Parent and Pediatrician Preferences for Type 1 Diabetes Screening in the U.S.

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OBJECTIVE

The purpose of this study was to use a discrete-choice experiment methodology to understand the relative importance of the attributes of screening tests for type 1 diabetes among parents and pediatricians in the U.S.

RESEARCH DESIGN AND METHODS

Online surveys presented hypothetical screening test profiles from which respondents chose their preferred test profile. Survey attributes were based on likely screening test options and included the mode of administration, where and when the test was conducted, the type of education and monitoring available to lower the risk of diabetic ketoacidosis (DKA), and whether a treatment was available that would delay onset of insulin dependence. Data were analyzed using random-parameters logit models.

RESULTS

Parents placed the highest relative importance on monitoring programs that could reduce the risk of DKA to 1%, followed by treatment to delay onset of insulin dependence by 1 or 2 years, and, finally, avoiding a $50 out-of-pocket cost. Pediatricians placed equal importance on monitoring programs that reduced a patient’s risk of DKA to 1% and on avoiding a $50 out-of-pocket cost for the screening test, followed by the option of a treatment to delay the onset of insulin dependence. The mode of administration and location and timing of the screening were much less important to parents and pediatricians.

CONCLUSIONS

Parents and pediatricians preferred screening tests that were accompanied by education and monitoring plans to reduce the risk of DKA, had available treatment to delay type 1 diabetes, and had lower out-of-pocket costs.

The prevalence of type 1 diabetes (T1D) in children has been increasing, with an estimated 1.45 cases per 1,000 children younger than 20 years in the U.S. (1). Approximately 58% of children experience diabetic ketoacidosis (DKA) at the time of T1D diagnosis (2). DKA develops after a variable period of prodromal symptoms of polyuria, polydipsia, weight loss, and fatigue. The prodromal period may be very short, unrecognized due to nonspecific symptoms, or absent in younger children. The mortality rate in children with DKA typically ranges from 0.15% to 0.3%, but can increase to 20–25% if cerebral edema is present (3). DKA at diagnosis in children and adolescents leads to extensive changes in brain structure and detrimental neurocognitive outcomes (4–7) as well as poor long-term glycemic control (8–10). A delay in diagnosis of T1D is the leading cause of DKA in children (3).
The progression of T1D can be partitioned into three stages. Stage 1 T1D includes asymptomatic β-cell autoimmunity marked by the presence of two or more islet autoantibodies, which advances to stage 2 with the advent of dysglycemia (11). Stage 3 T1D is defined as symptomatic diabetes. Prospective cohort studies have shown that 70% of individuals with stage 1 diabetes progress to stage 3 within 10 years, and the lifetime risk for progression to stage 3 approaches 100% (12). Although it is not routine practice to screen for islet autoantibodies, the results from screening tests could be used to identify children with islet autoantibodies associated with risk of development of stage 3 T1D. Early detection of T1D could decrease the accompanying complications of DKA, including short-term financial burdens and risk of death, as well as the long-term impacts on neurocognition and glycemic control. Screening also can mitigate other burdens of diagnosis, including the psychologic distress of receiving an unexpected diagnosis for a chronic condition and the need for providing education during the diagnosis communication. Although there is initial anxiety associated with a diagnosis from screening, the level of stress felt by parents of screened children significantly decreases compared with that of parents of unscreened children during the 1st year after T1D diagnosis (13).

When considering the attributes of a screening test, it is important to account for the preferences of parents and pediatricians. The U.S. Food and Drug Administration released guidance in 2016 that encourages the use of data on preferences of patients and caregivers in medical product development (14). Discrete-choice experiment (DCE) methodology is an effective approach to quantify the preferences of parents and pediatricians and has been used since before 1990 to obtain patients’ preferences for health care and for a wide range of health care topics (15–17).

The purpose of this study was to understand the relative importance to parents and pediatricians in the U.S. of the attributes associated with screening tests for T1D that would be administered to all children.

**RESEARCH DESIGN AND METHODS**

**Survey Development**

We used a DCE survey methodology in this study to quantify the relative importance to parents and pediatricians of screening test attributes for T1D. The preference study was conducted according to good research practice guidelines published by the International Society for Pharmacoeconomics and Outcomes Research (15) and was reviewed by the RTI International Institutional Review Board.

At the beginning of the study, the study team conducted qualitative interviews with 10 parents of children aged ≤17 years (n = 6 with no children with T1D; n = 4 with children with T1D) and 10 physicians (n = 3 endocrinologists; n = 7 pediatricians) to gain insight into the potential benefits and risks or concerns associated with T1D screening tests (18). Interview responses were used to finalize a list of attributes for the DCE. Interview participants favored screening for T1D in all children, but parents and physicians had concerns about the details of the test, including test accuracy, mode of administration, cost, and what happens after a positive test result. The interview results suggest that additional education is needed to inform parents and physicians of the benefits of education and monitoring to reduce hospitalizations and DKA at onset, because several interview participants felt screening was less valuable if there was no treatment available.

Using the list of potential attributes generated during the qualitative interviews, the study team chose the final set of attributes and levels for the DCE questions with input from expert clinicians based on likely future screening test options. Five attributes were selected: three attributes to describe the test (mode of administration, where and when the test was conducted, and cost) and two attributes to describe the options for a child who tested positive (the type of education and monitoring to lower the risk of DKA and whether a treatment was available that would delay onset). Table 1 lists the attributes and levels used to create the DCE questions.

The survey instrument started with questions about the respondent’s experience with T1D and knowledge about the disease. On the basis of feedback during the qualitative interviews, the survey included descriptions of T1D, the differences between T1D and type 2 diabetes mellitus, DKA, and what it was like to care for a child with T1D. Published literature was used to inform the description of the potential improvement in DKA risk with education and monitoring (19–23). The parent and pediatrician versions of the survey contained the same attributes and levels, which were described using patient-friendly language for parents and medical terminology for pediatricians. The survey included questions about attributes as well as comprehension questions to assess respondents’ understanding of the survey instrument (see Survey Excerpts, Supplementary Material).

Each DCE question offered respondents a choice between two hypothetical screening test profiles (example DCE questions are shown in Supplementary Figs. 1 and 2), and each survey included eight DCE questions. Parents were asked which screening test they would choose for their child, and pediatricians were asked which screening test they would prefer to implement in their practice. After the DCE questions, the surveys contained additional questions about screening-test preferences and demographic questions. The survey instruments were refined during 15 in-person pretest interviews with parents and 15 telephone pretest interviews with pediatricians.

The final set of DCE questions included in each survey was generated with a commonly used D-optimal algorithm to construct a fractional factorial experimental design (24,25). The resulting design included 48 unique DCE questions that were assembled into six blocks of eight DCE questions each. The final experimental design was evaluated for level balance and orthogonality. The aim of this type of experimental design is to strike a balance between asking enough DCE questions of each respondent to estimate the model parameters for each attribute level while not overburdening the respondent with too many questions. Each respondent was randomly assigned to answer one of the blocks of eight questions and, to avoid having some questions systematically affected by learning and fatigue, the order of the eight choice questions in each block was also randomized for each respondent. The design was developed following good research practice guidelines published by the International Society for Pharmacoeconomics and Outcomes Research (26). The same experimental design was used for both the parent and pediatrician surveys.

**Study Population**

A quota sample of 1,000 parents and 500 pediatricians was recruited by M3, a
market research firm, from members of M3’s online U.S. nationwide panels and partner panels. To be eligible for inclusion, parents had to be aged ≥18 years, have a child younger than 18 years for whom they make medical decisions, be residents of the U.S., be able to read English, and provide informed consent. Pediatricians must have board certification, treat children more than half the time, be residents of the U.S., be able to read English, and provide informed consent. The consent process was similar for pediatricians and parents. Parents were compensated for their time completing the survey with panel points with a cash value of ~$4, and pediatricians received $63.

**Statistical Analysis**

Responses to DCE questions generated cross-sectional panel data that were analyzed using a random-parameters logit (RPL) model. To account for variation in preferences among individuals in the sample, RPL models estimate a distribution of preferences around each model parameter (27). The random parameters were assumed to be normally distributed and independent. The model relates the choices respondents make to the differences in the attribute levels across the alternatives in each DCE question (28). The resulting log-odds parameter estimates can be interpreted as preference weights that indicate the relative strength of preferences for each attribute level. The parent and pediatrician data sets were analyzed separately. All the levels in each attribute were effects coded, with the exception of cost, which was coded as a continuous variable (29). Cost was adjusted for income effects by multiplying cost by the natural log of the parent’s income (using the midpoint of the respondent’s income range) for the parent model. A Wald $\chi^2$ test was used to determine the statistical significance of differences between adjacent attribute levels ($P < 0.05$) for each attribute. The conditional relative importance of a change from one attribute level to another was calculated using the preference weights.

Differences in screening test preferences for parent and pediatrician subgroups (Supplementary Table 1) were analyzed using an RPL model with the same specifications as the full-sample model but with an interaction term for each subgroup. Differences in preferences between subgroups were tested using a log likelihood $\chi^2$ test of joint statistical significance for all interaction terms ($P < 0.05$). As with the full sample results, a Wald $\chi^2$ test was used to determine the statistical significance of differences between adjacent attribute levels ($P < 0.05$) for each attribute in each subgroup.

Finally, to examine the importance of the screening test attributes compared with the attributes that describe options for a child who tests positive, we used the results from the RPL model to predict the probability that the average respondent would choose screening tests with different attribute levels (27). Screening test A represented a screening test with the most preferred test attributes and the least preferred scenarios if the child tested positive. Screening test B represented a screening test with the least preferred test and the most preferred scenarios if the child tested positive. Table 2 lists the levels used for analyzing the predicted probability of selecting screening tests A and B.

**RESULTS**

A total of 1,866 potential parent respondents met eligibility criteria and consented to participate. Of those who consented to participate, 1,628 (87.2%) met the study quota requirements and 1,514 completed the survey. Respondents were excluded for completing the survey too quickly ($n = 480$) or without variability in answers ($n = 32$), leaving 1,002 respondents in the parent sample. A total of 705 potential pediatrician respondents met the eligibility criteria and consented to

| Table 1—Attributes and levels for the DCE questions in the pediatrician and parent surveys* |
| Attribute                                                                 | Level description                                                                 |
| How a child gets the test [How your child gets the test] | Saliva sample  
Finger prick  
Urine sample  
Venipuncture [Blood draw with a needle] |
| When and where a child gets the test [When and where your child gets the test] | Same day at your office or at your preferred lab [Same day at your doctor’s office or at their preferred lab]  
A different day at a separate lab or clinic |
| A family’s out-of-pocket cost for the screening test [Your personal out-of-pocket cost for the screening test] | None ($0)  
$5  
$30  
$50 |
| Level of education and monitoring provided [Education and monitoring through blood tests] | Education only  
Risk of DKA at time of diagnosis is 15–20%  
Education and blood tests every 6 months  
Risk of DKA at time of diagnosis is 3–4%  
Education and blood tests every 3 months  
Risk of DKA at time of diagnosis is 1% or less |
| An optional treatment is available to delay T1D | No treatment exists to delay T1D  
Optional treatment delays T1D by 1 year  
Side effect: nausea  
Optional treatment delays T1D by 2 years  
Side effect: 1–2% risk of serious infection |

*The brackets differentiate text used only in the parent survey; otherwise, both surveys used the same wording.
parents preferred tests conducted in the doctor’s office on the same day as the child’s appointment and that cost less. They preferred education and monitoring programs with a lower risk of DKA to education only, and they preferred scenarios in which the two optional treatments to delay onset of insulin dependence exist rather than a scenario in which no treatment exists.

Differences between the most and least preferred levels of each attribute convey the overall relative importance of that attribute, conditional on the attribute levels included in the survey. The change from education only with 15–20% risk of DKA to monitoring every 3 months with a ≤1% risk of DKA was the most important. Switching from no treatment available to a treatment that delays onset for 1 year with the side effect of nausea and moving from $50 out-of-pocket cost to $0 were the most important changes, and these changes were equally important. Moving from a scenario in which no treatment is available to a treatment that delays onset for 1 year with the side effect of nausea was the third most important. Switching from venipuncture to a urine sample and from having the test conducted on the same day at the pediatrician’s office or preferred laboratory to a different day at a separate laboratory or clinic were relatively less important given the range of levels presented in the survey.

Several parent subgroups demonstrated significantly different preferences. Respondents who had T1D or who had a child with T1D (n = 164) had statistically significantly different preferences compared with the rest of the sample (n = 838; test for joint significance of all interaction terms, P = 0.0009). Respondents with and without T1D experience preferred scenarios in which the two optional treatments to delay onset of insulin dependence exist over a scenario in which no treatment exists.

For pediatricians, the change from education only with 15–20% risk of DKA to monitoring every 3 months with a ≤1% risk of DKA and the change from $50 out-of-pocket cost to $0 were the most important changes, and these changes were equally important. Moving from a scenario in which no treatment is available to a treatment that delays onset for 1 year with the side effect of nausea was the third most important. Switching from venipuncture to a urine sample and from having the test conducted on the same day at the pediatrician’s office or preferred laboratory to a different day at a separate laboratory or clinic were relatively less important given the range of levels presented in the survey.

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whereas parents without T1D experience rated cost as similar in importance to the existence of a treatment to delay onset of insulin dependence. Respondents who had a child aged ≤5 years (n = 544) had statistically different preferences compared with the rest of the sample (n = 684; P = 0.0272). Parents with children who had insurance other than Medicaid (n = 318) had statistically different preferences compared with the rest of the sample (n = 684; P = 0.0272). Parents with children who did not have insurance or had Medicaid did not differentiate between methods. None of the pediatrician subgroups tested had statistically significant differences in preferences.

Predicted Choice Probabilities
For the tests presented in Table 2, on average, parents, including all the parent subgroups examined, and pediatricians were more likely to choose screening test B, a screening test with the least preferred test attributes and the most preferred scenarios if the child tested positive, over screening test A, a screening test with the most preferred test attributes and the least preferred scenarios if the child tested positive (Fig. 2). Pediatricians were somewhat more likely than parents to select screening test A, but the probability of selecting screening test B was still much higher.

CONCLUSIONS
To support the development of screening paradigms and to identify potential barriers to implementation of broad-based screening for T1D, we conducted a DCE survey to assess the preferences of parents and pediatricians for the features of T1D screening tests and their interest in T1D screening tests for all children. The results suggest that parents placed the highest relative importance on monitoring programs that reduced the risk of DKA to 1%, followed by the option of a treatment to delay the onset of insulin dependence by 1 or 2 years, and, finally, avoiding a $50 out-of-pocket cost. The mode of administration and location and timing of the test were much less important to parents. Pediatricians placed approximately equal importance on monitoring programs for patients that reduced the risk of DKA from 15 to 20% to 1% and on avoiding a $50 out-of-pocket cost. The mode of administration and location and timing of the test were much less important to parents. Pediatricians placed approximately equal importance on monitoring programs for patients that reduced the risk of DKA from 15 to 20% to 1% and on avoiding a $50 out-of-pocket cost.
Parents and pediatricians placed greater value on monitoring programs to lower the risk of DKA at diagnosis and a treatment to delay onset of insulin dependence than on test attributes. This finding was consistent with the qualitative interviews conducted to support the development of the DCE, during which physicians and parents ranked as important features of screening tests the existence of a plan to monitor children who test positive, education of families, and the availability of a treatment to delay onset (18). In support of these outcomes, previous studies have shown that education of families can result in a reduction of DKA (30,31), and the recent landmark teplizumab study has shown that a delay in diagnosis is possible (32). Although the feasibility of attaining DKA rates <1% has not been shown, this study was specifically designed to assess preferences to evaluate the relative importance between attributes. Although reduction of DKA to a rate <1% was more desirable than reduction of rates <3%, the result was not significant. This suggests the current methods we have for screening and monitoring to reduce DKA rates to 3–4% are acceptable to parents and physicians as an outcome for screening.

In addition, other benefits of screening could include minimizing long-term deteriorations to neurocognition and glycemic control by reducing the prevalence of DKA. Finally, screening for T1D also could identify potential participants for inclusion in trials of therapies intended to prevent or delay stage 3 T1D. If parents were offered a free test that was administered using their preferred mode and at their preferred location, 98% indicated they would have their child screened for T1D. Although 98% involvement in a screening program seems high, some respondents may have expressed a willingness to screen, because the question presented the most favored attributes (i.e., inclination to screen may not necessarily carry over from the ideal scenario to the real world). Among pediatricians, 94% said they would be likely or very likely to include a screening test for T1D as part of their practice if their preferred test was available, was recommended by the American Academy of Pediatrics, and was reimbursed by insurance.

In the absence of an approved therapy to prevent T1D, cost-effectiveness research analyzing the cost savings from a reduction in DKA could support insurance coverage and implementation of universal screening for T1D in children. In a recent cost-effectiveness study (33), researchers found a cost of $4,700 per case of T1D detected for children and adolescents enrolled in a screening program and $14,000 per case detected for routine screening in Denver, CO. The authors estimated that a 20% reduction in DKA events combined with 0.1% improvements in HbA1c levels would be needed for the program to reach a value threshold of $50,000–$150,000 per quality-adjusted life-year, and screening may be cost-effective in areas with a high prevalence of DKA. Furthermore, the JDRF T1D Fund, along with Health Advances, recently modeled the direct medical savings of a reduction in DKA at diagnosis (34).

There are several limitations associated with this study design. The survey presented hypothetical scenarios to respondents, which does not replicate the experience of talking with a doctor about test options or include all possible test attributes. Accordingly, decisions made in the survey may not fully predict decisions made in a clinical setting where other considerations may come into play. The duration of benefit for a disease-modifying therapy and side effects were combined in one attribute, limiting insights from this study into how respondents might trade off duration of benefit and side effects. However, in a DCE survey conducted by DiSantostefano et al. (35) among parents to elicit preferences for treatments to delay insulin dependence in children, duration of benefit, risk of serious infection, and chance of nausea were included. The results of that study demonstrated parents’ risk tolerance for treatments to delay insulin dependence and acceptable trade-offs between duration of benefit and side effects. In addition, although the sample recruitment included quotas for the child’s age, the preferences of the sample may not be representative of the broader population of parents or pediatricians. The percentage of parents in the parent sample who reported having T1D or a child with T1D was higher than expected for a general population sample and may have influenced screening preferences, and the subgroup analysis reports some differences in preferences around cost and the treatment to delay onset of insulin dependence. Similarly, the relatively high percentage of parents who identified as White, having a more than a high school education, being well insured, and having a high income...
may affect the generalizability of the results. For example, the subgroup analysis revealed some differences in preferences for parents of children with no insurance or with Medicaid. Finally, the use of a web panel to recruit parents and pediatricians may have limited the representativeness of the sample and the generalizability of the results. However, research has shown that results from online stated-preference surveys, in general, are not statistically significantly different from those elicited through face-to-face interviews (36,37).

In conclusion, parents and pediatricians participating in this study preferred screening tests that include education and monitoring plans to reduce the risk of DKA, have a treatment to delay T1D available, and have lower out-of-pocket costs. As T1D screening becomes more common, additional research on preferences, especially among different populations, can help identify opportunities for education and potential barriers to implementation.

The idea of implementing general population screening programs for T1D into the standard of care is relatively new, so discussions regarding translation into clinical care are still in the nascent stages. The data presented here could be used in discussions with payers and policy organizations to provide evidence of the need, preferences, and willingness of parents and pediatricians to participate in screening programs.

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