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ARTICLE

# Increasing risk of psychiatric morbidity after childhood onset type 1 diabetes: a population-based cohort study

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## Abstract

**Aims/hypothesis** The aim of this study was to investigate psychiatric morbidity following childhood onset of type 1 diabetes.
**Methods** In a matched, population-based cohort study based on Danish national registers, we identified children and adolescents who had been diagnosed as an in- or outpatient with type 1 diabetes before the age of 18, and afterwards diagnosed with a psychiatric disorder ($n = 5084$). Control individuals were matched according to sex and date of birth ($n = 35{,}588$). The Cox proportional hazards model was used to assess associations between type 1 diabetes and the incidence of psychiatric disorders as well as the effects of age at onset and duration of type 1 diabetes on the risk of subsequently developing psychiatric morbidities.
**Results** An increased risk of being diagnosed with mood disorders and anxiety, dissociative, eating, stress-related and somatoform disorders was observed in both sexes in the years following type 1 diabetes onset, with the highest risk observed five years or more after onset (HR 1.55 [95% CI 1.38, 1.74]). The risk of psychoactive substance-misuse disorders increased significantly only in boys, and the risk of personality disorders increased only in girls.
**Conclusions/interpretation** In the years following type 1 diabetes onset, an increased risk of eating disorders, anxiety and mood disorders, substance misuse, and personality disorders was found. These findings highlight a clinical need to monitor the mental health of children and adolescents in the years following type 1 diabetes onset to identify and treat psychiatric problems associated with type 1 diabetes.

**Keywords** Adolescents · Anxiety · Children · Comorbidity · Eating disorder · Mood disorder · Personality disorder · Psychiatric illness · Substance misuse · Type 1 diabetes mellitus

**Abbreviations**

| | |
|---|---|
| ADHD | Attention deficit hyperactivity disorders |
| ASD | Autism spectrum disorders |
| IR | Incidence rate |
| ISPAD | International Society for Paediatric and Adolescent Diabetes |
| NPR | National Patient Register (of Denmark) |

## Introduction

The psychological burden associated with type 1 diabetes in children and adolescents is reflected by research demonstrating an increased risk of mental health problems, particularly depression, disturbed eating and anxiety disorders [1–7]. In

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## Research in context

**What is already known about this subject?**

- Type 1 diabetes in children and adolescents has been shown to be correlated with a range of psychiatric diagnoses
- The risk of psychiatric morbidity may be affected by onset age and duration of type 1 diabetes
- Most previous studies used small and highly selected populations and a limited range of outcomes. Two larger cohort studies did not account for differences between the sexes

**What is the key question?**

- Do children and adolescents have an increased risk of psychiatric morbidity, and in which diagnostic categories?

**What are the new findings?**

- Children and adolescents with type 1 diabetes have increased risk of a wide range of psychiatric diagnoses, with differences between the two sexes
- The risk may vary depending on the onset age of type 1 diabetes, and may increase with duration of the disease

**How might this impact on clinical practice in the foreseeable future?**

- Clinicians should routinely address aspects of mental health when seeing children and adolescents with type 1 diabetes

addition, impaired health-related quality of life [8, 9], low adherence to treatment [10, 11], poor glycaemic control [12–14], hospitalisation [15], and an increased overall risk of complications and mortality have been observed in children and adolescents with type 1 diabetes and co-occurring mental health problems [16, 17]. In acknowledging the potentially high impact and long-term consequences of psychiatric problems in young people suffering from type 1 diabetes, the International Society for Paediatric and Adolescent Diabetes (ISPAD) has recommended heightened awareness and screening for mental health problems in children and adolescents with type 1 diabetes [18].

However, current knowledge on mental health problems in children and adolescents with type 1 diabetes is limited and based mainly on findings from small, selective, cross-sectional studies that use diverse measures to define mental health problems and psychopathology [3–5]. A greater understanding of the incidence and presentation of psychiatric symptoms both at type 1 diabetes onset and thereafter is required to address these mental health problems in clinical practice and to guide appropriate interventions. Therefore, longitudinal data are needed that prospectively explore the occurrence of a wide spectrum of psychiatric disorders from type 1 diabetes onset [19, 20]. Two such studies have recently been published: (1) A large population register-based case-cohort study from Sweden followed children and adolescents for more than five years after type 1 diabetes onset [6]. The study demonstrated that the overall risk of psychiatric disorders in the type 1 diabetes individuals was double that in age- and sex-matched control individuals, and that the risk was greatest in the first year after type 1 diabetes onset. The risk also increased across diagnostic groups that included mood, eating, substance misuse, behavioural, anxiety and stress-related disorders, attention deficit hyperactivity disorders (ADHD), suicide attempts and intellectual disabilities; (2) Another population-based register study that followed a cohort of Australian children and adolescents with type 1 diabetes confirmed that the risk of psychiatric disorders doubled [7].

In the present study, our objective was to enhance our understanding of the psychiatric risks associated with type 1 diabetes in children and adolescents by exploring data from Danish national registers, with a focus on any differences between the sexes, the duration of diabetes, and age at type 1 diabetes onset.

## Methods

**Study design** This study is a population-based, matched cohort study, using data from two nationwide Danish registers.

The study population was identified using the Danish Civil Registration System, which contains information on everyone living in Denmark. The system includes each individual's personal identification number, their sex, date of birth and vital status. The personal identification number is used in all national registers, which means they can be accurately cross-referenced [21, 22].

The National Patient Register (NPR) contains information on all contacts at public hospitals in Denmark, for inpatients since 1977, and for outpatients since 1995 [23]. In Denmark, all children and adolescents treated for type 1 diabetes are diagnosed and treated at public hospitals. In addition, children

and adolescents with major mental health problems are referred and diagnosed in public hospital settings [24]. The diagnoses recorded in NPR are the result of examinations and diagnostic classification done by medical doctors in accordance with ICD-10 (www.who.int/classifications/icd/en/) [23]. In this study, we defined type 1 diabetes mellitus as ICD-10 codes E10-E16 as recorded in the NPR.

Our study population consisted of children born in Denmark who had been diagnosed with type 1 diabetes before the age of 18 years and during the period 1996 to 2013. Children and adolescents who had been diagnosed with a psychiatric disorder prior to the diagnosis of type 1 diabetes, and children and adolescents not living in Denmark at the time of the type 1 diabetes diagnosis, were excluded. The total number of children and adolescents with type 1 diabetes included in the study was 5,084, and 48% of them were female.

The inclusion date for children and adolescents with diabetes was defined as the date of type 1 diabetes diagnosis, and the individual's age on that date was defined as their age at inclusion.

Control individuals were randomly selected from the background population, matched by their sex and date of birth. Children and adolescents who were not born and living in Denmark, who had diabetes-related diagnoses (ICD-10 codes E10–E16) before the age of 18 years, or who had been diagnosed with a psychiatric disorder, were excluded. Control individuals were assigned the same inclusion date and age at inclusion as their matched counterparts with diabetes. We included seven control individuals for each individual with type 1 diabetes. The total number of control individuals included was 35,588, and 48% of them were female.

**Psychiatric morbidity** Psychiatric morbidity was defined as a psychiatric disorder diagnosed within the NPR, after the onset of type 1 diabetes. All ICD-10 F-diagnoses (F00–F99) of mental health were included [24]. The major diagnostic groups were: psychoactive substance misuse (F10–F19), psychotic disorders (F20–F29), mood disorders (F30–F39), anxiety, dissociative, stress-related and somatoform disorders (F40–F48), eating disorders (F50), personality disorders (F60–F69), intellectual disability (F70–F79), specific developmental disorders (F80–F83), autism spectrum disorders (ASD) (F84), unspecified developmental disorders (F88–F89), hyperkinetic disorder (F90) and other behavioural disorders (F91–F98). In addition, the ICD-10 suicide attempt diagnoses (X60–X84) were included.

**Follow up** For each individual, the study follow-up period began on the inclusion date and ended on the date when one of the following occurred: Diagnosis of a psychiatric disorder, emigration from Denmark (as reported in the Danish Civil Registration System), death, or termination of the study period (31 December 2013). Each participant could be counted only once in the analysis for overall risk of any psychiatric disorder. When calculating the risk of specific psychiatric disorders, each participant could figure in several categories if they had more than one diagnosis, but only once in each category.

**Statistical analysis** Statistical analyses were performed using STATA/IC for Windows (ver.14.0; StataCorp, College Station, TX, USA). Risk estimates were calculated using the Cox proportional hazards model, using calendar dates to measure time. We adjusted for age at inclusion and modelled continuous variables using cubic splines to allow for nonlinear correlations [25, 26]. We used robust estimations of standard error to allow for the possibility of intragroup correlations, and defined a group as the child or adolescent with diabetes together with the corresponding control individuals. The Cox proportional hazards assumption was examined for diabetes as a dichotomous independent variable, and there were no violations. Separate analyses were carried out for girls and boys.

We examined the association between age at onset of type 1 diabetes and the risk of psychiatric disorders, stratifying into four groups by age at inclusion (0–4 years, 5–9 years, 10–14 years and 15–17 years).

Finally, the association between duration of type 1 diabetes and any psychiatric disorder was analysed, stratified by three observation time intervals: within the first year; one to five years; and five years or more after the inclusion date. For each of these intervals, any individuals who had been diagnosed with a psychiatric disorder prior to the start of the time interval were excluded.

## Results

This study included 5084 children and adolescents with type 1 diabetes and 35,588 controls. Of the total 40,672 individuals, 48% were female (Table 1). The mean age of girls at inclusion (± SD) was 9.6 years (±4.4), and the mean follow-up time was 7.8 years (±4.9). The mean age of boys at inclusion (± SD) was 10.2 years (±4.6), and the mean follow-up time was 7.8 years (±5.1).

**Incidence of psychiatric disorders within the study group** Among the children and adolescents with type 1 diabetes, a total of 586 (incidence rate [IR] = 15.0 per 1000 person-years) were diagnosed with a psychiatric disorder, compared with 2969 control individuals (IR = 10.7 per 1000 person-years) (Table 1).

When males and females were combined, anxiety disorders showed the highest incidence in individuals with type 1 diabetes and in control individuals. Among girls, mood disorders and other behavioural disorders were second most common, followed by personality disorders and eating disorders. These diagnoses showed the same patterns of incidence in both

**Table 1** Number of individuals, incidence and IR of psychiatric disorders in children and adolescents with type 1 diabetes and in control individuals

| | Children and adolescents with type 1 diabetes | | | | Control individuals | | | |
|---|---|---|---|---|---|---|---|---|
| | n | Observation time (years) | Incidence | IR[a] | n | Observation time (years) | Incidence | IR[a] |
| Girls | 2423 | 18,420 | 301 | 16.3 | 16,961 | 132,046 | 1495 | 11.3 |
| Boys | 2661 | 20,599 | 285 | 13.8 | 18,627 | 146,037 | 1474 | 10.1 |
| Total | 5084 | 39,018[b] | 586 | 15.0 | 35,588 | 278,084[b] | 2969 | 10.7 |

[a] IR per 1000 people per year

[b] Values do not add up because of rounding

individuals with type 1 diabetes and control individuals. Among boys, ADHD and ASD were among the most frequent diagnoses, in both individuals with type 1 diabetes and control individuals (Table 2).

**Risk of psychiatric disorder after onset of type 1 diabetes** Compared with control individuals, the HR for any psychiatric disorder was 1.46 (95% CI 1.29, 1.64) in girls and 1.38 (95% CI 1.22, 1.56) in boys with type 1 diabetes (Table 2). Type 1 diabetes was associated with a two- to three-fold increase in the risk of eating disorders (HR in girls, 2.02 [95% CI 1.54, 2.64]; HR in boys, 3.73 [95% CI 1.71, 8.11]) and a 55–95% increase in the risk of mood disorders (HR in girls, 1.55 [95% CI 1.27, 1.89]; HR in boys, 1.95 [95% CI 1.52, 2.51]). Differences between females and males were observed. The risk of personality disorders was increased significantly only in girls (HR 1.72 [95% CI 1.33, 2.22]). Conversely, the risk of psychoactive substance-misuse disorders was increased significantly only in boys (HR 1.43 [95% CI 1.02, 1.99]).

Examining the risk of psychiatric disorders stratified by age at inclusion suggested an increasing risk from early to late childhood, with the highest risk seen in children with diabetes onset at ages ten to 14 years (HR 1.55 [95% CI 1.36, 1.76]). (Table 3).

Examining the effect of duration of diabetes on risk of psychiatric disorders suggested an increasing risk over time, with the highest risk occurring five years or more after diabetes diagnosis (HR 1.55 [95% CI 1.38, 1.74]) (Table 4).

## Discussion

**Principal findings** In this nationwide population-based case-cohort study of more than 5,000 Danish children and adolescents diagnosed with type 1 diabetes before their 18th birthday, we observed an increase in psychiatric morbidity following type 1 diabetes onset, with the highest risks observed more than five years after type 1 diabetes onset. The study showed a generally increased risk of psychiatric morbidity, as well as increased risk of specific psychiatric diagnoses, including mood disorders and anxiety, dissociative, eating, stress-related and somatoform disorders, psychoactive substance misuse (in boys only) and personality disorders (in girls only).

**Strengths and weaknesses** The major strengths of this study include its use of prospective data from a large nationwide population cohort, based on information from Danish national registers, which covers the entire population [21–23]. The data included the whole range of ICD-10 psychiatric disorders observed in children and adolescents [24, 27], which ensured that all psychiatric problems were represented without selection limitation.

The use of data from national patient registers ensured the inclusion of all individuals who had been in contact with in- and outpatient settings and emergency units at public hospitals. Psychiatric disorders are diagnosed by medical doctors in these settings in accordance with ICD-10 diagnostic criteria. In Denmark, referral and treatment at public hospitals is provided without charge to the individual, and selection to treatment due to social or economic factors is less likely [23].

The NPR does not include data from private specialists and general practitioners, and the number of children and adolescents diagnosed and treated for mental disorders in these settings is unknown. However, studies of lifetime incidence of psychiatric disorders in Danish children and adolescents [24] suggests that the incidence of severe disorders, including neurodevelopmental disorders and psychosis, is in line with the general population prevalence of the same disorders [28]. In contrast, the incidence of anxiety, depression and behavioural disorders is below the general population prevalence of these disorders [28]. This indicates that only a minority of young people with serious mental health problems are diagnosed outside hospital settings.

Our data does not include children and adolescents with mental health problems that do not exceed the threshold of clinical referral. Only a small proportion of all children and adolescents with mental health problems of any kind are referred for hospital evaluation or treatment [29], and the impact of type 1 diabetes on minor or subclinical mental health symptoms was not assessed in the present study. Accordingly, our findings reflect minimum estimates of risk especially in the non-diabetic children who are not under close medical care.

**Table 2** Incidence, IRs and HRs (95% CI) of psychiatric diagnoses in children and adolescents with type 1 diabetes compared with control individuals

| | Girls | | | | | Boys | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Individuals with type 1 diabetes | | Control individuals | | | Individuals with type 1 diabetes | | Control individuals | | |
| | Incidence | IR[a] | Incidence | IR[a] | HR (95% CI) | Incidence | IR [a] | Incidence | IR[a] | HR (95% CI) |
| Any psychiatric disorder (F00-F99) | 301 | 16.3 | 1495 | 11.3 | 1.46 (1.29, 64) | 285 | 13.8 | 1474 | 10.1 | 1.38 (1.22, 1.56) |
| Psychoactive substance misuse (F10-F19) | 16 | 0.8 | 82 | 0.6 | 1.37 (0.81, 2.33) | 41 | 1.9 | 202 | 1.3 | 1.43 (1.02, 1.99) |
| Psychotic disorders (F20-F29) | 22 | 1.1 | 136 | 1.0 | 1.14 (0.72, 1.79) | 27 | 1.3 | 180 | 1.2 | 1.05 (0.71, 1.57) |
| Mood disorders (F30-F39) | 118 | 6.2 | 543 | 4.0 | 1.55 (1.27, 1.89) | 80 | 3.7 | 290 | 1.9 | 1.95 (1.52, 2.51) |
| Anxiety, dissociative, stress-related and somatoform disorders (F40-F48) | 147 | 7.7 | 771 | 5.7 | 1.36 (1.14, 1.61) | 100 | 4.7 | 496 | 3.3 | 1.43 (1.15, 1.77) |
| Eating disorders (F50) | 66 | 3.4 | 233 | 1.7 | 2.02 (1.54, 2.64) | 9 | 0.4 | 17 | 0.1 | 3.73 (1.71, 8.11) |
| Disorders of personality and behaviour (F60-F69) | 74 | 3.8 | 305 | 2.2 | 1.72 (1.33, 2.22) | 23 | 1.1 | 147 | 1.0 | 1.10 (0.71, 1.70) |
| Intellectual disability (F70-F79) | 7 | 0.4 | 68 | 0.5 | 0.72 (0.33, 1.58) | 17 | 0.8 | 107 | 0.7 | 1.11 (0.67, 1.86) |
| Specific developmental disorders (F80-F83) | 7 | 0.4 | 54 | 0.4 | 0.91 (0.42, 1.97) | 26 | 1.2 | 165 | 1.1 | 1.11 (0.73, 1.68) |
| Autism spectrum disorders (F84) | 14 | 0.7 | 114 | 0.8 | 0.86 (0.49, 1.50) | 53 | 2.5 | 339 | 2.3 | 1.09 (0.82, 1.46) |
| Other/unspecified developmental disorders (F88-F89) | 3 | 0.2 | 40 | 0.3 | 0.53 (0.16, 1.70) | 7 | 0.3 | 38 | 0.3 | 1.29 (0.58, 2.89) |
| Attention deficit hyperactivity disorder (F90) | 40 | 2.0 | 250 | 1.8 | 1.12 (0.81, 1.56) | 63 | 2.9 | 496 | 3.3 | 0.89 (0.68, 1.15) |
| Other behavioural disorders (F91-F99) | 89 | 4.6 | 419 | 3.1 | 1.50 (1.20, 1.88) | 89 | 4.2 | 492 | 3.3 | 1.28 (1.02, 1.60) |
| Suicide attempt (X60-X84) | 18 | 0.9 | 90 | 0.7 | 1.41 (0.85, 2.34) | 8 | 0.4 | 40 | 0.3 | 1.41 (0.68, 2.96) |

[a] IR per 1000 people per year

Being already within the healthcare system, children and adolescents treated for type 1 diabetes are considered to have a lower threshold of referral for other health problems, including mental health concerns. This could lead to an overall increased risk of being diagnosed with a psychiatric disorder after the onset of type 1 diabetes and thereby an increased risk ratio. We found an increased risk ratio over time, which may reflect an increasing psychological burden over time experienced by young people diagnosed with type 1 diabetes. Still, the higher likelihood of detection of psychiatric disorders in children and adolescents with type 1 diabetes, relative to children in the general population, represents a potential referral bias in our study, as in the previously published register-based studies [6, 7].

Changes in diagnostic practices and classification could also influence the apparent incidence and prevalence of psychiatric disorders over time. Throughout our observation period, only one diagnostic system (ICD-10) was used in Denmark, and this likely mitigates the effects of any changes in diagnostic practices. Any changes are also likely to affect both individuals with diabetes and control individuals to the same extent.

It is a limitation of our study that we did not have access to data to explore the possible influences of socioeconomic

**Table 3** Number of individuals, total observation time, incidence, IRs, and HRs (95% CI) of psychiatric disorders in children and adolescents with type 1 diabetes compared with control individuals, grouped by age at inclusion

| | | Individuals with type 1 diabetes | | | Control individuals | | | |
|---|---|---|---|---|---|---|---|---|
| Age at inclusion | n | Observation time (years) | Incidence | IR [a] | Observation time (years) | Incidence | IR [a] | HR (95% CI) |
| 0–4 years | 7211 | 7570 | 82 | 10.8 | 52,552 | 436 | 8.3 | 1.31 (1.04, 1.65) |
| 5–9 years | 12,042 | 11,507 | 174 | 15.1 | 82,392 | 911 | 11.1 | 1.37 (1.17, 1.60) |
| 10–14 years | 15,432 | 14,390 | 259 | 18.0 | 103,712 | 1216 | 11.7 | 1.55 (1.36, 1.76) |
| 15–17 years | 5987 | 5551 | 71 | 12.8 | 39,428 | 406 | 10.3 | 1.25 (0.98, 1.60) |
| All ages | 40,672 | 39,018 | 586 | 15.0 | 278,084 | 2969 | 10.7 | 1.41 (1.30, 1.54) |

[a] IR per 1000 people per year

**Table 4** Number of individuals, total observation time, incidence, IRs and HRs (95% CI) of psychiatric disorders in children and adolescents with type 1 diabetes compared with control individuals, grouped by time after inclusion date

| | | Individuals with type 1 diabetes | | | Control individuals | | | |
|---|---|---|---|---|---|---|---|---|
| Time after inclusion date | n | Observation time (years) | Incidence | IR [a] | Observation time (years) | Incidence | IR [a] | HR (95% CI) |
| <1 year | 40,672 | 39,018 | 47 | 1.2 | 278,084 | 269 | 1.0 | 1.23 (0.90, 1.67) |
| 1–5 years | 37,657 | 38,813 | 194 | 5.0 | 276,657 | 1087 | 3.9 | 1.26 (1.09, 1.47) |
| >5 years | 26,275 | 34,466 | 345 | 10.0 | 246,837 | 1613 | 6.5 | 1.55 (1.38, 1.74) |

[a] IR per 1000 people per year

variables and family history of psychiatric illness. A recent Swedish study investigated a population comparable with ours, using a similar methodology, but adjusting for both socioeconomic factors and family history of psychiatric diagnoses. No significant changes in risk estimates were found when adjusting for potential socioeconomic and family confounders in this study [6], suggesting that these factors affect the risk of psychiatric morbidity evenly in children and adolescents with type 1 diabetes and in their peers without diabetes. In line with these findings, we have no reasons to think that a lack of socioeconomic and family psychiatric data has significantly influenced our results and conclusion.

**Relation to other studies** Our results supplement those from previous research based on smaller, more selective samples [1, 4, 5], and add to the knowledge gained from two recent population-based register studies from Sweden and Australia. The Swedish study included a large sample of individuals with type 1 diabetes diagnosed at a mean age of 9.3 years according to ICD-8, ICD-9 (www.icd9data.com/2007/Volume1) and ICD-10 criteria, and had a mean follow-up time of 5.8 years [6]. The Australian study included a smaller sample of individuals with type 1 diabetes diagnosed at a mean age of 9.5 years according to ICD-9 and ICD-10 criteria [7]. The mean age at type 1 diabetes onset was similar in all three studies. Our study investigated individuals referred and diagnosed in both inpatient and outpatient settings, as did the Swedish and the Australian studies. The Australian study excluded children who had diagnoses prior to type 1 diabetes onset, as did our study, whereas the Swedish study adjusted for prior psychiatric diagnoses in the risk analysis. Our study was consistent with those from Sweden and Australia in observing an overall increase in the risk of ICD-10 psychiatric disorders; however, the HR was lower in our study (HR for boys, 1.4 [95% CI 1.2, 1.6]; HR for girls, 1.5 [95% CI 1.3, 1.6]) compared with the results based on ICD-10 diagnoses in the Swedish study (HR 1.9 [95% CI 1.8, 2.0]), and those based on ICD-9 and ICD-10 diagnoses in the Australian study (HR 2.5 [95% CI 2.1, 2.9]). Across the main diagnostic categories, our findings match those from the Swedish and Australian studies [6, 7] in demonstrating a significantly increased risk of anxiety, mood disorders and other behavioural disorders, and a particularly high risk of eating disorders. Previous studies using smaller sample sizes found associations between type 1 diabetes and an increase in internalising symptoms, anxiety, depression [1, 2, 4, 8, 10], and eating disorders [9, 16, 30–32]. Notably, we found that following type 1 diabetes onset, the most prevalent psychiatric morbidity was eating disorders, and that boys were particularly at risk compared with their peers without diabetes. While most of the current literature on eating disorders in individuals with type 1 diabetes is focused on girls and women, our findings underline the differences between females and males in psychiatric illnesses and the dangers of overlooking either sex. Neither the Swedish nor the Australian population-based studies stratified individuals based on sex [6, 7].

In our study, boys had an increased risk of substance-misuse disorders after type 1 diabetes onset. This finding is consistent with results from the Swedish study that demonstrated an increased risk of substance-misuse disorders, although it did not differentiate between sexes. Although there are limited data on substance misuse among adolescents with diabetes, substance use and insulin misuse are described as common in adolescents with type 1 diabetes, and particularly among type 1 diabetes individuals with depression [33].

We observed an increased risk of personality disorders in girls only. The Australian study found an overall increase in the risk of personality disorders of more than two-fold, although it did not differentiate between sexes. These disorders were not included in the Swedish study.

An increased risk of suicide attempts observed in the Swedish study [6] was not replicated in our study. However, our analysis was based on relatively few cases ($n = 26$), and may not have had the power to detect an increased risk. A recent systematic review on suicide risk in children and adolescents with type 1 diabetes was inconclusive [34].

Our study found no significant increase in the risk of psychosis, which is consistent with results from previous population-based studies [6, 7]. Contrary to the Swedish study, we found no increased risk of intellectual disability, ASD or ADHD. These neurodevelopmental disorders are typically diagnosed before the age of ten years [24], and are associated with an increased risk of complex comorbid mental

disorders throughout an individual's lifetime [35]. As our focus was de novo onset of psychiatric illness, we excluded individuals diagnosed prior to type 1 diabetes onset, which may explain the differences.

We found a non-significant tendency for increased risk of psychiatric illness over time following type 1 diabetes onset. This may suggest that the challenges of coping with a chronic disease may increase the emotional stress on the child in a way that accumulates rather than diminishes over time. In contrast, the Swedish study observed the opposite trend: a non-significant decline in risk over time, with the highest risk of psychiatric morbidity observed in the first year after type 1 diabetes onset [6]. The authors suggested this reflected increased contact with the hospitals and doctors and the general distress associated with the type 1 diabetes diagnosis. The higher HRs observed in the Swedish study could also be explained by a higher detection rate of latent mental health issues already present at type 1 diabetes onset.

Our findings also suggest that age at type 1 diabetes onset may affect the risk of psychiatric morbidity, with the highest risk occurring at ten to 14 years of age (Table 3). The Swedish study reported an increased risk of psychiatric morbidity with increasing age at type 1 diabetes onset, using age of onset ≥12 years as the oldest age stratum [6]. A possible explanation for these observations is that onset of type 1 diabetes in the developmentally sensitive periods of pre-adolescence and adolescence may coincide with the social and emotional stresses and strains of life-changing events to increase the risk of anxiety, mood disorders and eating disorders [28].

**Implications of the study** The present study confirms that a range of mental health problems may co-occur with type 1 diabetes in both male and female children and adolescents. There was a notable increase in the risk of anxiety disorders, eating disorders and depression. These disorders are thought to develop as a result of imbalances in stress-resilience mechanisms [35] and are potentially preventable by appropriate interventions at an early stage. Clinicians need to be aware of the early symptoms of anxiety and depression, and the symptoms of disturbed eating patterns, body dissatisfaction, and an obsessional preoccupation with weight in both boys and girls. Eating disorders may be particularly difficult to identify if omission of insulin is misinterpreted as non-adherence to treatment for other reasons [31, 32]. In addition, clinicians should be aware that mental health problems in young people with type 1 diabetes may present with atypical emotional and reactive symptoms including substance misuse and behavioural problems, which may mask depression, suicidal behaviour and personality disorders.

Despite ISPAD's recommendations that mental health concerns are included in the treatment of children and adolescents with type 1 diabetes [18], there are no evidence-based guidelines or studies on how to implement screening for the range of mental health problems and psychiatric disorders typically found in young people [29]. Therefore, studies are needed that examine the possibility and effects of early detection, together with the effects of shared-care interventions on behalf of young individuals with type 1 diabetes, within a clinical setting. There is also a need for research into strategies that can manage a range of mental health problems as part of collaborations and shared-care initiatives between paediatricians and child and adolescent mental health services. Improving our knowledge of mental health problems in children and adolescents with type 1 diabetes will be fundamental in assisting health professionals to generate interventions that improve the lives of young patients coping with the demands of diabetes treatment, and facing the challenges they experience in everyday life.

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**Data availability statement** The datasets analysed in this study are available from the corresponding author upon reasonable request.

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**Duality of interest** The authors declare that there is no duality of interest associated with this manuscript.

**Contribution statement** GT, KB and AMS conceived and designed the study, and wrote, edited and reviewed the manuscript. DD and JT researched and analysed data, and wrote, edited and reviewed the manuscript. JS and SMS contributed to the discussion and interpretation of data, and wrote, edited and reviewed the manuscript. All authors gave final approval for publication.

GT takes full responsibility for the work as a whole, including the study design, access to data and the decision to submit and publish the manuscript.

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