Parental anxiety after 5 years of participation in a longitudinal study of children at high risk of type 1 diabetes

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Funding information
Lion Club International; Skåne County Council Foundation for Research and Development; Strategic Research Area Exodiab; SUS Funds; Swedish Childhood Diabetes Foundation; Swedish Diabetes Association; Swedish Foundation for Strategic Research; The Kristianstad Central Hospital Research and Development Fund; The Royal Physiographic Society; Vetenskapsrådet; Diabetes Association

Abstract
Aim: Parents of children participating in screening studies may experience increased levels of anxiety. The aim of this study was to assess parental anxiety levels after 5 years of participation in the Diabetes Prediction in Skåne study. Associations between parental anxiety about their child developing type 1 diabetes and clinical, demographic, and immunological factors were analyzed.

Method: Mothers and fathers of participating 5-year-old children answered a questionnaire regarding parental anxiety associated with their child's increased risk of type 1 diabetes. Anxiety levels were assessed using the State Anxiety Inventory scale. Data were analyzed using logistic and multinomial regression.

Results: Parents of 2088 5-year-old children participated. Both parents answered the questionnaire for 91.2% (n = 1904) of children. In 67.1% of families, neither parent reported being anxious that their child had an increased risk of developing type 1 diabetes. Anxiety was higher in mothers of children positive for autoantibodies (OR 2.21 95% CI 1.41, 3.48, P < .001) and those perceiving their child had a higher risk for type 1 diabetes (2.01; 1.29, 3.13, P = .002). Frequency of worry was associated with parental anxiety (mothers 5.33; 3.48, 8.17, P < .001, fathers 5.27; 3.51, 7.92, P < .001). Having a family member with type 1 diabetes and having lower education level were also associated with increased anxiety.

Conclusions: Diabetes in the family, the child's autoantibody status, education level, frequency of worry and risk perception where associated with higher parental anxiety. These findings add to our understanding of the impact of screening for type 1 diabetes in children on parental anxiety.

Keywords
anxiety, autoantibodies, child, diabetes mellitus, genetic testing

1 | INTRODUCTION

Screening for risk is of uncertain benefit in diseases with no established cure or prevention like type 1 diabetes. Nevertheless, the...
Type 1 diabetes is one of the most common chronic pediatric diseases, and its incidence is increasing in Sweden and worldwide. Sweden has the second highest incidence of type 1 diabetes in genetically susceptible children after Finland. Children in Sweden who develop type 1 diabetes are being diagnosed at increasingly younger age regardless of gender. What triggers the progressive autoimmune destruction of the pancreatic beta cells is still unknown. However, during the autoimmune process, islet autoantibodies to glutamic acid decarboxylase (GAD65), insulinoma-associated protein 2 (IA-2A), insulin (IAA), and zinc transporter 8 (ZnT8A) can be detected in the blood and used as risk biomarkers for developing type 1 diabetes. The risk of developing type 1 diabetes increases with the number of different positive islet autoantibodies: 12.7%, 61.6%, and 79.1% of children with one, two, and three or more autoantibodies, respectively, will develop type 1 diabetes within 10 years.

Parental anxiety has been previously investigated in relation to genetic risk of type 1 diabetes and autoantibody development, but of those studies focused most on mothers. Parental anxiety increases both at the time the parents are informed about their child's genetic risk and when they receive information about autoantibody positivity. In the few studies looking at both parents, mothers reported greater anxiety than fathers. Johnson et al. reported high anxiety among parents coming from families with a family member with type 1 diabetes when their high risk child participated in clinical trials. Another study showed that both maternal and paternal anxiety increase with the number of autoantibodies, with parents of children with multiple autoantibodies reporting the highest anxiety levels. Some studies have indicated that anxiety decreases over time, while a recent large international study indicated that 43% of mothers and 34% of fathers still report high levels of anxiety 3 years after their child was informed about the first islet autoantibody. Other factors associated with parental concern and anxiety surrounding the child's risk of disease development are educational level, parental age, employment status, and if the parents underestimate the child's risk. Except for the publication based on data from The Environmental Determinants of Diabetes in the Young (TEDDY) study 2017, most of the studies were small, with a short follow-up and mostly in mothers. In that study, the authors investigated both mothers' and fathers' anxiety over time related to their child's autoantibody status in a large international cohort. In our study, we investigated both maternal and paternal anxiety in the parents of children at increased risk of type 1 diabetes after 5 years of participation in a prospective follow-up study. The aim was to determine the level of parental anxiety regarding their child's risk of developing type 1 diabetes and to examine variables associated with parental anxiety. We hypothesize that parental anxiety is associated with the child's autoantibody status, parental risk perception, and the frequency of parental worry.

2 | METHODS

2.1 | The DiPiS study

The Diabetes Prediction in Skåne (DiPiS) study screened 35,683 children at birth for their risk of developing type 1 diabetes between September 2000 and August 2004 at the five maternity clinics in the south of Sweden. DiPiS is a prospective, longitudinal study of children at increased risk of type 1 diabetes to identify potential environmental risk factors. The increased risk of type 1 diabetes was based on a calculated risk score based on genetic risk (HLA genotype), presence of maternal infections during pregnancy, maternal diabetes, cord blood autoantibodies, and high or low relative birthweight. Children were followed annually from 2 years until 15 years of age with a blood draw and a questionnaire for both parents. The blood sample was analyzed for GAD65A, IA-2A, IAA, and ZnT8A. If one islet autoantibody was detected, the family was contacted by phone by a nurse to inform them about a small increase in the risk of their child developing type 1 diabetes. Those families were not contacted again if autoantibody status remained stable. Children developing more than one autoantibody or progressing from one to multiple autoantibodies were contacted by a pediatrician and informed about the increased risk of the child developing type 1 diabetes. Those families were offered a more frequent follow-up schedule with blood sampling every 3 months for HbA1c, plasma glucose, and an annual oral glucose tolerance test.

At the 3-year follow-up, the parents were asked if they would like to know their child's genetic risk. Parents were informed by a letter containing information on genetic risk: either <1/100, 1/100, 2/100, and 3/100, where 2/100 and 3/100 indicated a high genetic risk for developing type 1 diabetes. The DiPiS study has been described in detail elsewhere.

The Ethics Review Board at Lund University, Lund, Sweden approved the DiPiS study. Written informed consent was obtained from all participating parents.

2.2 | Study population

This study included children who had been followed in the DiPiS study for at least 5 years, where at least one of the parents had filled out the 5-year questionnaire with at most three of six items missing in the SAI, and where at least one blood sample had been analyzed for islet autoantibodies. The final dataset was comprised of n = 2088 children, n = 2059 mothers, and n = 1933 fathers.
2.3 | Sociodemographic and parental lifestyle measures

Information about the parents' educational level and social status was collected from a questionnaire collected at 2 months, while information about employment and support from other persons was collected from the annual questionnaires from 2 years of age. Education was grouped into either low (elementary school and gymnasium) or high (university). Information regarding diabetes in the immediate family was recorded from both the 2-month and the 5-year questionnaires. An FDR was defined as a mother, father, or a full sibling with type 1 diabetes.

2.4 | Parental worry and anxiety about the child's type 1 diabetes risk

The State-Trait Anxiety Inventory (STAI) contains 40 items, 20 assessing the state anxiety (State Anxiety Inventory scale, SAI-how the person feels right now), and the other 20 assessing trait anxiety (State Trait Inventory scale, STI-how the person generally feels). Several studies have described a six-item short-form SAI (SAI-6). The six-item SAI scale can be converted to the 20-item SAI scale for comparison, with the six-item and 20-item SAI results being highly correlated. Prior studies using the 20-item SAI classify a parent with a score >40 as highly anxious. In our study, parental anxiety about the child's risk for type 1 diabetes was measured annually using the SAI-6 questionnaire, with the score rescaled to correspond to the 20-item SAI.

Parental frequency of worry was assessed using the following question: "How often do you worry that your child will develop type 1 diabetes?", with possible answers being never, rarely, sometimes, often, and very often. Responses were then grouped into 1 (never worried), 2 (rarely worried), and 3 (sometimes, often, or very often worried).

2.5 | Risk perception

Both parents, in separate questionnaires, answered the following question: "Compared to other children, do you think that your child's risk of developing diabetes is much lower, slightly lower, about the same, a little higher, or much higher?". The responses were grouped into lower risk (much lower and slightly lower risk), same risk (about the same), and higher risk (a little higher and much higher risk).

2.6 | Statistical analyses

The SAI score was treated both as a three-level variable and as a binary variable. The SAI score was dichotomized into "higher anxiety" (SAI > 40) and "lower anxiety" (SAI ≤ 40). The three-level SAI score was categorized as follows: "lowest anxiety" (SAI 22.05), "moderate anxiety" (SAI 24-40), and "higher anxiety" (SAI > 40). An SAI score of exactly 22.05 was obtained for n = 470 (22.8%) mothers and for n = 588 (30.4%) fathers, where the lowest category of anxiety was selected for all questions, which means very calm, not at all worried, very relaxed, not at all tense, very at-easy and not at all nervous. We hypothesized that parents who answered that way were in some way different from those who did not. We therefore treated individuals with a score of exactly 22.05 as a separate group. The next higher score in our dataset was 24.67, hence the three-level scoring definition. The autoantibody status was said to be "positive" if at least one autoantibody was detected.

Multinomial regression was used for the analyses with the three-level SAI outcome and logistic regression was used with the binary SAI score as the outcome. Three models were fit for mothers and fathers separately for each outcome. Model 1 estimated the association between anxiety and autoantibody positivity adjusting for potential confounders (HLA risk, FDR, and child gender); model 2 estimated the association between anxiety and the parent's perception that their child was at a higher risk of developing type 1 diabetes, adjusting for potential confounders (autoantibody positivity, HLA risk, FDR status, and education); and model 3 estimated the association between anxiety and how often the parent felt worried about their child developing the disease, adjusting for potential confounders (autoantibody positivity, HLA risk, FDR status, education, working status, level of support, perceived risk, and if the parents were living together with the child or not). The three-level SAI score was used in the main analysis and the binary SAI score in the sensitivity analysis. P-values were based on the Wald test. R version 3.5.0 (r-project.org) and SPSS version 24 (IBM SPSS, IBM Corp., Armonk, New York) were used for the statistical analyses.

3 | RESULTS

The study population consisted of n = 2088 children; 1053 girls and 1035 boys. The majority of children were from the general population with no history of type 1 diabetes in the family (n = 1855, 88.8%), while 175 (8.4%) had an FDR with the disease. Information on FDR was missing for 58 (2.8%) children. In the majority of cases, both parents completed the questionnaire (n = 1904, 91.2 %), with 29 questionnaires answered only by the fathers and 155 only by the mothers. A total of 2059 (98.6%) mothers and 1933 (92.6%) fathers completed the SAI in the questionnaires. Table 1 describes the distribution of all variables used in the analysis, stratified by maternal and paternal anxiety levels.

When the parents filled out the 5-year questionnaire, their knowledge about the risk of their child developing type 1 diabetes was based on HLA testing and autoantibody results from the 2, 3, and 4-year blood samples. Up to 4 years of age, 1986 (95.1%) children were negative for islet autoantibodies, 79 (3.8%) had one autoantibody, and 23 (1.1%) were positive for multiple autoantibodies. The HLA group distributions were similar for <1/100 (32.1%), 1/100 (26.1%), and 2/100 (29.7%), with the 3/100 group containing the
TABLE 1  Distribution of all variables used in the analysis, stratified by anxiety level of mothers and fathers separately (n mothers = 2059 and n fathers = 1933)

| Child characteristic | Mothers | Fathers |
|----------------------|---------|---------|
|                      | SAI 22.1 | SAI >22.1-40 | SAI >40 | SAI 22.1 | SAI >22.1-40 | SAI >40 |
|                      | 470 n (%) | 1169 n (%) | 420 n (%) | 588 n (%) | 1059 n (%) | 286 n (%) |
| Gender               |          |          |          |          |          |          |
| Male                 | 247 (52.6) | 565 (48.3) | 206 (49.0) | 294 (50.0) | 507 (47.9) | 154 (53.8) |
| Female               | 223 (47.4) | 604 (51.7) | 214 (51.0) | 294 (50.0) | 552 (52.1) | 132 (46.2) |
| FDR                  | 12 (2.6) | 90 (6.2) | 68 (16.2) | 22 (3.7) | 94 (8.9) | 43 (15.0) |
| GP                   | 445 (94.7) | 1048 (91.1) | 339 (80.7) | 553 (94.1) | 942 (89.0) | 233(81.5) |
| Missing              | 13 (2.7) | 31 (2.7) | 13 (3.1) | 13 (2.2) | 23 (2.1) | 10 (3.5) |
| Autoantibody status  |          |          |          |          |          |          |
| Positive             | 10 (2.1) | 52 (4.4) | 37 (8.8) | 20 (3.4) | 53 (5.0) | 21 (7.3) |
| Negative             | 460 (97.9) | 1179(95.6) | 383 (91.2) | 568 (96.6) | 1006 (95.0) | 265 (92.7) |
| HLA risk             |          |          |          |          |          |          |
| 0                    | 153 (32.6) | 367 (31.4) | 137 (32.6) | 180 (30.6) | 338 (31.9) | 104 (36.4) |
| 1                    | 126 (26.8) | 319 (27.3) | 93 (22.1) | 156 (26.5) | 270 (25.5) | 73 (25.5) |
| 2                    | 136 (28.9) | 340 (29.1) | 137 (32.6) | 175 (29.8) | 326 (30.9) | 74 (25.9) |
| 3                    | 54 (11.5) | 139 (11.9) | 53 (12.7) | 74 (12.6) | 124 (11.6) | 34 (11.9) |
| Missing              | 1 (0.2) | 4 (0.3) | 0 (0.0) | 3 (0.5) | 1 (0.1) | 1 (0.3) |
| Parent characteristic |          |          |          |          |          |          |
| Education            |          |          |          |          |          |          |
| High                 | 232 (49.4) | 600 (51.3) | 175 (41.7) | 213 (36.2) | 417 (39.3) | 85 (29.7) |
| Low                  | 230 (48.9) | 554 (47.4) | 238 (56.7) | 364 (61.9) | 628 (59.3) | 201 (70.3) |
| Missing              | 8 (1.7) | 15 (1.3) | 7 (1.6) | 11 (1.9) | 14 (1.3) | 0 (0.0) |
| Working              |          |          |          |          |          |          |
| Yes                  | 378 (80.4) | 937 (80.2) | 312 (74.3) | 554 (94.2) | 1006 (95.0) | 260 (90.9) |
| No                   | 73 (15.5) | 170 (14.5) | 74 (17.6) | 20 (3.4) | 26 (2.5) | 15 (5.4) |
| Missing              | 19 (4.0) | 62 (5.3) | 34 (8.1) | 14 (2.4) | 27 (2.5) | 11 (3.7) |
| Parents live together|          |          |          |          |          |          |
| Yes                  | 439 (93.4) | 1074 (91.9) | 379 (90.2) | 556 (94.6) | 999 (94.3) | 267 (93.4) |
| No                   | 27 (5.7) | 91 (7.8) | 40 (9.5) | 28 (4.8) | 44 (4.2) | 15 (5.2) |
| Missing              | 4 (0.9) | 4 (0.3) | 1 (0.3) | 4 (0.6) | 16 (1.5) | 4 (1.4) |
| Support              |          |          |          |          |          |          |
| Have support         | 390 (83.0) | 920 (78.7) | 309 (73.6) | 534 (90.8) | 900 (85.0) | 230 (80.4) |
| Need more            | 77 (16.4) | 244 (20.9) | 109 (25.9) | 50 (8.5) | 151 (14.3) | 54 (18.8) |
| Missing              | 3 (0.6) | 5 (0.4) | 2 (0.5) | 4 (0.7) | 8 (0.7) | 2 (0.8) |
| Live together with the child |          |          |          |          |          |          |
| Yes                  | 459 (97.7) | 1132 (96.8) | 404 (96.2) | 559 (95.1) | 1010 (95.4) | 270 (94.4) |
| Part time/no         | 10 (2.1) | 34 (2.9) | 14 (3.3) | 29 (4.9) | 44 (4.2) | 14 (4.9) |
| Missing              | 1(0.2) | 3 (0.3) | 2 (0.5) | 0 (0.0) | 5 (0.4) | 2 (0.7) |
| Risk perception      |          |          |          |          |          |          |
| Higher               | 27 (5.7) | 214 (18.3) | 180 (42.9) | 25 (4.3) | 176 (16.6) | 79 (27.6) |
| Same                 | 277 (58.9) | 742 (63.5) | 184 (43.8) | 344 (58.5) | 638 (60.2) | 155 (54.2) |
| Lower                | 164 (34.9) | 211 (18.0) | 55 (13.1) | 214 (36.4) | 241 (22.8) | 52 (18.2) |
| Missing              | 2 (0) | 2 (0.2) | 1 (0.2) | 5 (0.8) | 4 (0.4) | 0 (0.0) |

(Continues)
| Table 1 | Mothers | Fathers |
|---------|---------|---------|
|         | SAI 22.1 | SAI >22.1-40 | SAI >40 | SAI 22.1 | SAI >22.1-40 | SAI >40 |
|         | Lowest anxiety | Moderate anxiety | Higher anxiety | Lowest anxiety | Moderate anxiety | Higher anxiety |
|         | n = 470 | n = 1169 | n = 420 | n = 588 | n = 1059 | n = 286 |
| Frequency of worry about T1D | | | | | | |
| Never | 326 (49.0) | 275 (23.5) | 38 (9.0) | 467 (79.5) | 397 (37.5) | 53 (18.5) |
| Rarely | 139 (14.8) | 648 (55.4) | 129 (30.7) | 110 (18.7) | 519 (49.0) | 106 (37.1) |
| Sometimes/often | 5 (1.0) | 243 (20.8) | 240 (57.1) | 9 (1.5) | 143 (13.5) | 119 (41.6) |
| Missing | 0 (0.0) | 3 (0.3) | 13 (3.2) | 2 (0.3) | 0 (0.0) | 8 (2.8) |

Abbreviations: FDR, first degree relative; GP, general population; HLA risk, risk based on HLA genotype; 0, <1/100; 1, 1/100; 2, 2/100; 3, 3/100.

Table 2: Mothers' SAI score modeled as a 3-level variable (lowest anxiety = 22.05, moderate anxiety = [22.05, 40], higher anxiety = [40, 69.21]) with the "moderate anxiety" group treated as the reference

| Mothers | SAI >22.1-40 vs 22.1 | SAI >40 vs >22.1-40 |
|---------|----------------------|---------------------|
| OR (95% CI) | P value | OR (95% CI) | P value |
| Model 1 (n = 1997) | | | |
| Autoantibody positive vs negative | 1.98 (0.99, 3.97) | .052 | 2.21 (1.41, 3.48) | <.001 |
| HLA risk | | | |
| 0 | Reference | | Reference |
| 1 | 1.11 (0.83, 1.48) | .472 | 0.88 (0.64, 1.20) | .419 |
| 2 | 1.05 (0.79, 1.39) | .742 | 1.15 (0.86, 1.54) | .345 |
| 3 | 1.10 (0.75, 1.60) | .631 | 1.04 (0.71, 1.52) | .851 |
| FDR vs GP | 3.24 (1.75, 6.00) | <.001 | 2.35 (1.67, 3.32) | <.001 |
| Gender male vs female | 0.81 (0.65, 1.01) | .063 | 1.05 (0.83, 1.32) | .688 |
| Model 2 (n = 1964) | | | |
| Risk perception | | | |
| Lower | Reference | Reference |
| Same | 1.98 (1.54, 2.55) | <.001 | 0.91 (0.64, 1.30) | .606 |
| Higher | 4.81 (3.01, 7.67) | <.001 | 3.17 (2.15, 4.66) | <.001 |
| Autoantibody positive vs negative | 1.64 (0.81, 3.31) | .167 | 1.88 (1.16, 3.03) | .009 |
| HLA risk | | | |
| 0 | Reference | Reference |
| 1 | 1.10 (0.82, 1.47) | .537 | 0.90 (0.65, 1.24) | .505 |
| 2 | 0.99 (0.75, 1.32) | .962 | 1.12 (0.83, 1.51) | .478 |
| 3 | 1.11 (0.75, 1.64) | .591 | 0.99 (0.66, 1.47) | .946 |
| FDR vs GP | 1.93 (1.01, 3.67) | .046 | 1.26 (0.86, 1.85) | .231 |
| Education | | | |
| Low | Reference | Reference |
| High | 1.08 (0.86, 1.35) | .514 | 0.61 (0.48, 0.78) | <.001 |
| Model 3 (n = 1846) | | | |
| Frequency of worry | | | |
| Never | Reference | Reference |
| Rarely | 5.27 (4.06, 6.85) | <.001 | 1.28 (0.85, 1.95) | .240 |
| Sometimes/often | 53.2 (19.4, 146.2) | <.001 | 5.33 (3.48, 8.17) | <.001 |
| Autoantibody positive vs negative | 1.37 (0.64, 2.95) | .417 | 1.88 (1.13, 3.12) | .015 |
We did not observe an association between high anxiety levels and participation in the DiPiS study (n = 1380, 67.1%) for the majority of mothers and fathers, but in 147 families (7.1%) both parents were anxious that their child would develop type 1 diabetes in the future. Results from the three multinomial regression models with three-level SAI score as the outcome are shown in Tables 2 and 3. For mothers, having a child with islet autoantibody positivity (at least one autoantibody) compared to having a child with no detected autoantibodies was associated with higher anxiety (SAI >40 vs >22.1-40): OR = 2.21 (95% CI = 1.41, 3.48, P < .001), adjusted for gender, HLA risk, and FDR status. When additionally adjusted for the perceived type 1 diabetes risk, parental education, frequency of parental worry, working status, level of support, and if the parents live together with the child or not, the association between anxiety and FDR was not statistically significant. Belonging to an FDR family was also associated with having moderate anxiety compared to lower anxiety when adjusting for autoantibody status, HLA risk and gender, mothers (3.24; 1.75, 6.00, P < .001) and fathers (2.48; 1.54, 4.01, P < .001; Tables 2 and 3).

20.4% of mothers and 14.5% of fathers perceived that their child had a higher risk than other children of developing type 1 diabetes. Being a parent perceiving that their child had a higher risk of developing type 1 diabetes was associated with being more anxious in both mothers (3.17; 2.15, 4.66, P < .001) and fathers (1.97; 1.26, 3.07, P = .003), adjusting for autoantibody positivity, HLA risk, FDR status,
| Fathers                          | SAI >22.1-40 vs 22.1 | SAI >40 vs >22.1-40 |
|--------------------------------|----------------------|--------------------|
|                                | OR (95% CI)          | P value            |
|                                |                      | OR (95% CI)        | P value            |
| **Model 1 (n = 1882)**         |                      |                    |
| Autoantibody positive vs negative | 1.41 (0.83, 2.41)   | .204               |
| HLA risk                       |                      |                    |
| 0                              | Reference            |                    |
| 1                              | 0.98 (0.74, 1.29)    | .872               |
| 2                              | 1.00 (0.77, 1.30)    | .990               |
| 3                              | 0.90 (0.64, 1.28)    | .564               |
| FDR vs GP                      | 2.48 (1.54, 4.01)    | <.001              |
| Gender male vs female          | 0.90 (0.74, 1.11)    | .329               |
| **Model 2 (n = 1849)**         |                      |                    |
| Risk perception                |                      |                    |
| Lower                          | Reference            |                    |
| Same                           | 1.68 (1.33, 2.12)    | <.001              |
| Higher                         | 5.79 (3.55, 9.44)    | <.001              |
| Autoantibody positive vs negative | 1.25 (0.73, 2.16)   | .421               |
| HLA risk                       |                      |                    |
| 0                              | Reference            |                    |
| 1                              | 0.96 (0.72, 1.27)    | .767               |
| 2                              | 0.95 (0.73, 1.25)    | .716               |
| 3                              | 0.88 (0.61, 1.26)    | .475               |
| FDR vs GP                      | 1.31 (0.78, 2.19)    | .310               |
| Education                      |                      |                    |
| Low                            | Reference            |                    |
| High                           | 1.13 (0.90, 1.40)    | .288               |
| **Model 3 (n = 1786)**         |                      |                    |
| Frequency of worry             |                      |                    |
| Never                          | Reference            |                    |
| Rarely                         | 5.25 (4.04, 6.82)    | <.001              |
| Sometime/often                 | 15.55 (7.71, 31.4)   | <.001              |
| Autoantibody positive vs negative | 0.91 (0.50, 1.67)   | .771               |
| HLA risk                       |                      |                    |
| 0                              | Reference            |                    |
| 1                              | 1.03 (0.76, 1.41)    | .846               |
| 2                              | 0.95 (0.71, 1.28)    | .759               |
| 3                              | 0.88 (0.59, 1.31)    | .538               |
| FDR vs GP                      | 1.11 (0.63, 1.96)    | .728               |
| Risk perception                |                      |                    |
| Lower                          | Reference            |                    |
| Same                           | 1.65 (1.27, 2.13)    | <.001              |
| Higher                         | 3.86 (2.25, 6.62)    | <.001              |
| Education                      |                      |                    |
| Low                            | Reference            |                    |
| High                           | 1.18 (0.93, 1.51)    | .175               |
TABLE 3 (Continued)

| Fathers | SAI >22.1-40 vs 22.1 SAI >40 vs >22.1-40 |
|---------|----------------------------------------|
| Working | OR (95% CI) | P value | OR (95% CI) | P value |
| No      | Reference | 0.65 (0.32, 1.31) | .226 | 2.00 (0.96, 4.19) | .066 |
| Yes     |           |                     |      |                     |      |
| Support | Have support | Reference | 2.03 (1.38, 2.97) | <.001 | 1.30 (0.89, 1.90) | .174 |
|         | Need more  | Reference |                     |      |                     |      |
| Live together with the child | No | Reference | 1.56 (0.87, 2.79) | .132 | 1.31 (0.63, 2.73) | .464 |
|         | Yes        |           |                     |      |                     |      |

Note: Comparing fathers with the moderate to fathers with lowest anxiety level, and fathers with higher anxiety to the ones with moderate anxiety. The sample sizes shown next to each model are the number of subjects with complete data available for each analysis out of a total n = 1933. Abbreviations: FDR, first degree relative; GP, general population; HLA risk, genetic risk based on HLA genotype, 0, <1/100; 1, 1/100; 2, 2/100; 3, 3/100.

TABLE 4 Parental anxiety in mothers and fathers modeled separately, comparing parents with higher anxiety to parents with a lower anxiety level

| SAI ≥40 vs <40 | Mothers (n = 2059) | Fathers (n = 1933) |
|----------------|-------------------|--------------------|
|                | OR (95% CI) | P value | OR (95% CI) | P value |
| Model 1        | (n = 1997) | (n = 1882) |
| Autoantibody positive vs negative | 2.58 (1.65, 3.97) | <.001 | 1.81 (1.05, 3.00) | .026 |
| HLA risk       |                |          |                |          |
| 0              | Reference | 0.90 (0.67, 1.22) | .516 | 0.94 (0.67, 1.32) | .724 |
| 1              |          | 1.16 (0.88, 1.54) | .287 | 0.77 (0.55, 1.07) | .121 |
| 2              |          | 1.06 (0.73, 1.53) | .750 | 0.84 (0.53, 1.28) | .424 |
| 3              |          | 2.97 (2.12, 4.15) | <.001 | 2.28 (1.54, 3.33) | <.001 |
| FDR vs GP      | 0.99 (0.79, 1.24) | .940 | 1.22 (0.94, 1.58) | .137 |
| Gender male vs female | | | |

Model 2 (n = 1964) (n = 1849)

| Risk perception | Mothers (n = 2059) | Fathers (n = 1933) |
|-----------------|-------------------|--------------------|
| Autoantibody positive vs negative | 2.06 (1.28, 3.27) | .002 | 1.57 (0.90, 2.63) | .098 |
| HLA risk        |                   |                   |                   |
| 0               | Reference | 0.91 (0.67, 1.25) | .580 | 0.93 (0.66, 1.30) | .656 |
| 1               |          | 1.11 (0.83, 1.49) | .482 | 0.74 (0.53, 1.04) | .085 |
| 2               |          | 1.01 (0.68, 1.49) | .964 | 0.82 (0.52, 1.26) | .373 |
| 3               |          | 1.39 (0.95, 2.02) | .085 | 1.32 (0.85, 2.03) | .208 |
| FDR vs GP       | 0.62 (0.49, 0.79) | <.001 | 0.61 (0.45, 0.81) | .001 |
| Education       |                   |                   |                   |
| Low             | Reference |                   |                   |                   |
| High            | 0.62 (0.49, 0.79) | <.001 | 0.61 (0.45, 0.81) | .001 |

Model 3 (n = 1846) (n = 1786)

| Frequency of worry | Mothers (n = 2059) | Fathers (n = 1933) |
|--------------------|-------------------|--------------------|
| Autoantibody positive vs negative | 2.28 (1.53, 3.46) | <.001 | 2.58 (1.81, 3.72) | <.001 |
| HLA risk           |                   |                   |                   |
| 0                  | Reference |                   |                   |                   |
| 1                  |          | 1.11 (0.83, 1.49) | .482 | 0.74 (0.53, 1.04) | .085 |
| 2                  |          | 1.01 (0.68, 1.49) | .964 | 0.82 (0.52, 1.26) | .373 |
| 3                  |          | 1.39 (0.95, 2.02) | .085 | 1.32 (0.85, 2.03) | .208 |
| FDR vs GP          |                   |                   |                   |
| Low                | Reference |                   |                   |                   |
| High               | 0.62 (0.49, 0.79) | <.001 | 0.61 (0.45, 0.81) | .001 |

(Continues)
and parental education level. When also adjusting for frequency of parental worry, working status, level of support, and if the parents lived together with the child or not, among parents perceiving that their child had a higher risk of developing the disease, only mothers seemed to be more anxious (mothers: 2.01; 1.29, 3.13, \( P = .002 \); fathers: 1.33; 0.82, 2.16, \( P = .249 \)) compared to those who did not perceive that their child's risk of developing type 1 diabetes was elevated. Based on model 2 and 3, both mothers and fathers who reported moderate anxiety were more likely to perceive that their child had a higher or comparable risk of developing type 1 diabetes than parents reporting lower anxiety levels (Tables 2 and 3).

A majority of parents of children participating in the DiPiS study stated that they never or rarely worried about the risk that their child would develop type 1 diabetes (mothers n = 1555 (75.5 %) and fathers n = 1652 (85.5%)). However, both mothers and fathers who stated that they sometimes or often worry about their child developing type 1 diabetes were significantly more anxious than parents who did not worry at all (5.33; 3.48, 8.17, \( P < .001 \) for mothers and 5.27; 3.51, 7.92, \( P < .001 \) for fathers), adjusting for autoantibody positivity, HLA risk, FDR status, parental education, working status, level of support, parental risk perception, and if the parents lived together with the child or not. Also, fathers who stated that they rarely worried about their child developing type 1 diabetes were more likely to be anxious compared to fathers who never worried (fathers 1.48; 1.02, 2.14, \( P = .039 \)). Parents who reported moderate anxiety were more likely to state that they rarely, sometimes or often worry about their child developing type 1 diabetes than parents reporting lower anxiety levels (Table 2 and 3).

Highly educated parents seemed to be less anxious that their child would develop type 1 diabetes (mothers 0.61; 0.48, 0.78, \( P < .001 \); fathers 0.59; 0.44, 0.79, \( P < .001 \)), when adjusting for autoantibody status, HLA risk, FDR status, and parental risk perception. Even when adjusting for frequency of parental worry, autoantibody status, HLA risk, FDR status, working status, level of support, parental risk perception and if the parents lived together with the child or not, higher education was associated with lower parental anxiety (mothers 0.72; 0.55, 0.94, \( P = .017 \); fathers 0.67; 0.49, 0.92, \( P = .012 \); Tables 2 and 3). No significant differences in anxiety level were found between parents in the lower anxiety group and the ones with moderate anxiety. Fathers who reported moderate anxiety were more likely to state that they would like more support in taking care of their child than fathers reporting lower anxiety levels (2.03; 1.38, 2.97, \( P < .001 \), but

| SAI ≥40 vs <40 | Mothers (n = 2059) | Fathers (n = 1933) |
|----------------|-------------------|-------------------|
| Autoantibody positive vs negative | 1.94 (1.16, 3.21) | 1.16 (0.64, 2.03) |
| HLA risk | Reference | Reference |
| 0 | 0.78 (0.54, 1.10) | 1.03 (0.71, 1.49) |
| 1 | 1.09 (0.79, 1.51) | 0.84 (0.58, 1.20) |
| 2 | 0.90 (0.58, 1.38) | 0.84 (0.51, 1.33) |
| 3 | 1.08 (0.71, 1.63) | 1.09 (0.67, 1.74) |
| FDR vs GP | Reference | Reference |
| Lower | 0.97 (0.66, 1.44) | 1.25 (0.87, 1.81) |
| Same | 2.28 (1.48, 3.55) | 1.66 (1.03, 2.70) |
| Higher | Reference | Reference |
| Education | Reference | Reference |
| Low | 0.74 (0.57, 0.97) | 0.70 (0.51, 0.95) |
| High | 1.23 (0.87, 1.72) | 1.79 (0.85, 3.52) |
| Working | Reference | Reference |
| No | 1.14 (0.84, 1.55) | 1.48 (1.01, 2.15) |
| Yes | Reference | Reference |
| Support | Reference | Reference |
| Have support | 0.75 (0.36, 1.65) | 1.41 (0.72, 3.01) |
| Need more | 1.14 (0.84, 1.55) | 0.97 (0.66, 1.44) |
| Live together with the child | Reference | Reference |
| No | 1.08 (0.71, 1.63) | 1.09 (0.67, 1.74) |
| Yes | 2.28 (1.48, 3.55) | 1.66 (1.03, 2.70) |

**Note:** This analysis corresponds to the analyses presented in Tables 2 and 3 and serves as a sensitivity analysis.

**Abbreviations:** FDR, first degree relative; GP, general population; HLA risk, genetic risk based on HLA genotype, 0, <1/100; 1, 1/100; 2, 2/100; 3, 3/100.
this association was not observed in mothers, adjusting for autoantibody status, HLA risk, FDR status, parental risk perception, parental education, frequency of parental worry, working status, and if the parents lived together with the child or not. Gender of the child, HLA risk, working or not and whether the parents were living together with the child or not was not found to be associated with parental anxiety in any of the models (Tables 2 and 3).

Table 4 shows the sensitivity analyses with the binary SAI score as the outcome. Results for maternal anxiety were consistent for the three-level and the binary SAI outcomes. Specifically, higher anxiety was associated with the same covariates in the model with binary SAI score as the outcome when comparing mothers with higher anxiety to those with moderate anxiety in the three-level model. For fathers, the results were consistent with the model with the three-level SAI score as the outcome, except for fathers with a child with autoantibodies. This covariate was associated with greater anxiety only in the model with the binary SAI score.

4 | DISCUSSION

Our primary aim was to determine the level of parental anxiety regarding their child's risk of developing type 1 diabetes after 5 years of participation in a prospective follow-up study.

For most parents, their child's participation in the DIPiS study was not associated with high parental anxiety. However, some factors were associated with higher anxiety: parents from an FDR family, a child with autoantibody positivity, perceiving that the child had a high risk of type 1 diabetes, frequent worriers, and parents with lower education level. Most parents did not think that their child's risk of developing type 1 diabetes was higher than other children.

Parents from FDR families were more anxious than parents without close relatives with type 1 diabetes, consistent with the previous literature. 

Several studies have reported that parents of children developing type 1 diabetes were more anxious before any risk information had been given revealed that FDR parents estimated the risk of their child developing type 1 diabetes as higher than other parents. This result seems to be the same after participating in the study for 5 years.

Previous studies have reported that parents of children developing autoantibodies are more anxious and perceive that their child's risk of developing type 1 diabetes had increased. In our study, these results were confirmed only in the analysis comparing mothers with higher anxiety to mothers with moderate anxiety levels. This might be because only a small number of children had developed autoantibodies before the age of five, thus the analytical power to detect a difference between these groups was low. However, our results may also depend on the way the parents were informed about their children's autoantibody status. In the DIPiS study, parents of children with one autoantibody were informed once by telephone by a nurse and then not again unless the results changed. Parents of children who had developed two or more autoantibodies were informed by a pediatrician and were followed-up more frequently. The reason for the difference between mothers and fathers may be that, in most cases, the mother was contacted by phone and received the information about the test results and about the increased risk for type 1 diabetes. The information they received may also differ from other studies and the way that information was delivered to the parents. Such information should be taken into consideration when interpreting and comparing the results from different studies. Johnson et al. reported that parental anxiety increased with the number of autoantibodies. We did not perform a corresponding analysis using our dataset, as only a few children developed multiple autoantibodies.

Several studies have found an association between anxiety and risk perception. Our study of worry and risk perception during the screening years of DIPiS showed that parents participating in the DIPiS study for 1 year were more worried if they thought that their child had a higher risk of developing type 1 diabetes. At year 1, none of the parents had been informed about the genetic risk or autoantibody status of the child. We can now confirm that parents who believe that their child is at high risk remain more anxious after 5 years of participation in the DIPiS study, despite having a better understanding of their child's risk of type 1 diabetes based on genetic risk and autoantibody status. It is interesting to note that we did not find an association between anxiety and the HLA group. This may be because the information was given only once or that it was not sufficiently clear and easy to understand. Our results are consistent with the results of studies from New Zealand (n = 114) and Finland (n = 949), which showed that information about the child's genetic risk did not increase maternal anxiety regardless of whether the child was at increased risk of type 1 diabetes.

Several studies have shown that other factors, such as the level of education, being a single parent, maternal age, working status, and ethnicity, may affect parental concern. In the ABIS study, a Swedish study similar to DIPiS, mothers with a less stable social situation such as lower educational level and unemployment were more likely to be anxious. Here we confirmed that educational level is an important factor for both maternal and paternal anxiety. Low educational level, in addition to feeling that they needed more support, was also associated with paternal anxiety. Other sociodemographic factors such as working status and living together with the child were not found to be associated with anxiety.

In addition to investigating parental anxiety, we also asked how often parents felt worried about their children developing type 1 diabetes, which, to our best knowledge, has not been investigated before in this context. Reporting worries “sometimes” or “often” was strongly linked to anxiety. This may be important and useful when screening for anxiety in similar studies.
Most previous studies investigating parental concerns and risk perception only considered one parent, usually the mother. The strength of our study is that it gave both parents the opportunity to answer the questionnaires individually and, in 91% of families, both parents responded. In the few studies that have compared maternal and paternal anxiety that their child will develop type 1 diabetes, mothers were found to be more anxious than fathers. In the present study, mothers seemed to be more anxious than fathers. Furthermore, by studying mothers and fathers, we were able to investigate factors associated with anxiety in both parents. An increase in maternal anxiety was observed when the child developed one or several autoantibodies, this association was not observed in the fathers.

Since our study shows that differences exist between maternal and paternal anxiety for type 1 diabetes, future studies should take both parents’ views into account using separate questions and questionnaires. Most previous studies are of the mother’s view of perception of risk and anxiety, but we expect the father’s perception and anxiety to similarly affect the family and be important when analyzing stress factors in families. In this context, the result of our study provides additional insights into the factors associated with anxiety levels in the parents during the screening and follow-up of children at high risk for type 1 diabetes.

In DiPiS, parents were informed about their child’s genetic risk of type 1 diabetes once, by a letter at the age of three. The parents’ understanding of risk based on HLA might have been improved if that information was reiterated at a later point in the study, for example, at the time when the parents were informed that their child developed autoantibodies. In addition to sharing the information about the genetic risk more than once, the provided information needs to be accessible to both parents and the information must be presented in a way that is easy to read and understand. Further studies on risk perception after the information has been given will be important to evaluate if the provided information is assimilated by the parents. It may also be important that the families only received information verbally once after the child turned single autoantibody positive in DiPiS. Providing information in a written form and resending it annually might be useful, both to increase the parents awareness of their child’s risk and to ensure that both parents receive the same information.

In conclusion, based on this longitudinal study of children at high risk for type 1 diabetes and their parents, having a family member with type 1 diabetes, having a child with autoantibodies, thinking that their child has a high risk of developing type 1 diabetes, higher frequency of worry and low education level where associated with higher parental anxiety about the child’s risk for type 1 diabetes. These findings add to our understanding of the impact of screening of type 1 diabetes and autoimmune diseases in childhood on family anxiety. This knowledge can be used when designing new research studies, to be prepared for parental reactions and to plan for necessary resources to help parents with higher anxiety levels.

ACKNOWLEDGEMENTS

Our research is supported in part by the Swedish Childhood Diabetes Foundation, Swedish Diabetes Association, SUS funds, Lion Club International, district 101-S, The royal Physiographic society, the Kristianstad central hospital Research and development fund, the Skåne County Council Foundation for Research and Development, Swedish Research Council, Strategic Research Area Exodiab and Swedish Foundation for Strategic Research. The supporting sources had no role in the study design, the collection, analysis or interpretation of the data, writing the manuscript or the decision to submit the manuscript for publication. The members of the DiPiS study group are: C. Andersson, R. Bennet, I. Jönsson, M. Ask, J. Bremer, C. Brundin, C. Cilio, C. Hansson, G. Hansson, S. Ivarsson, B. Jonsdottir, Á Lernmark, B. Lindberg, B. Lernmark, M. Lundgren, M Maziarz, J Melin, A. Ramelius, I. Wigheden, U.-M. Carlsson, A. Svärd (Department of Clinical sciences Malmö, Lund University, Sweden) A. Carlsson (Department of Clinical sciences Lund, Lund university, Sweden), E. Cedervall (Department of Paediatrics, Ångelholm hospital, Sweden), B. Jönsson (Department of Paediatrics, Ystad Hospital, Sweden), K. Larsson (Department of Paediatrics, Kristianstad Central Hospital, Sweden) and J. Neiderud (Department of Paediatrics, Helsingborg Hospital, Sweden). We thank all the participating parents and children in the DiPiS study.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

5 | AUTHOR CONTRIBUTIONS

J.M. contributed to the study and the analysis design, performed analyses, conducted the literature search and wrote the manuscript. M.M. conducted the data analyses, contributed to the interpretation of the data and edited the manuscript. C.A.A. revised the manuscript. M.L. interpreted data, contributed to and edited the manuscript. H.E.L. designed the study, was involved in data collection, interpreted data, contributed to, and edited the manuscript. All authors have read and gave final approval of the version to be published.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Melin J, Maziarz M, Andrén Aronsson C, Lundgren M, Elding Larsson H. Parental anxiety after 5 years of participation in a longitudinal study of children at high risk of type 1 diabetes. Pediatr Diabetes. 2020;21:878-889. https://doi.org/10.1111/pedi.13024