Costs of Public Health Screening of Children for Presymptomatic Type 1 Diabetes in Bavaria, Germany

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OBJECTIVE

We sought to evaluate costs associated with public health screening for presymptomatic type 1 diabetes in 90,632 children as part of the Fr1da study in Bavaria and in forecasts for standard care.

RESEARCH DESIGN AND METHODS

We report on resource use and direct costs for screening-related procedures in the Fr1da study coordination center and laboratory and in participating pediatric practices and local diabetes clinics. Data were obtained from Fr1da study documents, an online survey among pediatricians, and interviews and records of Fr1da staff members. Data were analyzed with tree models that mimic procedures during the screening process. Cost estimates are presented as they were observed in the Fr1da study and as they can be expected in standard care for various scenarios.

RESULTS

The costs per child screened in the Fr1da study were €28.17 (95% CI 19.96; 39.63) and the costs per child diagnosed with presymptomatic type 1 diabetes were €9,117 (6,460; 12,827). Assuming a prevalence of presymptomatic type 1 diabetes of 0.31%, as in the Fr1da study, the estimated costs in standard care in Germany would be €21.73 (16.76; 28.19) per screened child and €7,035 (5,426; 9,124) per diagnosed child. Of the projected screening costs, €12.25 would be the costs in the medical practice, €9.34 for coordination and laboratory, and €0.14 for local diabetes clinics.

CONCLUSIONS

This study provides information for the planning and implementation of screening tests for presymptomatic type 1 diabetes in the general public and for the analysis of the cost-effectiveness of targeted prevention strategies.

Type 1 diabetes is a chronic autoimmune disease characterized by destruction of the insulin-producing pancreatic β-cells and requires lifelong treatment with insulin (1). The worldwide prevalence of type 1 diabetes in individuals <20 years of age was estimated to be 0.4% in 2019 (2,3), and incidence rates are rising in many countries (1,3). The clinical onset of type 1 diabetes is often associated with diabetic ketoacidosis (DKA), which is a severe acute complication that can be life-

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threatening and is mainly caused by a delayed diagnosis of type 1 diabetes. The frequency of DKA at the onset of the disease has increased in the last two decades and is >20% in Germany and >45% in the U.S. (4–6).

The health and economic consequences of type 1 diabetes and DKA are significant. People with type 1 diabetes have an increased risk for various micro- and macrovascular complications (1,7) and a lower life expectancy (8) and experience a significant decrease in health-related quality of life (9,10). Presence of DKA at the time of clinical diagnosis is associated with worsened long-term blood glucose control and increases the risk of vascular complications and memory deficits (8,11–13). Excess annual medical expenditure per person with type 1 diabetes is estimated to be $6,288 in the U.S. (14), and €3,745 in Germany (15). The annual excess health care costs associated with DKA in both countries have a similar dimension and are estimated to be $7,612 and €3,605 in the U.S. and Germany, respectively (16,17).

Diagnosing type 1 diabetes at an early, presymptomatic stage may lower the incidence rate of DKA and could reduce morbidity in patients (18,19). However, previous studies indicated that screening for presymptomatic type 1 diabetes is unlikely to be cost-effective if only the health and economic benefits associated with prevention of DKA at disease onset are considered, unless the screening costs are less than $1 (16,20). Cost analyses must therefore also consider the long-term positive effects of screening for improved blood glucose control and reduced patient morbidity (20). In addition, now that interventions that delay disease progression are becoming realistic in type 1 diabetes (21,22), the cost-effectiveness of screening and early diagnosis required for any kind of targeted prevention strategy needs to be assessed from yet another perspective.

There have been few attempts to perform population-based screening for presymptomatic type 1 diabetes (23). Consequently, there are only limited estimates of the costs of such public health screening (16,20). In 2015, we initiated the Fr1da study in Bavaria, Germany, which to date is the largest public health screening program for presymptomatic type 1 diabetes worldwide (24,25). The study is conducted in collaboration with pediatric practices in the context of routine child care and included >90,000 children at the time of our analysis.

Here, we present a detailed description of the costs associated with public health screening for presymptomatic type 1 diabetes in the Fr1da study research setting, including costs per child screened and costs per case diagnosed, and provide estimates of the corresponding costs that would be expected in standard care in Germany.

RESEARCH DESIGN AND METHODS

Study Participants

The Fr1da study offered screening for islet autoantibodies to children aged 1.75–5.99 years in Bavaria, Germany. Families of children who were positive for multiple islet autoantibodies (i.e., presymptomatic type 1 diabetes) were invited to participate in a program of diabetes education, metabolic staging, assessment of psychological stress associated with diagnosis, and prospective follow-up for progression to clinical diabetes. Details on the Fr1da study protocol have previously been published (24,25). The study was approved by the institutional review board at Technical University Munich. This analysis includes data from 90,632 children (median age 3.1 years; interquartile range 2.1–4.2; 47% girls) who participated in the Fr1da study between February 2015 and May 2019, of whom 280 (0.31%) were diagnosed with presymptomatic type 1 diabetes (25).

Procedures in the Fr1da Study

Recruitment, Consenting, and Blood Sampling

Study participants were recruited during medical checkups in pediatric practices. Primary care pediatricians offered screening to families, obtained written informed consent from the parents or legal guardian, and took a capillary blood sample from the child. Once a week, the pediatricians sent the collected blood samples by courier to the Fr1da study coordination center and laboratory. The coordination center provided pediatricians with study materials (i.e., information and consent forms, lancets, and blood collection tubes) and established a telephone hotline for additional information.

Blood Sample Processing, Islet Autoantibody Measurements, and Results Communication

In the Fr1da study coordination center and laboratory, the samples were processed and prepared for analysis. Processing included centrifugation of capillary blood samples to obtain serum. Data associated with the samples were entered into the study database. If necessary, the study center contacted the pediatricians to complete missing information. Sera were tested for the presence of autoantibodies to GAD (GADA), insulinoma-associated antigen-2 (IA-2A), and zinc transporter 8 (ZnT8A) with the 3 Screen Islet Cell Antibody ELISA (RSR Ltd., Cardiff, U.K.) (26,27). If the ELISA result was positive, GADA, IA-2A, ZnT8A, and insulin autoantibodies (IAA) were each tested for separately in the remaining serum with radiobinding assay (RBA) (28–30). If two or more distinct islet autoantibodies were detected in the RBAs, a venous blood sample was requested for confirmation and retested separately for GADA, IA-2A, ZnT8A, and IAA with RBAs. The results of the autoantibody measurements were reviewed and discussed by a physician, a scientist, and a laboratory technician during weekly consultation meetings. Children were diagnosed with presymptomatic type 1 diabetes if positive for two or more islet autoantibodies in both the screening and confirmation samples. In these cases, the child's pediatrician was informed of the diagnosis and autoantibody status. The pediatrician then informed the family and arranged contact with the Fr1da study coordination center.

Staging and Education

Children with presymptomatic type 1 diabetes were invited to participate in metabolic staging and an educational program at a pediatric diabetes clinic close to the family's home. An oral glucose tolerance test was performed for staging, and glycated hemoglobin (HbA_{1c}) was measured. Presymptomatic type 1 diabetes was classified as stage 1, 2, or 3 as previously advocated (31,32).

Design of Costing Approach

We describe the direct medical costs that result from the Fr1da public health screening from a health care system perspective. For this purpose, we adopted a

microcosting approach, in which we evaluated the time and resources associated with screening using respective prices or reimbursement rates within the German health care system. Specifically, we examined the extra costs per child screened for presymptomatic type 1 diabetes. This included the cost of time for physicians, nurses, laboratory staff, and scientists, as well as the cost of materials used to inform families about the Fr1da study, obtain consent, draw capillary or venous blood, analyze samples, and report results. Furthermore, this included the cost of staging and educating children with presymptomatic type 1 diabetes at a local diabetes clinic.

In our analysis, we subdivided the costs per child screened in the Fr1da study into three categories: *1*) costs of sample acquisition, *2*) costs of sample analysis and result communication, and *3*) costs of staging and education. Within the first two categories, we distinguished between costs for participating pediatricians and for the Fr1da study coordination center and laboratory. Costs for metabolic staging and education of children diagnosed with presymptomatic type 1 diabetes were incurred only by local diabetes clinics.

To determine these costs, we described the patient flow and associated resource uses within the three categories of the screening process in respective tree models. Main data sources were the Fr1da study documents detailing the sequence of tests and communication for each of the 90,632 participating children, an online survey returned by 134 of the 682 participating primary care pediatricians, and documentation of time sheets and interviews with Fr1da study coordination center and laboratory staff.

Assessment of Costs and Probability of Screening Procedures

Costs were estimated through identification of all events during the screening process that were associated with any resource use (e.g., time or material). For each identified event, we assessed the amount of resources consumed and multiplied this amount by the unit costs of the respective resource.

The amount of resources was assessed in different ways. Regarding time spent by pediatricians, we used survey data (Supplementary Material) that contained information on who (i.e., nurse or pediatrician) performed a specific procedure (e.g., blood collection) at the practice and how much time it took. In the analysis, we used 75% of the time estimated by doctors to take into account an overestimation, as previously described (33,34). Furthermore, the data were whiskered excluding the upper and lower 5% of response values. Regarding time spent by staff at the Fr1da study coordination center and laboratory, we conducted interviews and reviewed time sheets to estimate the time needed for logistics (e.g., hotline or data management), sample processing, antibody measurements, and evaluation of test results. An overview of the estimated resource units used per child screened can be found in Supplementary Table 1.

The cost of medical staff time used was estimated with federal income statistics for nurses', laboratory workers', and scientists' time costs (35,36) and data from a representative survey on the economic situation of ambulatory physicians (Zentralinstitut für die kassenärztliche Versorgung in der Bundesrepublik Deutschland Praxis Panel [ZiPP]), including income statistics for pediatricians (37). The material costs were drawn from the cost plan of the Fr1da study. Costs for staging and education were drawn from the uniform valuation standard (Einheitlicher Bewertungs-maβstab [EBM]) of the National Association of Statutory Health Insurance Physicians (Kassenärztliche Bundesvereinigung [KBV]) (38). Details on the estimated costs per unit can be found in Supplementary Table 2.

The cost per procedure was multiplied by the respective probability of occurrence. The main data sources for the probability assessment were Fr1da study documents, which included tracking of the sequence of tests and communication (e.g., sample requests) regarding every sample.

Assessment of Uncertainty

We used empirical distributions on key cost and probability parameters to estimate the uncertainty around our cost estimates. To estimate respective 95% CIs, we drew 1,000 random values of the respective distributions. Likewise, we conducted 1,000 simulations of the different models, simultaneously drawing random values from all underlying cost and probability distributions.

Scenarios for Islet Autoantibody Screening in Routine Care

Further to the analysis of costs as observed in the Fr1da study, we adapted the analysis model to mimic screening for presymptomatic type 1 diabetes in standard care in Germany. For the projected standard care scenario, we considered only 50% of the costs associated with obtaining informed consent in the Fr1da study and assumed that negative screening results would be communicated to families only if a second blood sample was requested to confirm the initial screening results. Furthermore, we assumed that all children diagnosed with presymptomatic type 1 diabetes would receive metabolic staging and diabetes education as part of standard care.

In addition, several other scenarios were analyzed. First, we repeated the analysis under standard care conditions but included higher (€4.96 per minute) or lower (€1.24 per minute) pediatrician time costs, as these costs vary across countries. Second, we analyzed the standard care scenario with higher (€3.60 per test) or lower (€1.40 per test) costs for the 3 Screen Islet Cell Antibody ELISA—a range based on the expected market price of the test kit when purchased outside of a research setting where special discounts are granted.

RESULTS

Cost of Screening for Presymptomatic Type 1 Diabetes as Observed in the Fr1da Study

The costs associated with screening in the Fr1da study were estimated for *1*) sample acquisition, *2*) sample analysis and result communication, and *3*) staging and education and are summarized in Fig. 1 (cost of each measure) and Table 1 (total cost per child), with the calculation of costs explained in Supplementary Table 3.

Costs for Sample Acquisition

A total of 90,632 children were recruited to participate in screening for presymptomatic type 1 diabetes (Fig. 1*A*). Per child, the pediatric practice incurred an average of €12.77 for obtaining informed consent, €3.40 for the collection of a capillary blood sample, and €0.72 for packaging the sample. The average time required for sample acquisition in the pediatric practice was 14 min, including information and consent (5.14 min),

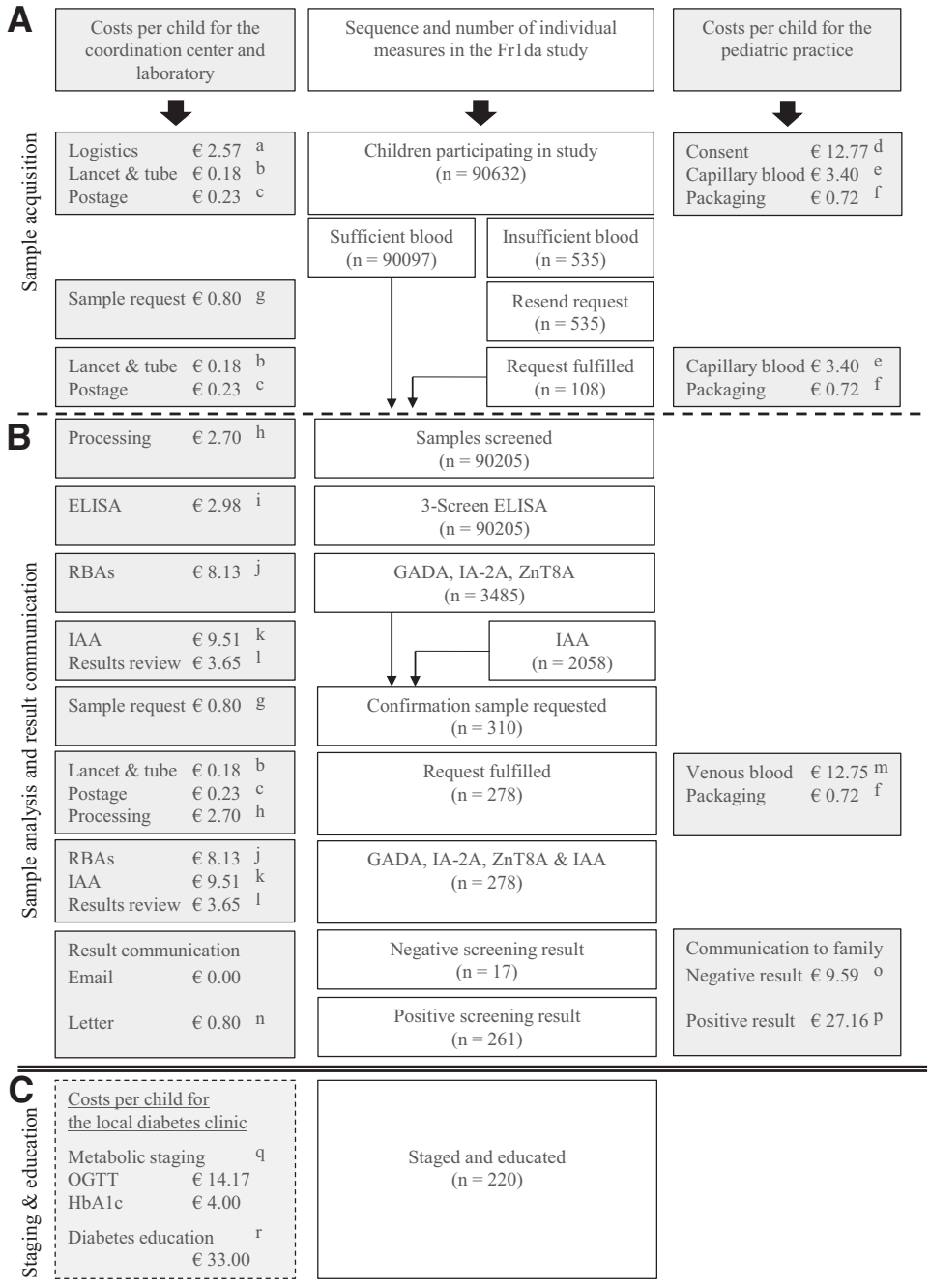

Figure 1—Flowchart of the sequence and number of individual measures in screening children for presymptomatic type 1 diabetes, and associated cost items and average costs per child, as observed in the Fr1da study for sample acquisition (*A*), sample analysis and results communication (*B*), and staging and education (*C*). Costs incurred are listed separately for the Fr1da study coordination center and laboratory (boxes on the left), the pediatric practice (boxes on the right), and the local diabetes clinic (box bottom left). Indicated is how often the respective measure was carried out (boxes in the middle). Index letters to the right of each cost item refer to information in Supplementary Table 3 on the calculation of costs per measure. OGTT, oral glucose tolerance test; 3-Screen ELISA, 3 Screen Islet Cell Antibody ELISA measuring GADA, IA-2A, and ZnT8A.

capillary blood collection (4.00 min), and packaging of samples (4.90 min). These activities were performed by physicians in 100%, 23%, and 6% of cases, respectively, and by nurses for the remaining proportions. The costs of the Fr1da study coordination center per child for sample acquisition were on average €0.18 in material costs for lancets and tubes, €0.23 in shipping costs per sample, and €2.57 in logistics and infrastructure costs.

From 535 children, the blood sample sent to the laboratory was not sufficient for screening, so the coordination center contacted the pediatrician and requested a new sample (€0.80 postage per child). A second screening sample was obtained from 108 of the 535 children, resulting in costs for time and materials for capillary blood collection and for packaging and shipping the samples (Fig. 1*A*).

The average total cost of sample acquisition per child enrolled in the

Table 1—Cost of screening for presymptomatic type 1 diabetes as observed in the Fr1da study

	Total costs	Pediatric practice	Coordination center and laboratory
Cost per child screened	€28.17 (19.96; 39.63)	€18.70 (10.82; 30.28)	€9.35 (8.18; 10.46)
Sample acquisition	€19.96 (12.16; 30.97)	€16.96 (9.25; 28.05)	€2.99 (2.25; 3.68)
Sample analysis and results communication	€8.10 (6.33; 11.03)	€1.74 (0.35; 4.66)	€6.36 (5.47; 7.20)
Metabolic staging and education*	€0.11 (0.10; 0.13)		
Cost per case diagnosed†	€9,117 (6,460; 12,827)	€6,052 (3,503; 9,801)	€3,028 (2,649; 3,385)

Data are means (95% CI). *Probabilistic cost per child screened for metabolic staging and education were completely accounted for as costs for the local diabetes clinics. †The costs per case diagnosed for the local diabetes clinic were €37.11 (95% CI 32.26; 41.98).

Fr1da study was €19.96 (95% CI 12.16; 30.97), of which €16.96 (9.25; 28.05) was for the pediatric practice and €2.99 (2.25; 3.68) for the coordination center and laboratory (Table 1).

Costs for Sample Analysis and Results Communication

For each of the 90,205 blood samples received with sufficient volume for screening (Fig. 1*B*), the average laboratory costs were €2.70 for sample processing (including €0.18 in material costs and €0.07 for queries to the pediatric practice) and €2.98 for the ELISA test (including €1.20 in material costs). In addition, the average costs for RBA testing of GADA, IA-2A, and ZnT8A in 3,763 samples were €8.13 (including €5.50 in material costs) and of IAA in 2,336 samples were €9.51 (including €6.50 in material costs). For the review and interpretation of RBA results by a medical specialist, a scientist, and a laboratory staff member, an average cost of €3.65 (for 1 min) per sample was estimated. Following data review, the pediatricians of 310 children were contacted by the coordinating center because two or more islet autoantibodies were detected positive in the screening sample, and an additional venous blood sample was requested for confirmation in each case (€0.80 postage per child). Nineteen children developed clinical type 1 diabetes before the confirmatory sample was collected. A venous blood sample was obtained from 278 children. Pediatricians incurred average costs of €12.75 per venous blood draw. As previously described for capillary blood, other costs were associated with sample collection materials, sample packaging and shipping, sample processing and RBA testing, and assessment of results. Of the 278 venous blood samples, 261 were confirmed as positive for multiple islet autoantibodies in RBAs, and the children were diagnosed with presymptomatic type 1 diabetes. The child's pediatrician received a letter with the findings and diagnosis (€0.80 postage per child), while negative screening results were communicated by automated e-mail (€0.00). The average cost of the pediatrician to communicate the diagnosis to the family was estimated at €27.16 (time costs only). In addition, pediatricians discussed a negative screening result in the confirmatory sample with families in 18% of cases, which was associated with a time cost of €9.59 per case (€1.73 per negative result).

The average total cost of sample analysis and result communication per child enrolled in the Fr1da study was €8.10 (95% CI 6.33; 11.03), of which €1.74 (0.35; 4.66) was for the pediatric practice and €6.36 (5.47; 7.20) for the coordination center and laboratory (Table 1).

Costs for Staging and Education

A total of 220 children diagnosed with presymptomatic type 1 diabetes received metabolic staging and education at local diabetes clinics (Fig. 1*C*). The costs for an oral glucose tolerance test and HbA_{1c} measurement were €14.17 and €4.00, respectively (38). The cost per child and family educated was estimated at €33.00. The average total cost of staging and education per child enrolled in the Fr1da study was €0.11 (95% CI 0.10; 0.13) (Table 1).

Composite Cost of Screening for Presymptomatic Type 1 Diabetes

The average total cost of screening for presymptomatic type 1 diabetes per child enrolled in the Fr1da study was €28.17 (95% CI 19.96; 39.63), of which €18.70 (10.82; 30.28) was incurred by the pediatric practice, €9.35 (8.18; 10.45) by the coordination center and laboratory, and €0.11 (0.10; 0.13) by the local diabetes clinic (Table 1).

Overall, 280 (0.31%) of 90,632 children were diagnosed with presymptomatic type 1 diabetes. The average cost per diagnosed child was €9,117 (95% CI 6,460; 12,827) (Table 1).

Estimated Cost of Screening for Presymptomatic Type 1 Diabetes in Standard Care in Germany

In a simulated standard care scenario for Germany, assuming the same prevalence of presymptomatic type 1 diabetes of 0.31% as in the Fr1da study, the average cost per child for screening was estimated at €21.73 (95% CI 16.76; 28.19), including €9.34 (8.29; 10.42) for laboratory costs, €12.25 (7.24; 18.52) for pediatrician costs, and €0.14 (0.12; 0.15) for local diabetes clinics to perform metabolic staging and education for children diagnosed with presymptomatic type 1 diabetes (Table 2). In this model, 50% of the costs incurred in the Fr1da study for obtaining informed consent were included, negative autoantibody results in the initial screening sample were not communicated to families, and all children with presymptomatic type 1 diabetes underwent staging and education. The estimated average cost per diagnosed child was €7,035 (95% CI 5,426; 9,124) (Table 2).

Alternative models were based on the standard care scenario but included calculations of higher (plus 100%) or lower (minus 50%) pediatrician time costs or estimation of lower or higher costs for the 3 Screen Islet Cell Antibody ELISA (Table 2). The average cost per child for screening for presymptomatic type 1 diabetes ranged from €15.70 (95% CI 13.28; 18.51) up to €33.80 (23.72; 47.43) in these models. Results of the analysis showed that screening costs

Table 2—Cost of screening for presymptomatic type 1 diabetes as estimated for standard care in Germany

Simulated standard care scenarios	Total costs	Pediatric practice	Coordination center and laboratory
Cost per child screened (model A)*	€21.73 (16.76; 28.19)	€12.25 (7.24; 18.52)	€9.34 (8.29; 10.42)
Cost per case diagnosed†	€7,035 (5,426; 9,124)	€3,967 (2,344; 5,996)	€3,024 (2,684; 3,373)
Model A plus 100% pediatrician time costs	€33.80 (23.72; 47.43)	€24.21 (14.61; 37.28)	€9.45 (8.41; 10.53)
Model A minus 50% pediatrician time costs	€15.70 (13.28; 18.51)	€6.27 (4.07; 8.87)	€9.29 (8.26; 10.38)
Model A with lower 3-Screen ELISA costs (€1.4 per test)	€21.93 (19.96; 28.39)	€12.25 (7.24; 18.52)	€9.54 (8.49; 10.62)
Model A with higher 3-Screen ELISA costs (€3.6 per test)	€24.13 (19.16; 30.59)	€12.25 (7.24; 18.52)	€11.74 (10.69; 12.82)

Data are means (95% CI). 3-Screen ELISA, 3 Screen Islet Cell Antibody ELISA measuring GADA, IA-2A, and ZnT8A. *Probabilistic costs for metabolic staging and education were €0.14 (95% CI 0.12; 0.15) in the simulated standard care scenario and completely accounted for as costs for the local diabetes clinics. †The costs per case diagnosed for the local diabetes clinic were €44.02 (95% CI 38.19; 49.80).

were more sensitive to changes in physician time costs than to changes in ELISA test kit costs.

CONCLUSIONS

In this study, we provide detailed information on the costs associated with a public health screening for presymptomatic type 1 diabetes in Germany. We report these costs as observed in the Fr1da study, totaling €28.17 per child studied, and specifically as incurred by participating pediatricians, the study coordination center and laboratory, and local diabetes clinics. In addition, we estimate the total costs that would be expected for screening as part of standard care in the German health care system to be €21.73 per child screened. We believe that our data provide useful reference values for the planning and implementation of screening tests for presymptomatic type 1 diabetes in the general population and for assessing the cost-effectiveness of targeted prevention strategies.

Our study has two major strengths. First, the Fr1da study is the largest population-based screening study to date for presymptomatic type 1 diabetes without prior selection for genetic risk or family history (24,25). Second, in the current study we used various data sources for a microcosting approach within the Fr1da study. This includes detailed information on the cost of acquiring, processing, and analyzing samples and communicating results, as well as the cost of metabolic staging of children diagnosed with presymptomatic type 1 diabetes, combined with specific education for affected families. To our knowledge, such a granular cost analysis is unprecedented in the field of type 1 diabetes screening, and it allowed us to detail the direct medical costs associated with public health screening from a health care system perspective.

Besides the Fr1da study, another large-scale population-based screening program for the early detection of presymptomatic type 1 diabetes in children is currently underway in the U.S., the Autoimmunity Screening for Kids (ASK) Program in Denver, CO. In the ASK Program, the cost per screened child was recently estimated to be $47 in the observed data and $141 in routine care (20), which is overall higher than the costs for public health screening in the Fr1da study. However, in comparing the costs observed in the two studies, it should be noted that the study design and scope of the underlying data differ. In the Fr1da study, screening was implemented in a routine care setting in collaboration with outpatient pediatric practices, considered only children aged 2–5 years, and included >90,000 children at the time of analysis (25). The ASK Program covered a broader age range (2–17 years) and had ∼10,000 participants at the time of the economic analysis. In comparison with the ASK cost study by McQueen et al. (20), we used a more detailed cost assessment in our study, but most importantly, the cost of health care services are much higher in the U.S. than in Germany or other European countries (39). The significant cost difference between the observed and routine care scenarios in the ASK Program screening results from the large difference between the negotiated fee for laboratory services of $15 in the study and the assumed commercial price of $138 in routine care. For comparison, the negotiated material cost for the Fr1da study for the 3 Screen Islet Cell Antibody ELISA was €1.20 per sample tested. Negotiated costs for laboratory services are specific to the two studies, and a "real-world" price for the required laboratory services is not yet available. However, due to scaling effects, the cost of test kits is expected to decrease in the long-term as screening for presymptomatic type 1 diabetes becomes standard care in many health systems. In a simulated standard care scenario, we varied the material costs for the ELISA up to €3.60 per test and sample. The tripling of ELISA costs increased the projected cost per child screened from €21.73 to €24.13 (by 11%).

Because of wide variation in test characteristics, proportion of positive results, and treatment options for individuals who test positive, it is difficult to compare the costs of different public health screening programs. In Germany, the extended newborn screening that screens for 14 different diseases would be one possible comparator. In 2017, the frequency of a child having a positive screening result was 1 of 999 (∼0.1%) (40) compared with ∼0.3% in the Fr1da study (25). The costs of the newborn screening at the physician site, including information, capillary blood draw, and shipping, are €14.83 (38). The costs of laboratory sample analysis were €11.55 until 2016 (12 diseases) and increased to €16.38 and €24.70 after the introduction of screening for cystic fibrosis and severe combined immunodeficiency, respectively.

Further research is needed to determine whether the costs of early diagnosis of type 1 diabetes through screening in children are outweighed by associated reductions in future health care costs and improvements in quality of

life and life expectancy. Screening for presymptomatic type 1 diabetes combined with education and care for affected families is very likely to reduce the incidence of DKA at onset of type 1 diabetes (18,19,25). This would prevent the occurrence of life-threatening conditions and have a positive impact on long-term health outcomes for patients with type 1 diabetes (11–13). In addition, there are other benefits of diagnosing individuals at an early stage of type 1 diabetes. Screening and identifying such individuals are the prerequisite for targeted strategies to treat presymptomatic type 1 diabetes in the future (21,23).

It is important to acknowledge that the costs associated with screening for presymptomatic type 1 diabetes presented here are specific to Germany. Our sensitivity analyses show that results are sensitive to time costs of health care professionals. Previous studies have shown that respective costs are much higher in the U.S. compared with Germany and other European countries. However, there is much less variation within European countries (39). This must be taken into account in transferring the results of this study to other countries and health care systems.

Our study has limitations that must be considered. For the cost analysis of the Fr1da study, we excluded campaign costs, although there was substantial spending on public advertising and commercials, in pediatric practices, and online. Two main reasons for this decision were lack of valid data and that these costs would only be relevant in a study setting—not in standard care. Furthermore, we did not consider overhead or fixed costs such as costs for the building or general equipment, which may result in an underestimation of laboratory costs. In addition, time cost estimates are based on pediatricians' self-reported time spent on screening-related procedures, and despite appropriate adjustments, actual time costs may be over- or underestimated. Furthermore, time spent by nurses was also estimated by physicians. This increases the uncertainty around these estimates. If the screening were established in standard care, it would be more likely that the time spent per child screened could be less than in the Fr1da study. Finally, we did not include follow-up monitoring of children diagnosed with presymptomatic type 1 diabetes in our cost analyses; rather, we focused on the one-time expenditure per child for screening and staging.

In conclusion, our study results provide a cost estimate for public health screening for presymptomatic type 1 diabetes including detailed insights into the costs of each associated procedure. By virtue of presenting our microcosting approach in a transparent manner, the estimates can be easily adapted to other countries and scenarios. This information can help improve the effectiveness of screening and be provided for health policy planners seeking to implement similar screening elsewhere. In addition, the study results are important for assessment of the cost-effectiveness of targeted type 1 prevention strategies.

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