

How TEDDY Screens for Risk of Type 1 Diabetes

Minna Kiviniemi, Robert Hermann, Jussi Nurmi, Anette G. Ziegler, Mikael Knip, Olli Simell, Riitta Veijola, Timo Lövgren, Jorma Ilonen, and the TEDDY Study Group

("A High-Throughput Population Screening System for the Estimation of Genetic Risk for Type 1 Diabetes: An Application for the TEDDY (The Environmental Determinants of Diabetes in the Young) Study," published in *Diabetes Technology & Therapeutics* in 2007)

- Potential TEDDY subjects were chosen based on the presence of specific genes HLA DR and DQ present in their blood which is associated with the risk of developing type 1 diabetes.
- The TEDDY study designed a standardized screening system to identify which participants were at high-risk of developing type 1 diabetes. This screening system provides the TEDDY study with a practical approach to rapidly and economically screen thousands of samples.

Quality Assurance of Our Screening Methods

Paul Dantonio, Nancy Meredith-Molloy, William A. Hagopian, Jin Xiong She, Beena Akolkar, Suzanne K. Cordovado, Miyono Hendrix, L. Omar Henderson, W. Harry Hannon, and Robert F. Vogt

("Proficiency Testing of Human Leukocyte Antigen-DR and Human Leukocyte Antigen-DQ Genetic Risk Assessment for Type 1 Diabetes Using Dried Blood Spots," published in *Journal of Diabetes Science and Technology* in 2010)

- The Centers for Disease Control and Prevention (CDC) conduct two kinds of quality assurance programs for type 1 diabetes studies that use genetic testing to determine patient's risk: a voluntary quarterly proficiency testing (VQPT) program available to any laboratory and a mandatory annual proficiency testing (PT) challenge for TEDDY laboratories.
- The TEDDY labs all provided highly accurate and valid results for genetic risk assessment.

Predicting Why Participants with No Family History of Type 1 Diabetes Might Leave the Study Early

Suzanne Bennett Johnson, Hye-Seung Lee, Judy Baxter, Barbro Lernmark, Roswith Roth, and Tuula Simell for the TEDDY Study Group

("The Environmental Determinants of Diabetes in the Young (TEDDY) Study: predictors of Early Study Withdrawal Among Participants with No Family History of Type 1 Diabetes," published in *Pediatric Diabetes* in 2010)

- Several reasons were linked to participants with no family history of type 1 diabetes leaving the TEDDY study early within the first year. These included:
 - Country of residence: the U.S. and Germany had more families leave the study early than Finland and Sweden.
 - Mothers who withdrew early were more than 2 years younger than those who remained active in the TEDDY study.
 - Families with at-risk female infants were more likely to withdraw than those with at-risk male infants.

- Maternal lifestyle behaviors during pregnancy: mothers who smoked during their pregnancy, reported never drinking during their third trimester (as opposed to those who reported having an occasional drink), or who reduced their work hours, quit their jobs, or did not work at all while they were pregnant were more likely to leave the study early.
- Families were slightly more likely to withdraw when the father did not participate in the study.
- Mothers who were anxious about their infants' risk for developing type 1 diabetes, or who had underestimated their child's risk, were more likely to leave the study within the first year.
- The study group used this information to target TEDDY families at high risk for study withdrawal with additional support in an attempt to continue their participation. These findings could be also useful when applied to future pediatric studies that begin when the child is still an infant.

Comparing in Birth Size of High-risk Participants among the TEDDY Countries

Ylva Sterner, Hye-Seung Lee, Helena Larsson, Christiane Winkler, Wendy McLeod, Kristian Lynch, Desmond Schatz, Åke Lernmark for the TEDDY Study Group
 ("Country-specific birth weight and length in type 1 diabetes high-risk HLA genotypes in combination with prenatal characteristics," published in *Journal of Perinatology* in 2011)

- TEDDY researchers found that there was no difference in the birth size (weight and length) of children born with high-risk type 1 diabetes risk-associated genetic factors (human leukocyte antigen DR-DQ genotypes) amongst the 4 different TEDDY countries.
- The study may support the idea that environmental factors during pregnancy and early childhood may contribute to a child's risk for type 1 diabetes.

Developing Cost-effective Ways to Screen for a Large Study

William Hagopian, Henry Erlich, Åke Lernmark, Marian Rewers, Anette G. Ziegler, Olli Simell, Beena Akolkar, Robert Vogt, Alan Blair, Jorma Ilonen, Jeffrey Krischer, and Jin Xiong She

("The Environmental Determinants of Diabetes in the Young (TEDDY): Genetic Criteria and International Diabetes Risk Screening of 421,000 Infants," published in *Pediatric Diabetes* in 2011)

- TEDDY researchers developed a cost-effective screening plan for identifying children with specific high-risk type 1 diabetes risk-associated genetic factors (human leukocyte antigen DR-DQ genotypes). The screening centers revealed that this method was 99% accurate.

Who Enrolls in TEDDY?

Barbro Lernmark, Suzanne Bennett Johnson, Kendra Vehik, Laura Smith, Lori Ballard, Judy Baxter, Wendy McLeod, Roswith Roth, Tuula Simell on behalf of the TEDDY Study Group

("Enrollment Experiences in a Pediatric Longitudinal Observational Study: The Environmental Determinants of Diabetes in the Young (TEDDY) Study," published in *Contemporary Clinical Trials* in 2011)

- TEDDY infants are classified as being either in the general population (GP) or having a first degree relative with type 1 diabetes (FDR).
- TEDDY subjects were placed into one of three categories: enrolled (joined the study), excluded (rejected after inability to meet study requirements), or refused to enroll (family opted out of participation). However, reasons for refusal to enroll were similar across countries and GP/FDR populations.
- When compared, rates were different amongst countries: Sweden had the highest enrollment, the U.S. had the highest number of families excluded because they did not meet study requirements, and Finland had the highest number of families refusing participation.
 - Families were more likely to enroll if they were in a European country, had another child in TEDDY, the infant was an only child, or the mother was older. Also, FDR infants were more likely to enroll than GP infants.
 - The most common reason for exclusion was the inability to re-contact the family.
 - Reasons for refusal to enroll were typically issues with the study procedures, such as being uncomfortable with blood draws, or family issues, such as being too busy to keep up with the protocol.
- Country specific estimates are important for estimating enrollment numbers for long-term pediatric studies. This study suggests that researchers should underestimate enrollment when a study involves the general population, painful procedures, or makes multiple demands on families.