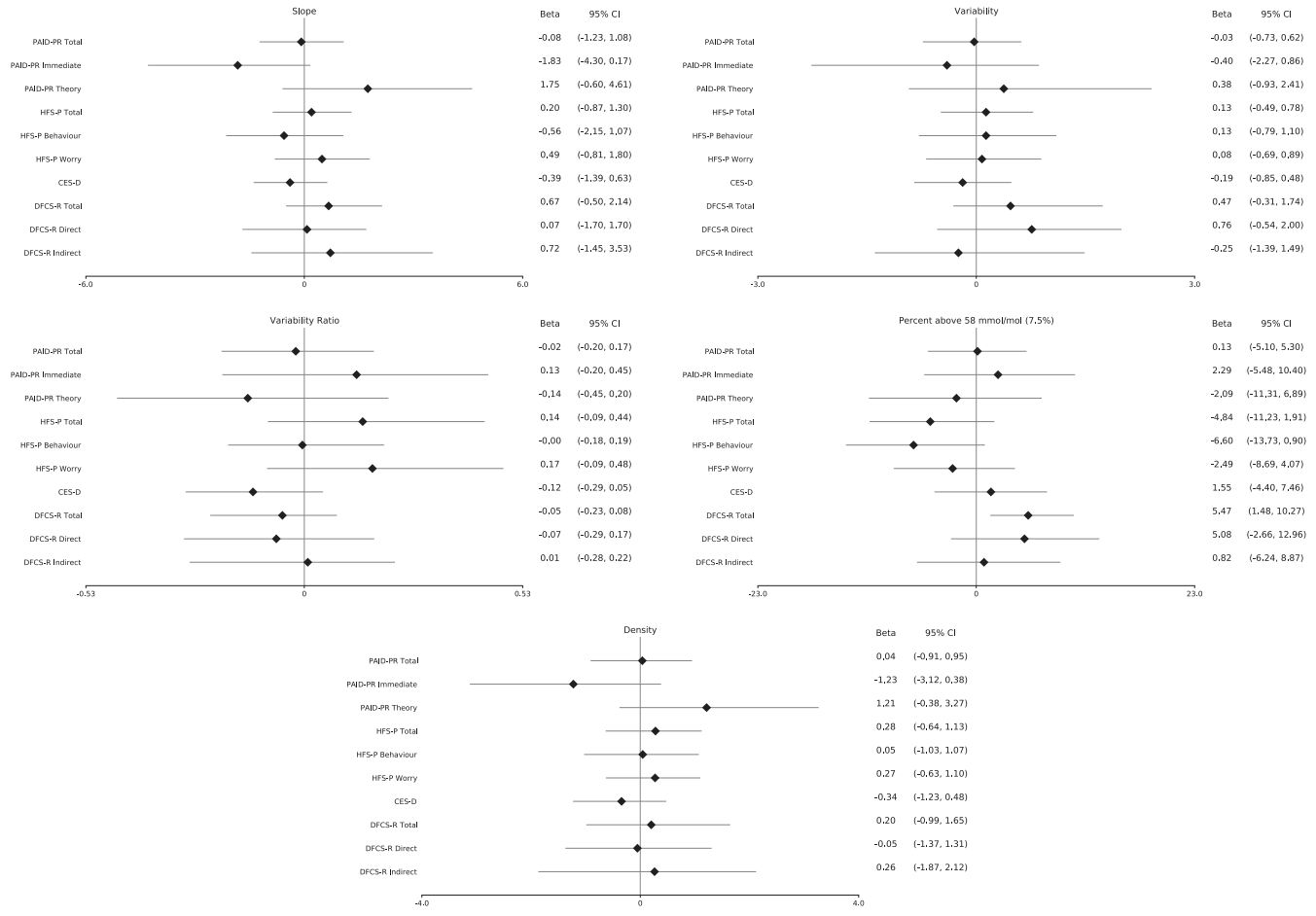

FIGURE 2 Beta estimates and 95% confidence intervals of the associations between baseline parent psychosocial variables and children's HbA1c derived features while controlling for child age, and sex, parent-child race/ethnicity, and clinic location

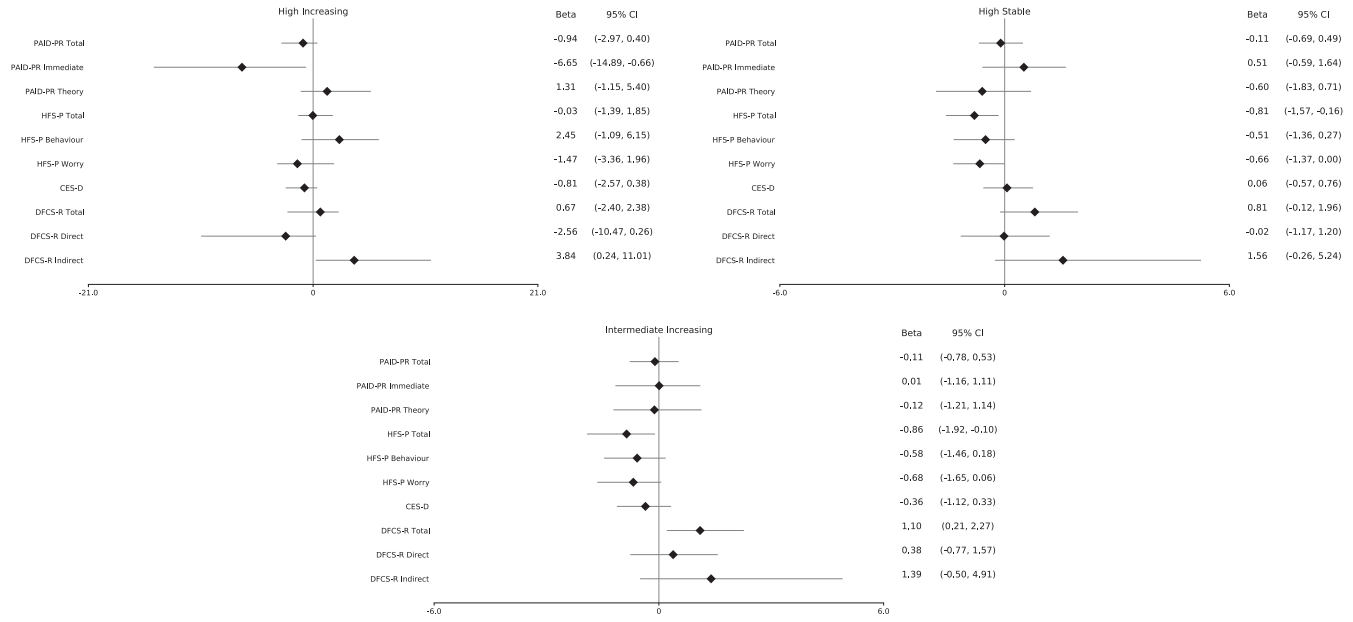

FIGURE 3 Beta estimates and the 95% confidence intervals of the multinomial logistic regressions for baseline parent psychosocial variables and children's HbA1c trajectory cluster. Models control for child age and sex, parent-child race/ethnicity, and clinic location. (reference cluster: Low Stable Trajectory. To the left of 0 indicates higher odds in favor of the reference cluster)

interventions targeting parents' fear and family conflict in the recent-onset period.[28,29]

This study has several strengths including its prospective longitudinal design in a relatively large sample of children from two large paediatric diabetes centres, its use of a central laboratory and validated, gold-standard methodology for processing all the children's HbA1c levels and its inclusion of parent psychosocial variables in the analyses. However, there are also some limitations. First, this study only used a follow-up period of 30 months, which limits an examination of longer-term changes in children's HbA1c levels. Second, because this study recruited children from two paediatric diabetes clinics versus a national registry, the sample may be relatively homogeneous and, therefore, the results may not extend to families from more diverse racial, ethnic or socioeconomic backgrounds. Third, while we used several strategies to maintain a high level of family engagement with our longitudinal study (e.g. incentives, email/phone calls and a newsletter),[30] we still experienced some attrition and data loss which could have negatively affected our power to detect other smaller effects. Fourth, the low prevalence of children in our sample with a high increasing HbA1c trajectory, although consistent with prior literature,[9,10] could have introduced bias in our associations and subgroup results. Fifth, we included several parent psychosocial variables and noted large variability in our effect size. Thus, we acknowledge a risk of type 1 error due to multiple hypothesis testing. Sixth, although prior research has found associations among sex, minority status and clinic site with HbA1c trajectories in youth with longer duration type 1 diabetes,[8] we elected to control for these variables versus discuss their unique associations because these variables are not behaviourally modifiable and we experienced a low prevalence of children populating some of these subgroups. Considering our sample limitations, we would encourage future, larger studies to continue explore how child race and sex and parent psychosocial variables may associate with child HbA1c trajectories in the recent-onset period to confirm and extend our results. Of note, we wish to acknowledge that race and ethnicity can be proxy measures of long-standing health, social and economic inequities in the USA.[31] Consequently, we would also encourage future studies consider the addition of variables that may better contextually frame trajectory differences due to systemic racism.

To conclude, we present novel results examining young school-age children's HbA1c levels and parent's psychosocial variables in the recent-onset period of type 1 diabetes. While our results are preliminary due to the size and discovery nature of the data set, they may have important clinical and research implications. Clinically, our results suggest the possibility of new subgroups of children with recent-onset type 1 diabetes based on distinct HbA1c trajectories. This may provide an evidence base for tailoring more intensive diabetes education and therapies to families of children at the highest risk for an increasing or high stable HbA1c trajectory. Our results also suggest parent-reported diabetes-specific family conflict could be a risk factor for suboptimal child HbA1c levels and trajectories, which may provide a new target to treat or prevent HbA1c excursion in at-risk children. The present results may also extend what clinicians and researchers know about the experiences of families of young school-age children with recent-onset type 1 diabetes and provide the evidence base to initiate larger cohort or registry-based studies to continue to develop predictive models of HbA1c trajectories in youth with recent-onset type 1 diabetes and explore how child race and ethnicity or parent psychosocial functioning may impact these models.

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CONFLICT OF INTEREST

Mark Clements is the Chief Medical Officer for Glooko and reports personal fees from Eli Lilly and Medtronic, outside the submitted work. All other authors have nothing to disclose.

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REFERENCES

1. American Diabetes Association. 13. Children and adolescents: standards of medical care in diabetes-2020. *Diabetes Care*. 2020;43(Suppl 1):S163-S182.
2. DiMeglio LA, Acerini CL, Codner E, et al. ISPAD clinical practice consensus guidelines 2018: glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. *Pediatr Diabetes*. 2018;19(Suppl 27):105-114.
3. Lind M, Svensson AM, Kosiborod M, et al. Glycemic control and excess mortality in type 1 diabetes. *N Engl J Med*. 2014;371(21):1972-1982.
4. Testa R, Bonfigli AR, Prattichizzo F, La Sala L, De Nigris V, Ceriello A. The, "Metabolic Memory" theory and the early treatment of hyperglycemia in prevention of diabetic complications. *Nutrients*. 2017;9(5):437.
5. Miller KM, Foster NC, Beck RW, et al. Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. *Diabetes Care*. 2015;38(6):971-978.

6. Driscoll KA, Raymond J, Naranjo D, Patton SR. Fear of hypoglycemia in children and adolescents and their parents with type 1 diabetes. *Curr Diab Rep*. 2016;16(8):77.
7. Pate T, Klemencic S, Battelino T, Bratina N. Fear of hypoglycemia, anxiety, and subjective well-being in parents of children and adolescents with type 1 diabetes. *J Health Psychol*. 2019;24(2):209-218.
8. Kahkoska AR, Shay CM, Crandell J, et al. Association of race and ethnicity with glycemic control and hemoglobin A1c levels in youth with type 1 diabetes. *JAMA Netw Open*. 2018;1(5).
9. Schwandt A, Hermann JM, Rosenbauer J, et al. Longitudinal trajectories of metabolic control from childhood to young adulthood in type 1 diabetes from a large German/Austrian Registry: a group-based modeling approach. *Diabetes Care*. 2017;40(3):309-316.
10. Clements MA, Schwandt A, Donaghue KC, et al. Five heterogeneous HbA1c trajectories from childhood to adulthood in youth with type 1 diabetes from three different continents: a group-based modeling approach. *Pediatr Diabetes*. 2019;20(7):920-931.
11. Moore JM, Snell-Bergeon JK. Trajectories of hemoglobin A1c and body mass index z-score over four decades among 2 to 18 year olds with type 1 diabetes. *Pediatr Diabetes*. 2019;20(5):594-603.
12. Prahalad P, Yang J, Scheinker D, Desai M, Hood K, Maahs DM. Hemoglobin A1c trajectory in pediatric patients with newly diagnosed type 1 diabetes. *Diabetes Technol Ther*. 2019;21(8):456-461.
13. Cengiz E, Cheng P, Ruedy KJ, et al. Clinical outcomes in youth beyond the first year of type 1 diabetes: results of the pediatric diabetes consortium (PDC) type 1 diabetes new onset (NeOn) study. *Pediatr Diabetes*. 2017;18(7):566-573.
14. Abdul-Rasoul M, Habib H, Al-Khouly M. 'The honeymoon phase' in children with type 1 diabetes mellitus: frequency, duration, and influential factors. *Pediatr Diabetes*. 2006;7(2):101-107.
15. Markowitz JT, Volkening LK, Butler DA, Antisdel-Lomaglio J, Anderson BJ, Laffel LM. Re-examining a measure of diabetes-related burden in parents of young people with type 1 diabetes: the problem areas in diabetes survey - parent revised version (PAID-PR). *Diabet Med*. 2012;29(4):526-530.
16. Shepard JA, Vajda K, Nyer M, Clarke W, Gonder-Frederick L. Understanding the construct of fear of hypoglycemia in pediatric type 1 diabetes. *J Pediatr Psychol*. 2014;39(10):1115-1125.
17. Radloff LS. The CES-D scale. *Appl Psychol Meas*. 1977;1:385-401.
18. Hood KK, Butler DA, Anderson BJ, Laffel LM. Updated and revised diabetes family conflict scale. *Diabetes Care*. 2007;30(7):1764-1769.
19. Khuu HM, Robinson CA, Goolsby K, Hardy RW, Konrad RJ. Evaluation of a fully automated high-performance liquid chromatography assay for hemoglobin A1c. *Arch Pathol Lab Med*. 1999;123(9):763-767.
20. Chiang JL, Kirkman MS, Laffel LM, Peters AL, Type 1 Diabetes Sourcebook A. Type 1 diabetes through the life span: a position statement of the American Diabetes Association. *Diabetes Care*. 2014;37(7):2034-2054.
21. Hennig C. Cluster-wise assessment of cluster stability. *Comput Stat Data An*. 2007;52(1):258-271.
22. Huber PJ. *Robust Statistics*. New York, NY: John Wiley & Sons, Inc; 1981.
23. Halsey LG. The reign of the p-value is over: what alternative analyses could we employ to fill the power vacuum? *Biol Letter*. 2019;15: https://doi.org/10.1098/rsbl.2019.0174
24. Reback J, McKinney W, Brockmendel J, et al. Pandas-dev/pandas: Pandas 1.0.1 (version v1.0.1). In: *Zenodo*. 2020. https://zenodo.org/record/3644238.
25. Virtanen P, Gommers R, Oliphant T. SciPy 1.0: fundamental algorithms for scientific computing in Python. *Nat Methods*. 2020;17:261-272.
26. Seabold S, Perktold J. Statsmodels: econometric and statistical modeling with python. *Proc of the 9th Python in Science Conf (SCIPY 2010)*. 2010:92-96.
27. Ceriello A. The emerging challenge in diabetes: the "metabolic memory". *Vascul Pharmacol*. 2012;57(5–6):133-138.
28. Wysocki T, Harris MA, Buckloh LM, et al. Randomized, controlled trial of behavioral family systems therapy for diabetes: maintenance and generalization of effects on parent-adolescent communication. *Behav Ther*. 2008;39(1):33-46.
29. Patton SR, Clements MA, Marker AM, Nelson EL. Intervention to reduce hypoglycemia fear in parents of young kids using video-based telehealth (REDCHiP). *Pediatr Diabetes*. 2020;21(1):112-119.
30. Bower P, Brueton V, Gamble C, et al. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. *Trials*. 2014;15:399.
31. Willi SM, Miller KM, DiMeglio LA, et al. Racial-ethnic disparities in management and outcomes among children with type 1 diabetes. *Pediatrics*. 2015;135(3):424-434.

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