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COMMENTARY

At high risk for early withdrawal: using a cumulative risk model to increase retention in the first year of the TEDDY study

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The Environmental Determinants of Diabetes in the Young (TEDDY) is a multicenter, multinational, epidemiologic study designed to identify possible environmental triggers of type 1 diabetes mellitus in children at increased genetic risk for the disease; more than 420,000 newborns were screened for human leukocyte antigen (HLA)–conferred genetic risk for type 1 diabetes; 21,589 were HLA eligible and 8,668 joined the TEDDY study [1]. Most participants (89%) have no first-degree relative with type 1 diabetes. Because both the identification of TEDDY-eligible infants and their participation in the TEDDY are time consuming and expensive for the investigators, families, and the funder, loss of these valuable participants from TEDDY is a major concern. We describe here the results of our efforts to identify general population families—at study inception—at high risk for withdrawal from TEDDY in the first year and to provide these families with a tailored intervention designed to improve study retention.

We used a cumulative risk model to identify families most likely to leave the TEDDY study. This model assumes that the total number of risks is more important than the particular risk factors comprising the total risk score [2–4]. Based on our prior analysis of predictors of withdrawal from TEDDY in the first year [5], nine risk factors measured at study inception were used to calculate a cumulative risk score for early withdrawal: child was an ethnic minority, young maternal age, maternal smoking during pregnancy, mother reduced work hours or did not work at all during pregnancy, total alcohol abstinence during pregnancy, maternal underestimation of child's diabetes risk, high maternal anxiety about the child's risk, missing data on the mother's initial study questionnaire, and the child's father failed to complete a brief initial study questionnaire. We selected a risk for early withdrawal cutoff score of $\geq$4 to identify those most likely to withdraw from the TEDDY study.

Beginning January 17, 2009, the Data Coordinating Center for TEDDY calculated the risk for early withdrawal score for each family based on data obtained at the child's first TEDDY visit and informed each site of any family with a risk for early withdrawal score of $\geq$4 within 3 months of the child's first study visit. Each site then developed a plan, individually tailored for each family that was designed to enhance study retention. A variety of strategies were used, including assigning a particular member of the TEDDY team to work with families who were at high

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Table 1. Percent of general population participants withdrawing from TEDDY in the first year, before and after high risk for early withdrawal score notification with tailored intervention was initiated

All participants					
Cohort	**Risk for early withdrawal**	**Total *N***	**% Withdrawn**	**Within-cohort *P*-value**	**Between-cohort *P*-value**
Comparison (C)					
No risk notification and	Low (score <4)	1,053	4.8		C low vs. I low: 0.161
no tailored intervention	High (score ≥4)	426	12.7	C high vs. C low: <0.0001	C high vs. I high: <0.0001
Intervention (I)					
Risk notification plus	Low (score <4)	1,204	3.7		
tailored intervention	High (score ≥4)	524	4.4	I high vs. I low: 0.467	
US participants					
Cohort	Withdrawal risk	Total *N*	% Withdrawn	Within-cohort *P*-value	Between-cohort *P*-value
Comparison (C)					
No risk notification and	Low (score <4)	485	4.3		C low vs. I low: 0.030
no tailored intervention	High (score ≥4)	248	11.7	C high vs. C low: <0.0001	C high vs. I high: <0.0001
Intervention (I)					
Risk notification plus	Low (score <4)	552	2.0		
tailored intervention	High (score ≥4)	294	3.7	I high vs. I low: 0.128	
European participants					
Cohort	Withdrawal risk	Total *N*	% Withdrawn	Within-cohort *P*-value	Between-cohort *P*-value
Comparison (C)					
No risk notification and	Low (score <4)	568	5.3		C low vs. I low: 0.862
no tailored intervention	High (score ≥4)	178	14.0	C high vs. C low: <0.0001	C high vs. I high: 0.002
Intervention (I)					
Risk notification plus	Low (score <4)	652	5.1		
tailored intervention	High (score ≥4)	230	5.2	I high vs. I low: 0.926	

Abbreviation: TEDDY, The Environmental Determinants of Diabetes in the Young.
Statistical comparisons were conducted using the chi-square test.

risk for early withdrawal to provide consistency of interactions and enhance family engagement, hiring a retention coordinator who contacted the high-risk families between TEDDY visits to enhance rapport and increase a sense of support for the family, addressing individual family concerns (eg, childcare for other children in the family, timing of the TEDDY visit, transportation to the TEDDY clinic), and increased communications between TEDDY visits (eg, thank you notes, reminder postcards).

To evaluate the impact of this strategy, we compared the intervention cohort to the previous study cohort for whom there was no risk for early withdrawal score calculation or tailored intervention (Table 1). As expected, in the comparison cohort, the withdrawal rates were significantly higher in the high compared with the low risk for early withdrawal group. In the intervention cohort, the withdrawal rates were lower, and there was no significant difference between the high and low risk for early withdrawal groups. Separate analyses for the European and US sites highlight the consistency of these results. Comparisons across cohorts document the significant decline in withdrawal rates for individuals with risk for early withdrawal scores ≥4 associated with risk notification followed by a tailored intervention. For the US sites, there was also a weaker but significant decline in withdrawal rates for the low-risk group (risk for early withdrawal score <4) in the intervention cohort compared with the low-risk group in the nonintervention comparison cohort.

We recognize that our findings are limited by the use of a pre–post rather than randomized study design. However, retaining these families in the TEDDY study was so important that we elected to apply the intervention to all high-risk families rather than randomly assigning them to an intervention or no intervention condition. We view the findings as promising and useful to others designing or implementing similar epidemiologic studies. To our knowledge, there have been no other attempts to use a cumulative risk model to identify study participants at risk for study withdrawal at study inception and to use this information to initiate efforts to improve retention. Individually tailored programs are demanding on study staff, and focusing such efforts on those at the highest risk for study withdrawal may be one cost-effective solution. Alternatively, such an approach could be used as exclusionary criteria at the time of study enrollment, recognizing the limitations such an approach would place on the generalizability of study findings.

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