Adherence to oral glucose tolerance testing in children in stage 1 of type 1 diabetes: The TEDDY study

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Abstract

Objective: To examine adherence to the oral glucose tolerance test (OGTT) in multiple islet autoantibody children in stage 1 of developing type 1 diabetes (T1D).

Methods: Children are followed from birth in The Environmental Determinants of Diabetes in the Young (TEDDY) study. Completion of an OGTT is recommended every 6 months in children 3 years of age who are multiple islet autoantibody positive. Factors associated with adherence to the OGTT protocol were examined.

Results: The average subject level adherence with the OGTT protocol was 62% although there were large differences across countries; Finnish participants and older children from Sweden were more adherent than participants from the United States and Germany. Factors associated with nonadherence included having a first-degree relative with T1D, using a local laboratory rather than

a TEDDY center for the OGTT, and maternal underestimation of the child's risk for T1D. Children were more adherent to the OGTT if their mothers: were more satisfied with TEDDY participation, reported monitoring the child for T1D by checking blood glucose levels at home, and viewed participating in TEDDY as the primary way they were monitoring the child for T1D.

Conclusions: In a study of children in stage 1 of T1D, adherence to an OGTT protocol was suboptimal despite extensive efforts to communicate the child's high risk to parents. These findings provide important guidance for development of strategies to improve methods for detecting progression or the development of T1D in high-risk pediatric populations.

Keywords

genetic studies; genetic risk; stage 1 type 1 diabetes

1 | INTRODUCTION

Progression of type 1 diabetes (T1D) transpires across three stages in which the presence of two or more T1D-related autoantibodies, normal glycemia, and no symptoms defines stage 1.[1] Progression to stage 2 is characterized by the development of glucose intolerance, but no clinical symptoms. Stage 3 is characterized by diagnosable T1D with obvious onset of clinical symptoms. However, progression from stage 1 to a clinical diagnosis of T1D in stage 3 is highly variable and may take months or decades.[2,3] Although routine screening for T1D is not currently recommended, there is reduced risk for diabetic ketoacidosis at the time of diagnosis in young children who are at very high risk for developing T1D and who are screened regularly.[4] Eliminating diabetic ketoacidosis is essential to prevent cerebral edema, the leading cause of death in children who present with diabetic ketoacidosis,[5,6] changes in white brain matter, and impairments in cognitive functioning.[4]

Currently, the oral glucose tolerance test (OGTT) is the gold standard method for identifying impaired glucose tolerance and diagnosing diabetes. Yet studies of adherence rates to recommended OGTTs are rare and limited to pediatric cystic fibrosis, overweight and obese patients and pregnant women.[7–17] Factors associated with nonadherence to an OGTT in pregnant women include demographic factors (younger age, single marital status, poor education, financial concerns), personal factors (higher parity, higher body mass index postpartum, smoking, procrastination, not wanting to know results despite being at high-risk for diabetes), and health system factors (inadequate recommendations about need for screening by healthcare staff, poor laboratory conditions).[4,11,12] No studies have focused on determining factors associated with OGTT adherence in pediatric populations. Because the OGTT is the gold standard for diagnosing any type of diabetes and is critical for determining staging in T1D, it is important to identify factors associated with completion of recommended OGTT protocols, particularly in pediatric populations at very high risk for T1D.

The Environmental Determinants of Diabetes in the Young study (TEDDY) is an international observational study designed to identify environmental triggers of T1D autoimmunity or onset in a population of genetically at-risk children followed for up to 15 years. An OGTT is included in the longitudinal design of TEDDY for children ≥ 3 years of

age who have 2 autoantibodies and are therefore in stage 1 of developing T1D.[18] The overall purpose of the current study was to examine adherence to the OGTT protocol in these TEDDY children and identify factors associated with OGTT adherence.

2 | RESEARCH DESIGN AND METHODS

2.1 | The TEDDY study

Between 2004 and 2010, TEDDY families were recruited from the general population and from first-degree relatives with T1D at six centers (United States: Colorado, Georgia/ Florida, and Washington; Europe: Finland, Germany, and Sweden). More than 420,000 infants were screened at birth via human leukocyte antigen genotyping, and 21,589 infants with T1D-related genotypes were eligible for TEDDY participation. Of those, 8676 joined TEDDY before 4.5 months of age. After enrollment, families participate in TEDDY study visits every 3 months during the first 4 years of the child's life and every 6 months thereafter if the child does not develop islet autoantibodies; children who are islet autoantibody positive continue to attend quarterly visits. Children are followed until 15 years of age or until T1D onset. The TEDDY protocol is demanding and includes collection of biological samples (e.g., blood, saliva, stool); records of the child's diet, illnesses, and life stressors; and measures of parent/child psychosocial functioning. TEDDY is supported by the National Institutes of Health and approved by each center's institutional review or ethics board.[14]

All TEDDY centers have one or more clinical sites where study visits occur. Germany is unique—almost all participants are first-degree relatives of people with T1D and participate in TEDDY through their medical provider's office. Only about 20% of German participants go to the German TEDDY center. In the United States, and occasionally in Finland and Sweden, participants who move away from their TEDDY sites are permitted to remain in TEDDY through a long distance protocol where blood draws for TEDDY assays are completed in a local laboratory and sent to a TEDDY site.

2.2 | Study population

As of April 30, 2017, of the 8676 TEDDY participants enrolled in this study, 542 (6.3%) were multiple islet autoantibody positive. The total number of children who were multiple islet autoantibody positive and 3 years of age was 451. The final sample of children (N = 437) included in the analysis were: (1) multiple islet autoantibody positive; (2) 3 years of age; and (3) had > 1 TEDDY study visit after becoming multiple islet autoantibody positive where an OGTT was scheduled to be performed.

2.3 | Reporting autoantibody positivity to families and monitoring for T1D

Islet autoantibody testing for glutamic acid decarboxylase, insulin, insulin antigen 2, and zinc transporter eight autoantibodies was conducted at each TEDDY visit, quarterly in the first 4 years and at least biannually thereafter. Parents of children with a first islet autoantibody positive test result were told that their child's risk for T1D may have increased slightly but that positive results sometimes return to normal levels. If at subsequent study visits, the child's islet autoantibody positive test result reverted to negative, parents were told that islet autoantibody positive test results often change across time and that their child's

negative result does not indicate a reduction in the child's risk for T1D unless future test findings are negative. If children tested positive for one islet autoantibody a second time, parents were informed that their child's risk of T1D had increased (e.g., "your child's risk of T1D is 15 out of 100"). For children testing positive for multiple persistent islet autoantibodies, parents were informed that their child's T1D risk had increased further (i.e., "out of 100 children with your child's test results, 50 will go on to develop T1D"), were given information about signs and symptoms of T1D, and encouraged to discuss the increased risk with their medical provider. In Sweden, parents were told that their child's risk had increased, but a specific number was not communicated until September of 2014, when Sweden began to use the same risk numbers (50 out of 100) as other sites.

TEDDY study centers varied in terms of whether parents of children who were multiple islet autoantibody positive were asked to conduct home glucose checks. At the United States and German centers, parents of these children were given glucose meters and instructed to check the child's blood glucose periodically (e.g., once a week or if they noticed clinical signs of T1D). In Finland, one clinical center (Tampere) instructed every parent with a child who was multiple islet autoantibody positive to engage in blood glucose monitoring, whereas two other Finnish clinical centers only provided this instruction to families whose child showed signs of progression toward T1D (e.g., impaired OGTT) or to families who expressed a desire to monitor glucose levels. In Sweden, parents were not given a blood glucose meter unless there were clinical signs of T1D.

2.4 | OGTT procedures

All TEDDY children   3 years of age who become multiple autoantibody positive at any time during the study are asked to complete an OGTT every 6 months as part of the TEDDY protocol with instructions to have the child fast, except for water, for up to 8 hours before the OGTT. Oral glucose, a solution in flavored water in a dose of 1.75 g/kg body weight to a maximum of 75 grams in children, is consumed within 5 minutes. More than 90% of participants completed a two-point OGTT performed by a venipuncture with a venous blood sample collection for glucose and insulin at 0 and 120 minutes. A small number (n = 39) completed a six-point OGTT, in which an intravenous line was inserted and venous samples were collected at −10, 0, 30, 60, 90, and 120 minutes. A small number (n = 30) of Swedish participants were occasionally given an intravenous glucose tolerance test instead of an OGTT as a separate protocol; these participants were included in the analyses. OGTTs occurred at the participant's TEDDY center during the TEDDY study visit with the exception of most German participants and those on the long distance protocol; these participants traveled to a local lab to have the OGTT completed and samples were then shipped to a TEDDY center.

3 | MEASURES

3.1 | OGTT adherence

To distinguish OGTT adherence from overall TEDDY visit adherence, determination of OGTT adherence was limited to completed TEDDY visits at which an OGTT was due. If the child had an OGTT, the child received a score of 1 (completed) for that visit. If the child did

not have an OGTT, the child received a score of 0 (not competed) for that visit. If no TEDDY study visit occurred at a recommended time point, then no binary observation was determined. Thus, each participant has several binary observations (OGTT completed = 1, OGTT not completed = 0) at approximately 6 month intervals. The number of OGTT opportunities available to each child differed and depended on when they entered TEDDY and when they became multiple islet autoantibody positive.

3.2. | Variables tested for associations with OGTT adherence

3.2.1 | Demographic variables—Demographic information was obtained from maternal interviews and questionnaires. Child variables included: sex, first-born status, and ethnic-minority status.[19] In the United States, ethnic-minority status is determined by: (1) whether the child's mother's first language is not English; (2) mother born outside the United States; or (3) child is a member of a Hispanic or ethnic-minority group. European countries do not use race or Hispanic or other ethnic classification systems; therefore, for European children ethnic-minority status is determined by: (1) mother's first language, or (2) country of birth is different than that of the TEDDY country in which the child resides. Child age was determined at the time of each scheduled OGTT. Maternal variables included age at child's birth, marital status (married or living together vs. single parent), education level (primary education or high school, trade school or some college, graduated from college), and crowding as an indicator of socioeconomic status (number of persons in household divided by number of rooms in the house).

3.2.2 | TEDDY specific variables—TEDDY country included the United States, Finland, Germany, and Sweden.

TEDDY cohort was defined as the year in which the child entered TEDDY.

Long distance protocol was coded yes if the child was participating in TEDDY on a long distance protocol instead of coming to a TEDDY center. Approximately 10% of the study sample was on a long distance protocol, most from Germany (n = 24) or the United States (n = 13). Use of the long distance protocol in Finland (n = 2) and Sweden (n = 3) was rare.

Maternal study satisfaction was assessed annually using three questions: (1) "Overall, how do you feel about having your child participate in the TEDDY study,;" (2) "Do you think your child's participation in the TEDDY study was a good decision:" and (3) "Would you recommend the TEDDY study to a friend." The items were significantly correlated and consequently were summed to create a total satisfaction score (Cronbach's α coefficient = 0.80). Scores ranged from 0 to 6 with lower scores indicating greater satisfaction with TEDDY.

3.2.3 | Child medical variables—First-degree relative with T1D was coded yes if the TEDDY child had a parent or sibling with T1D.

Glycemic control was measured by a blood draw for hemoglobin A1C (A1C) at the same time an OGTT was conducted. A1C represents the child's average glucose level during the

preceding 2.5 to 3 months. Throughout TEDDY, parents are informed of their child's A1C results.

Body mass index z-score (zBMI) was calculated by age from height and weight measurements obtained at each TEDDY study visit based on CDC growth charts.[20]

3.2.4 | Maternal psychosocial and lifestyle variables—Since mothers accompanied their children to a TEDDY study appointment 80% of the time, maternal psychosocial and lifestyle variables were included.[19]

Maternal smoking (yes/no) was assessed via questionnaire.

Maternal depressive symptoms were assessed annually using the depression subscale from the well-being questionnaire[21] (Cronbach's α coefficient = 0.70). Higher scores indicate more depressive symptoms.

Maternal anxiety about children's T1D risk was assessed annually with a six-item questionnaire adapted from the 20-item state scale of the State Trait Anxiety Inventory (STAI;[22] Cronbach's α coefficient = 0.93[23,24]). Mothers were asked to respond to the state anxiety questions while thinking specifically about their child's risk for T1D. The six-item score was then converted to a total score comparable to the 20-item state anxiety score. Higher scores indicate higher anxiety symptoms.

Maternal T1D risk perception accuracy was assessed annually by questionnaire[19] using the following item: "Compared with other children, do you think your child's risk for developing diabetes is (mark only one answer)—"much lower," "somewhat lower," "about the same," "somewhat higher," or "much higher?" Mothers answering "much lower," "somewhat lower," or "about the same" were classified as inaccurate, whereas those answering "somewhat higher" or "much higher" were classified as accurate.

Maternal beliefs that T1D risk can be reduced was assessed annually by questionnaire. Mothers were asked to agree or disagree with three statements on a five-point Likert-type scale (1 = strongly agree to 5 = strongly disagree): (1) "I can do something to reduce my child's risk of developing diabetes;" (2) "Medical professionals can do something to reduce my child's risk for developing diabetes;" and (3) "It is up to chance or fate whether my child develops diabetes." Responses to statements 1 and 2 were reversed scored and then summed with the response to statement 3 so that higher scores indicated greater belief that risk of T1D could be reduced (Cronbach's α coefficient = 0.62).

Maternal actions taken to prevent T1D was assessed by the following item: "Sometimes people do things to try to stop their child from getting diabetes. Sometimes people do nothing special to try to prevent diabetes in the child. Have you done anything to try to stop or prevent your child from getting diabetes?" Mothers who answered yes were coded 1 and those who answered no were coded 0.

Maternal report of monitoring the child for T1D was assessed annually by the following item: "In the past year have you done anything to monitor or keep an eye on your child's risk

of developing diabetes?" Responses were then coded into types of monitoring behaviors. For the purposes of this study, we used two of the most commonly reported behaviors intended to monitor for T1D, participation in TEDDY (yes/no) and glucose monitoring (yes/no).

3.3 | Analytic plan

To take advantage of the longitudinal data available in TEDDY, we used generalized estimating equations (GEE), a semiparametric approach, which is ideal for use with longitudinal data when the question of interest is whether there are differences between groups on a particular variable, in this case OGTT adherence. In addition, GEE accounts for missing data so that listwise deletion does not occur. For this study, we were interested in identifying variables associated with OGTT adherence (coded as 1) versus nonadherence (coded as 0) across time. A linear slope model using age in years was examined. The logit link function and the first order autoregressive covariance working correlation were used for all analyses. Standard errors of the parameter estimates were from the empirical sandwich estimate.

Model building used a hierarchical approach with fixed covariates considered prior to time-varying covariates, and main effects considered prior to interactions. Forward stepwise regression was used to determine the variables in the model. If a fixed covariate was significant ($p < 0.05$), the interaction of that covariate and age was examined and included in the model if it was also significant. Other second order interactions of the fixed covariates were examined using a higher threshold ($p < 0.01$) for significance. No third or higher order interactions of the chosen covariates were examined.

Retention of these study participants in TEDDY was high, only 3.8% of the 437 participants chose to discontinue participation in TEDDY. Their data were included in the analysis.

4 | RESULTS

4.1 | Descriptive statistics

Participant characteristics including demographics, TEDDY specific variables, child medical variables, and maternal psychosocial and lifestyle variables are found in Table 1.

4.2 | OGTT adherence rates

The average number of OGTT visits completed was 7.1 ± 4.2 (median = 7.0; range = 1–19) and the average subject level adherence rate across all countries was $62\% \pm 33.5\%$ (median = 75%; range = 0–100%). Average subject level adherence rates varied by TEDDY country with highest rates occurring in Finland (78%) and Sweden (73%) and lowest rates occurring in the United States (49%) and Germany (48%).

4.3 | Factors associated with OGTT adherence

Mothers who perceived their child as at increased risk for T1D ($p = < 0.001$) and who reported monitoring the child for T1D by participating in TEDDY ($p = 0.004$) or blood glucose checking at home checking ($p = 0.004$) were more adherent to the OGTT protocol. In addition, higher adherence to the OGTT protocol was associated with greater maternal

satisfaction with the TEDDY study ($p = < 0.001$). There was also a country by child age interaction ($p = < 0.001$) (Table 2). Finnish participants and older participants from Sweden were far more likely to adhere to the OGTT protocol than participants from the United States (Table 3). Trends in the German data are not discernible due to small sample sizes.

Being a first-born child ($p = 0.005$), having a first-degree relative with T1D ($p = 0.005$), and being on the long distance protocol ($p = 0.003$) were associated with lower adherence to the OGTT protocol. In addition, mothers who underestimated their child's risk for T1D ($p = < 0.001$) were less likely to be adherent to the OGTT protocol.

5 | CONCLUSIONS

To our knowledge, this is the first study to examine OGTT adherence in children who are multiple autoantibody positive and therefore in stage 1 of developing T1D. Although mothers of these children were informed of their child's high risk for developing T1D, OGTT adherence was low; on average, children completed only 62% of their scheduled OGTTs. Because we wanted to focus on OGTT adherence, and not study visit adherence, we limited our data to TEDDY visits completed at which an OGTT was scheduled per protocol. If the child came to the TEDDY visit and completed the OGTT, the child was scored as OGTT adherent; if the child came to the TEDDY visit and did not complete the OGTT, the child was scored as nonadherent. This approach may have actually overestimated OGTT adherence since missed TEDDY visits where excluded from the analysis. It is certainly possible that families may have chosen to miss a TEDDY visit in order to avoid the OGTT.

Adherence varied considerably by country with participants from Finland and older children from Sweden having the highest adherence; Germany and the United States had the lowest adherence. Finland has the highest worldwide incidence of T1D[25] followed by Sweden.[26] Higher OGTT adherence in these TEDDY countries may reflect parents' heightened awareness of T1D, cultural differences in health care delivery, and cultural acceptance of research participation.

Age was associated with OGTT adherence only in Sweden where adherence improved as the child got older. It is worth noting that prior to September 2014, Sweden informed families of their T1D risk without giving specific numbers but after that date, Sweden began using the same numbers as other TEDDY sites (50/100). An analysis of the impact of this change indicated a highly significant increase in adherence after the numerical estimate of risk was provided. This finding suggests that how T1D risk is communicated to families may have a significant effect on OGTT adherence. TEDDY recently changed the risk estimate provided to parents of multiple autoantibody positive children from 50/100 to 70/100 based on the best available current science. It is yet to be determined if this change further improves OGTT adherence.

German children's very low OGTT adherence is consistent with a prior TEDDY study showing poor adherence to food record completion at the German site.[27] However, most of the German participants in this study were on the long distance protocol, which was strongly associated with lower OGTT adherence. The long distance protocol required participants to

go to a local lab for their OGTT and to have the OGTT samples delivered to the TEDDY center by the lab or by the parent. A protocol that permitted an OGTT to be completed at a local lab without the requirement of sending the OGTT samples to the TEDDY center may have been more successful. It is also possible that the personal connection that TEDDY participants have with the TEDDY staff at the TEDDY sites, in contrast to an unknown person in a local laboratory who would collect these samples, contributed to better OGTT adherence.

The only demographic factor associated with OGTT adherence was whether the child was the mother's first child. The effect was relatively small; however, it is possible that mothers are more hesitant to subject their first child to the invasive procedures required of an OGTT.

The only child medical variable related to OGTT adherence was having a first-degree relative with T1D. Although TEDDY participants who have a first-degree relative with T1D are more likely to remain in TEDDY,[19] they are less adherent to two of the most demanding aspects of the TEDDY protocol—completing food records[27] and completing OGTTs. Perhaps parents who are already familiar with T1D believe they can detect its onset in their at-risk child and every 6 month OGTTs are not necessary. It is also possible that the burden of caring for someone in the family with T1D may have made the demands of an OGTT less acceptable.

Maternal study satisfaction with TEDDY was very high with 70% of the sample indicating they were completely satisfied with TEDDY. However, even minor dissatisfaction with TEDDY was associated with poorer OGTT adherence. Attending to participants concerns about the TEDDY protocol, even if minor, may lead to optimal OGTT adherence.

Mothers who had a better understanding of their child's T1D risk were more adherent with the OGTT protocol. Despite extensive efforts to inform parents of their multiple islet autoantibody positive child's high T1D risk, 21% of mothers of these children in stage 1 of T1D underestimated their child's T1D risk.[19] Risk communication is very challenging and the literature is replete with examples of risk underestimation in T1D as well as other diseases.[28–30] These findings suggest the need to develop better risk communication and intervention tools for targeted populations who have difficulty understanding this complex concept. Our experience in Sweden suggests that using numerical estimates of risk may be one important strategy since use of such estimates improved OGTT adherence compared to the use of simple descriptors of increased risk. Improving communication about the value of the OGTT as a tool for monitoring and diagnosing T1D may be an important addition to the communication strategy both in research settings and in clinical situations where a patient's risk for T1D is known.

Mothers who reported using TEDDY to monitor their child for T1D and mothers who reported home blood glucose monitoring as an action to monitor the child for T1D were more adherent with the child's OGTT protocol. Although sites varied in terms of instructions for home blood glucose monitoring, our experience in Finland is informative. One site in Finland instructed parents to home blood glucose monitor and two sites did not. The difference in OGTT adherence between these sites was large and significantly different

suggesting that providing blood glucose meters may be one strategy to improve OGTT adherence. These findings suggest that provider behavior and family factors may be important for OGTT adherence.

The results of this study should be considered in the context of its strengths and limitations. This study did not assess participant attitudes toward the OGTT protocol per se—the need to fast, unpleasant sugary taste of the OGTT mixture, its length, and required blood volume— all of which could have played a role in nonadherence. This study also focused on mothers' psychosocial data; children's attitudes and beliefs are likely to play an important role in OGTT adherence but were not available in this study. However, children's data will be available in the future since TEDDY children provide psychosocial data when they reach 10 years of age. We also did not interview parents and children about their OGTT experience, which could have identified additional factors relevant to efforts to improve adherence. Several study nurses reported that some mothers refused the OGTT because they believed that the glucose solution would cause T1D, suggesting an additional avenue of inquiry. Alternatively, continuous glucose monitors or postprandial monitoring through finger sticks may prove to be more acceptable and effective methods of detecting glucose variations and intolerance, but future studies in this area are needed. Despite these limitations, this study has a number of strengths including being the first to document OGTT adherence in children in stage 1 of T1D, its large sample size, inclusion of participants from multiple countries, and longitudinal design.

In conclusion, adherence to completing OGTTs, the gold standard for diagnosing T1D, was suboptimal in children who are in stage 1 of T1D, despite extensive efforts to communicate the child's high risk to parents. These findings should help guide intervention strategies to improve OGTT adherence in both research and clinical settings in pediatric populations at very high risk for T1D. For example, our experiences suggest that when an OGTT is recommended by a provider in an outpatient clinical setting, but not completed by the patient, providing risk education in the form of actual numbers and more detailed explanation about the purpose of the OGTT and that it cannot precipitate T1D, and recommending familiar personnel conduct the procedure may increase adherence to OGTT completion.

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TABLE 1

Participant characteristics at time of OGTT eligibility

	N (Total = 437)	% or M ± SD (min, max)
Demographic variables		
Child's sex		
Female	180	41%
Male	257	59%
Mother's first child		
Yes	105	24%
No	329	76%
Child is a member of a minority group		
Yes	31	7%
No	397	93%
Mother's age	437	31.4 ± 4.9 (18, 45)
Mother's marital status		
Married or living together	411	95%
Single	23	5%
Mother's Education		
Primary or high school	64	15%
Trade school or some college	95	22%
College	272	63%
Crowding	434	0.7 ± 0.3 (0.3, 3.0)
TEDDY specific study variables		
Country		
United States	152	35%
Finland	106	24%
Germany	31	7%
Sweden	148	34%
Cohort (year of study entry)		
2004/2005	85	19%
2006	68	16%
2007	106	24%
2008	82	19%
2009/2010	96	22%
Long distance protocol		
Yes	42	10%
No	395	90%
Maternal study satisfaction[a]	433	1.4 ± 1.7 (0, 6)
Child medical variables		
First degree relative with T1D		
Yes	94	22%

	N (Total = 437)	% or M ± SD (min, max)
No	343	78%
Child age at second autoantibody positivity	437	4.0 ± 2.5
A1C	360	5.3 ± 0.3 (4.6, 6.2)
BMI z-score	413	0.2 ± 1.0 (−2.5, 2.6)
Maternal psychosocial and lifestyle variables		
Smoking status		
Yes	31	7%
No	403	93%
Depressive symptoms[b]	434	3.2 ± 2.2 (0, 10)
Anxiety about child's T1D risk[b]	432	38.0 ± 11 (22, 69)
T1D risk perception accuracy		
Inaccurate	90	21%
Accurate	342	79%
Belief that T1D risk can be reduced[b]	432	6.1 ± 2.3 (0, 12)
Actions taken to prevent T1D		
Yes	184	42%
No	252	58%
Monitoring child for T1D		
Participation in TEDDY	201	46%
Glucose checking	78	18%
Other	44	10%

Abbreviations: BMI, body mass index; OGTT, oral glucose tolerance test; T1D, type 1 diabetes; TEDDY, The Environmental Determinants of Diabetes in the Young.

[a] Lower scores indicate greater satisfaction.

[b] Higher scores indicate greater symptoms of depression and anxiety and higher beliefs.

TABLE 2

GEE estimates for fixed and time-varying covariates produced by forward stepwise regression

Covariate	Parameter	S.E.	95% CI	P-value
Demographic variables				
Mother's first child (reference = no)[c]	−0.2	0.1	−0.4, −0.1	.005
TEDDY specific study variables				
Country (reference = United States)[c]				<.001
Finland	1.2	0.4	0.5, 1.9	
Germany	0.1	0.6	−1.0, 1.3	
Sweden	−1.2	0.3	−1.8, −0.6	
Long distance protocol (reference = no)[c]	−0.7	0.2	−1.1, −0.4	.003
Satisfaction with TEDDY study[a,d]	−0.21	0.04	−0.29, −0.13	<.001
Child medical variables				
Age at time of OGTT[b,d]	0.07	0.03	0.00, 0.14	.054
First-degree relative with T1D (reference = no)[c]	−0.3	0.1	−0.5, −0.1	.005
Maternal psychosocial and lifestyle variables				
Inaccurate T1D risk perception (reference = accurate)[d]	−0.3	0.07	−0.44, −0.16	<.001
Monitoring: TEDDY participation (reference = no)[d]	0.18	0.06	0.07, 0.30	.004
Monitoring: glucose checking (reference = no)[d]	0.18	0.06	0.06, 0.30	.004
Interactions				
Country by age (reference = United States)				<.001
Finland	−0.12	0.05	−0.22, −0.02	
Germany	0.09	0.08	−0.08, 0.25	
Sweden	0.16	0.04	0.08, 0.24	

Abbreviations: CI, confidence interval; OGTT, oral glucose tolerance test; T1D, type 1 diabetes; TEDDY, The Environmental Determinants of Diabetes in the Young.

[a]Lower scores indicate greater satisfaction.

[b]Factor associated with a significant interaction.

[c]Fixed covariates.

dTime-varying covariates.

TABLE 3

OGTT adherence rates by country and age

Age (years) N adherent/ total N (%)	3	4	5	6	7	8	9	10	>10
United States	34/68 (50%)	76/141 (54%)	85/158 (54%)	89/155 (57%)	95/161 (59%)	67/132 (51%)	45/68 (51%)	24/59 (41%)	16/39 (41%)
Finland	47/59 (80%)	76/97 (79%)	80/103 (78%)	77/98 (79%)	89/112 (79%)	80/107 (75%)	62/88 (70%)	50/67 (75%)	48/62 (77%)
Germany	4/13 (31%)	13/26 (50%)	17/29 (59%)	22/30 (73%)	14/25 (56%)	13/21 (62%)	5/10 (50%)	7/11 (64%)	4/5 (80%)
Sweden	47/83 (57%)	88/141 (62%)	90/155 (58%)	111/172 (65%)	112/160 (70%)	116/158 (73%)	94/119 (79%)	79/87 (91%)	65/71 (92%)