

Reasons for Staying as a Participant in the Environmental Determinants of Diabetes in the Young (TEDDY) Longitudinal Study

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Abstract

Objective: To assess parents' opinions about their participation in the longitudinal, multicenter study - The Environmental Determinants of Diabetes in the Young (TEDDY) consortium.

Methods: A survey was given to parents who had been in the study for ≥ 1 year. Parents rated the importance of different reasons for staying in TEDDY and how well different study components were working. Parents were also asked if they had suggestions for making TEDDY better and if they ever had thought of leaving TEDDY and if so, why.

Results: Out of the 3336 eligible families, 2000 completed the survey (59.1%); most (77.6%) were mothers. Survey completion was more common in European than US TEDDY sites and was associated with greater maternal education, more accurate perceptions about their child's risk of type 1 diabetes, longer participation in TEDDY and excellent attendance at TEDDY visits. "Having someone watching the child for development of T1DM" was most important reason given for staying in the study; other important reasons included "Helping science discover causes of diabetes" and "Getting child's antibody results". Most parents were very satisfied with the different components of TEDDY and had not thought of leaving the study. A minority (24%) of parents acknowledged some thoughts of leaving TEDDY and cited the blood draws, being too busy/not having enough time, the demanding protocol, and food diaries as their reasons for considering leaving.

Conclusions: The study highlights factors important for successful implementation of demanding, longitudinal protocols. Friendly, devoted, skilled and knowledgeable staff with continuity makes the family comfortable. Keeping parents involved and informed on study progress is essential as is making procedures as smooth and painless as possible. Although the study is international the survey results were convergent across countries suggesting that the results have relevance to other similar studies to retain study participants.

Keywords: Natural history; Diabetes mellitus; Type 1 Diabetes; Clinical observational study; Participation

Introduction

Longitudinal research is advantageous to understanding the natural history of a disease and the possible role of gene-environment interactions. Participant retention and protocol compliance is important in order to maintain statistical validity and avoid bias. One of the most challenging aspects is keeping the participants enrolled until the study endpoint is reached.

The Environmental Determinants of Diabetes in the Young (TEDDY) study is a longitudinal multi-center, multi-national, epidemiological study, supported by the National Institutes of Health (NIH). The TEDDY consortium is comprised of 6 clinical centers, located in the United States (Washington, Colorado, Georgia/Florida), Finland, Sweden and Germany, and a data coordinating center in Tampa, Florida [1]. The primary objective of this study is identification of environmental exposures that are associated with increased risk of autoimmunity and type 1 diabetes mellitus (T1DM) [1].

The study cohort consists of children with elevated genetic risk for T1DM [2]. The cohort was established by screening newborns from the general population and from families with First-Degree Relatives (FDR) diagnosed with T1DM. Children are followed for environmental exposures and diet with a clinic visit every three to six months until age 15. Parents fill out questionnaires regarding demographics, health

histories and parents' worries and anxiety. Blood, stool, nasal swabs, saliva, urine, and other samples are collected [1]. Altogether, the TEDDY study is demanding for the child and the parents both in terms of the multiple components included in the study protocol and the longitudinal nature of the study.

The literature on why families/participants continue to stay in studies over time is limited especially for longitudinal natural history studies. Understanding the reasons why participants continue in a study enables the investigators to modify the study to accommodate participants' needs in order to facilitate study subjects' participation and reduce attrition. Previous studies show that potential to help others as well as personal benefits are very important motivators for study participants [3]. Previous studies also suggest while families highly

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Received May 15, 2012; Accepted May 24, 2012; Published May 31, 2012

Citation: Lernmark B, Lynch K, Ballard L, Baxter J, Roth R, Simell T, et al. (2012) Reasons for Staying as a Participant in the Environmental Determinants of Diabetes in the Young (TEDDY) Longitudinal Study. J Clin Trials doi:10.4172/2167-0870.1000114

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value intangible staff attributes such as friendliness, responsiveness and encouragement, study staff may underestimate the importance scheduling participating families to see the same staff at each study visit, as well as appointment reminders, center location, newsletters and commitment to the study [4]. In a community-based clinical trial studying the gastrointestinal health effects of drinking water, “being kept well informed” and that “the study was well run” were identified as particularly important by study participants [5].

This survey was designed to systematically collect information on TEDDY parents’ reasons for study participation, as well as their opinions about practical matters that might be possible to change or modify in order to avoid study withdrawal and improve compliance with the protocol. Findings of this study – and the survey approach per se – could be useful tools in other observational long-term studies.

Subjects and Methods

The screening and subsequent enrollment of children into TEDDY commenced in September 2004. During a six month interval between August 2008 and January 2009, the TEDDY Experience Questionnaire was given to families who had been in the study for more than a year. The parent(s) or person who brought the child to the study visit was asked to complete the questionnaire. If both parents came to the study visit, they could complete the questionnaire together. To assure confidentiality, the completed questionnaire was placed in a sealed envelope to be reviewed by study personnel not directly involved with the family. Each family was asked to complete the questionnaire only one time. Since children are scheduled for clinic visits every third month, the six month study window gave most families the opportunity to fill out the questionnaire. If a family wanted to complete the questionnaire at home and return it by mail, they were allowed to do so. However, most questionnaires were completed at the study visit.

In the questionnaire, the following questions and topics were addressed

1) Parents were asked to rate the importance of various reasons for staying in TEDDY; an open ended question permitted them to add additional reasons for participating; 2) Parents were asked how well potentially modifiable components of the study protocol were working; an open-ended question asked for additional suggestions for improving TEDDY and; 3) Parents were asked if they ever thought of leaving TEDDY and if yes, why.

Demographic data, study compliance records and other background data were obtained from the TEDDY database. Accuracy of maternal perceptions of the child’s T1DM risk as well as maternal anxiety – measured by a 6-item short form of the State Anxiety Scale (SAI) [6] – about the child’s getting T1DM were obtained from a TEDDY questionnaire completed at the 15 months TEDDY visit.

Statistical analysis

First, we used logistic regression to examine whether demographic factors (child gender, maternal education, country of birth), study compliance, child having a first degree relative with diabetes (FDR), maternal anxiety or worry about the child’s getting diabetes, and accuracy of maternal perceptions about the child’s T1DM risk were associated with parental questionnaire completion. Next we examined the most important reasons for staying in TEDDY and tested for country differences using chi-square. Finally, we used multiple logistic regression to identify demographic and psychosocial factors associated with thoughts of leaving the TEDDY study. All analyzes was performed in SAS 9.2. P-values less than 0.05 were considered statistically significant.

Results

During the 6 month study window, 3336 families had been in the TEDDY study for ≥ 1 year and were eligible to complete the questionnaire; 2000 (59.1%) families actually completed the questionnaire and most (77.6%) questionnaires were completed by the child’s mother. The mean age of TEDDY child in families who completed the survey was 32 months (range: 11-53 months). Questionnaire completion rates differed significantly by country: Sweden (74.2%); Finland (68.1%); Germany (58.8%); US (42.0%).

Multiple logistic regressions were used to examine who did and did not complete the questionnaire. European TEDDY country, higher maternal education, older child age, higher study compliance in the first year of TEDDY, and accurate maternal perceptions of the child’s T1DM risk were associated with completing the questionnaire (all p ’s <0.05). Table 1 provides the reasons parents described as “most important” for staying in TEDDY. “Having someone watching the child for development of T1DM” was the most common reason selected, followed by “Helping science discover causes of diabetes” and “Getting the child’s antibody results”. These were the top three reasons for staying in TEDDY for Finnish, German and the US parents. Swedish parents also selected “Having someone watching my child for

Reasons for staying in TEDDY	TEDDY country				
	FINLAND	GERMANY	SWEDEN	US	ALL
	N (%)	N (%)	N (%)	N (%)	N (%)
Knowing someone is watching my child for development of diabetes	330 (61.5)	93 (73.2)	667 (81.1)	400 (77.8)	1490 (74.5)
Helping science discover the causes of type 1 diabetes	299 (55.7)	75 (59.1)	593 (72.1)	395 (76.8)	1362 (68.1)
Getting my child’s antibody results	404 (75.2)	78 (61.4)	443 (53.9)	340 (66.1)	1265 (63.3)
Being seen by the same TEDDY staff at each visit	231 (43.0)	26 (20.5)	503 (61.2)	136 (26.5)	896 (44.8)
Knowing my child might be able to participate in future prevention studies	139 (25.9)	49 (38.6)	461 (56.1)	190 (37.0)	839 (42.0)
Total number of questionnaires	537	127	822	514	2000

Table 1: Most common reasons for staying in TEDDY: Number (%) of respondents describing the reason as “very important” by country.

the development of diabetes” and “Helping science discover the causes of type 1 diabetes” as their top two reasons for staying in TEDDY. However, Swedish parents rated “Being seen by the same TEDDY staff” of greater importance than parents from other countries and rated “Getting my child’s antibody results” as less important.

Although there were significant country differences, most parents were very satisfied with how different parts of TEDDY worked for the family (Table 2). Nevertheless, this survey approach which focused on potentially modifiable aspects of the TEDDY protocol highlighted potential areas of improvement within a country. For example, the data suggest that Finland might focus on day and time of visit scheduling, time needed to complete a TEDDY visit, and parking for the TEDDY visit as areas for improvement. In contrast, the data suggest that Sweden might focus on visit reminders and parking as areas of improvement while the US might focus on time to complete a visit, transportation to the visit, and parking.

Using an open-ended question, respondents were also given the opportunity to provide suggestions on how the TEDDY study could be improved. A total of 490 suggestions were given with some parents

giving multiple suggestions. The most common suggestions, made by at least 50 respondents, included improvements to diet records (14.4%) and stool sample collection (14.6%), incentives (13.3%), visit scheduling and reminders (13.8%), logistics associated with the clinic visit (17.9%), and the desire to have more information about TEDDY findings (15.1%). Comparatively more suggestions came from German parents (37% of parents provided at least one suggestion vs. 18% for other countries, $p < 0.001$).

Most parents (76%) reported they had never thought of leaving TEDDY. Those respondents who acknowledged thinking about leaving the TEDDY study did so for the following primary reasons: the blood draw (33.8%); too busy, not enough time (17.8%); protocol too demanding (15.5%); and food diary too demanding (12.6%). No reason was given by 4.1% of these respondents.

Using multivariate logistic regression to examine factors associated with thoughts of leaving TEDDY, we found that country and maternal age were significant predictors (data not shown) with more German (43.4%) and Finnish (33.0%) respondents having such thoughts compared to Swedish (14.7%) and US respondents (18.2%; $p < 0.0001$).

	TEDDY country				P-value ^a
	ALL	FINLAND	SWEDEN	US	
	N (%)	N (%)	N (%)	N (%)	
Working with the TEDDY staff					
Works Great/Not a problem	1818 (97.5)	514 (96.1)	806 (98.7)	498 (97.2)	
Works good most of the time	43 (2.3)	20 (3.7)	9 (1.1)	14 (2.7)	
Needs improvement	3 (0.2)	1 (0.2)	2 (0.2)	0 (0.0)	≤0.05
Getting questions answered					
Works Great/Not a problem	1757 (94.4)	495 (92.9)	764 (93.5)	498 (97.5)	
Works good most of the time	99 (5.3)	35 (6.6)	52 (6.4)	12 (2.3)	
Needs improvement	5 (0.3)	3 (0.6)	1 (0.1)	1 (0.2)	≤0.005
Wait before visit starts					
Works Great/Not a problem	1737 (93.5)	487 (91.4)	794 (97.2)	456 (89.8)	
Works good most of the time	113 (6.1)	45 (8.4)	21 (2.6)	47 (9.3)	
Needs improvement	8 (0.4)	1 (0.2)	2 (0.2)	5 (1.0)	<0.0001
Day or time visit is scheduled					
Works Great/Not a problem	1663 (89.3)	430 (80.4)	752 (91.9)	481 (94.5)	
Works good most of the time	192 (10.3)	102 (19.1)	64 (7.8)	26 (5.1)	
Needs improvement	7 (0.4)	3 (0.6)	2 (0.2)	2 (0.4)	<0.0001
Time to complete a visit					
Works Great/Not a problem	1584 (85.4)	447 (84.0)	722 (88.4)	415 (82.2)	
Works good most of the time	252 (13.6)	81 (15.2)	94 (11.5)	77 (15.2)	
Needs improvement	18 (1.0)	4 (0.8)	1 (0.1)	13 (2.6)	<0.005
Reminders for the visits					
Works Great/Not a problem	1386 (76.2)	413 (83.6)	524 (64.4)	449 (87.9)	
Works good most of the time	336 (18.5)	45 (9.1)	245 (30.1)	46 (9.0)	
Needs improvement	97 (5.3)	36 (7.3)	45 (5.5)	16 (3.1)	<0.0001
Transportation to the visit					
Works Great/Not a problem	1384 (74.7)	379 (70.8)	616 (75.5)	389 (77.6)	
Works good most of the time	431 (23.3)	139 (26.0)	193 (23.7)	99 (19.8)	
Needs improvement	37 (2.0)	17 (3.2)	7 (0.9)	13 (2.6)	≤0.05
Parking for a TEDDY visit					
Works Great/Not a problem	994 (54.3)	168 (31.5)	417 (52.6)	409 (80.8)	
Works good most of the time	593 (32.4)	238 (44.7)	280 (35.3)	75 (14.8)	
Needs improvement	245 (13.4)	127 (23.8)	96 (12.1)	22 (4.3)	<0.0001

^a p-value test across countries whether there is a difference in proportion of parents replying “works great/not a problem”

Note: Data from German families were excluded because German families participate through their local pediatrician’s office and by telephone; consequently these questions were not relevant to their experience. In contrast, for all other countries where participants come to a TEDDY study center for their TEDDY clinic visits.

Table 2: Respondent satisfaction with different components of the TEDDY study by country.

In addition, more educated respondents (24.0%) acknowledged such thoughts compared to those with a high school education or less (12.6%; $p < 0.0001$).

Discussion

Strength of the present study was that instead of investigating why families left the study, we explored their reasons for participation. Having someone who is watching the child for the development of diabetes and getting the child's antibody results were two of the most important reasons for staying in the TEDDY study, findings reported previously [7]. It is also important not to underestimate participants' altruistic objectives for participating in research [8]. In a phase III clinical trial [4], in addition to possible personal benefit, respondents often mentioned the possibility of helping others. In our study "help science discover the causes of diabetes" was one of the top three reasons respondents gave for participating in TEDDY. It is interesting that one of the suggestions for making TEDDY a better experience was to provide participants information about the progress of the study. Researchers have previously pointed out that keeping participants informed on what is happening in the study, including any new results, can be a very important aspect of retention. Hellard [5], in their community-based clinical trial, reported that keeping the family well informed about the study progress received the highest rating for keeping the participants in the study.

A majority of the parents who completed the questionnaire gave positive opinions about their participation; TEDDY staff members were often mentioned in a favorable way. This finding is consistent with the study by Dias et al [3] who attributed their high retention to the friendliness and responsiveness of the staff. The intensive protocol with four visits a year to the TEDDY clinic is demanding for many parents, but at the same time, it creates an important opportunity to build a relationship between the parents, the TEDDY study, and the study staff. The importance of this aspect of study procedure is highlighted by the findings from Sweden where "Being seen by the same TEDDY staff at each visit" was rated as one of the top three reasons for staying in TEDDY. Sweden is the only TEDDY country that has the same nurse sees the same child at each TEDDY visit and collects all samples and follows up data.

Families reported high satisfaction with most components of the study. However, surveying participants about potentially modifiable aspects of the study protocol may provide important insights as to where improvements could occur. Although parking seemed to be an issue for all sites, other potential areas of improvement differed across sites.

The fact that most participants had never thought of leaving TEDDY is an additional indicator that most respondents were satisfied with their study participation. More educated respondents and German respondents were more likely to acknowledge thoughts of possibly leaving TEDDY. TEDDY visits are done very differently in Germany than at the other TEDDY sites. Instead of coming to a TEDDY clinic, most of the participating German families have their data collected by phone and have the child's blood drawn at the child's pediatrician's office. Even if the TEDDY staff is in contact with the family over the phone and by mail on a regular basis, the person-to-person contact is missing for many German families – a factor that has previously been stressed as important for maintaining participation in longitudinal studies [3]. A greater proportion of German parents also

highlighted the blood draw as a reason for possible withdrawal from TEDDY. Getting the child's blood drawn at the child's pediatrician's office, might be a greater challenge to the family than the friendly and supportive environment consistently offered through a dedicated TEDDY clinic.

The blood draw and insufficient time to devote to the many TEDDY tasks were the most common reasons given for possibly leaving the TEDDY study. These findings are consistent with prior reports identifying similar reasons for why families fail to join longitudinal studies like TEDDY [8,9]. It appears that even when families join a longitudinal study, protocol issues including blood draws and extensive time demands remain important for study retention.

A weakness of our study was that 41% of the families did not return the questionnaire and that the number and proportion of returned questionnaires differed between countries and especially within the US sites (data not shown). More educated mothers with accurate perceptions of their child's T1DM risk, who had been in the TEDDY study longer and who rarely – if ever – missed a TEDDY visit, were more likely to return the questionnaire. We previously reported that mothers who accurately estimate their child's risk for T1DM are more likely to stay in the TEDDY study during the first year [10], a finding that is consistent with the current study's finding that mothers with accurate T1DM risk perceptions were more likely to return the questionnaire. Because more committed families were more likely to return the survey, the results are likely biased and represent the opinions of those most involved in the TEDDY study. Nevertheless, the opinions of those who are most committed to TEDDY offer important information about why families stay in longitudinal demanding studies like TEDDY. We believe the survey findings reported here highlight a number of factors important for successful implementation of demanding, longitudinal study protocols with pediatric populations. To meet friendly, devoted, skilled and knowledgeable study staff is the most often highlighted priority of the parents and to have continuity of the staff makes the family more comfortable. To keep the parents involved in the study by informing them about the progress of the study and any results that can be disclosed may be particularly helpful. If the study protocol involves procedures like blood draws every effort needs to be made to assure the procedure is as painless as possible. Although the TEDDY study is an international project including four countries, the survey results were strikingly convergent across countries suggesting that the results described here may have considerable relevance to other longitudinal studies with pediatric populations.

TEDDY Study Acknowledgements

The TEDDY Study Group (See appendix)

Funded by DK 63829, 63861, 63821, 63865, 63863, 63836, 63790 and UC4DK095300 and Contract No. HHSN267200700014C from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Child Health and Human Development (NICHD), National Institute of Environmental Health Sciences (NIEHS), Juvenile Diabetes Research Foundation (JDRF), and Centers for Disease Control and Prevention (CDC).

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