Association and Familial Coaggregation of Type 1 Diabetes and Eating Disorders: A Register-Based Cohort Study in Denmark and Sweden

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OBJECTIVE

To ascertain the association and coaggregation of eating disorders and childhood-onset type 1 diabetes in families.

RESEARCH DESIGN AND METHODS

Using population samples from national registers in Sweden (n = 2,517,277) and Demark (n = 1,825,920), we investigated the within-individual association between type 1 diabetes and eating disorders and their familial coaggregation among full siblings, half siblings, full cousins, and half cousins. On the basis of clinical diagnoses, we classified eating disorders into any eating disorder (AED), anorexia nervosa (AN) and atypical AN, and other eating disorder (OED). Associations were determined with hazard ratios (HRs) with 95% CIs from Cox regressions.

RESULTS

Swedish and Danish individuals with a type 1 diabetes diagnosis had a greater risk of receiving an eating disorder diagnosis (HR [95% CI] Sweden: AED 2.02 [1.80–2.27], AN 1.63 [1.36–1.96], OED 2.34 [2.07–2.63]; Denmark: AED 2.19 [1.84–2.61], AN 1.78 [1.36–2.33], OED 2.65 [2.20–3.21]). We also meta-analyzed the results: AED 2.07 (1.88–2.28), AN 1.68 (1.44–1.95), OED 2.44 (2.17–2.72). There was an increased risk of receiving an eating disorder diagnosis in full siblings in the Swedish cohort (AED 1.25 [1.07–1.46], AN 1.28 [1.04–1.57], OED 1.28 [1.07–1.52]); these results were nonsignificant in the Danish cohort.

CONCLUSIONS

Patients with type 1 diabetes are at a higher risk of subsequent eating disorders; however, there is conflicting support for the relationship between having a sibling with type 1 diabetes and an eating disorder diagnosis. Diabetes health care teams should be vigilant about disordered eating behaviors in children and adolescents with type 1 diabetes.

Type 1 diabetes is the predominant type of diabetes in childhood and adolescence. Research suggests that youth with type 1 diabetes have a higher risk of developing an eating disorder (1,2). Eating disorders are serious mental illnesses, with one of

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the highest mortality rates of any psychiatric disorders (3). Eating disorders can become chronic, and relapse can be life-interrupting to patients and their families (4).

Evidence points toward a general predisposition for children with autoimmune disorders to be at an increased risk of developing psychiatric disorders, including eating disorders (5). Compared with those without eating disorders, patients with type 1 diabetes and an eating disorder have a higher risk of poor glycemic control, a threefold increased risk of diabetic retinopathy, impaired social and family functioning, and elevated mortality (6–8). Given the severity of these outcomes, understanding the etiology of this comorbidity is critical for developing more effective approaches to treatment and prevention. As of now, there are no standard assessments for eating disorders within the context of type 1 diabetes; however, screening instruments do exist for this population (9). Moreover, treatment of co-occurring eating disorders and type 1 diabetes is often a complex balance of effectively managing both diseases. For instance, it is difficult to maintain adequate glycemic control during the refeeding stage of severe anorexia nervosa (AN) (10,11). Standardized screenings and treatment are needed for this comorbidity.

Evidence from twin-based studies shows that ~50% of the risk for type 1 diabetes and 50–82% of risk for eating disorders is heritable (12,13). Genome-wide association studies identified a locus for AN that was previously implicated in type 1 diabetes and autoimmune disorders, suggesting a potential genetic association between type 1 diabetes and AN (14,15). Yet, evidence for this association from familial studies remains limited. A Danish study has found within-individual and familial associations between autoimmune diseases, including type 1 diabetes, and all types of eating disorders (16). In a prior Swedish study, we also observed a within-individual association between type 1 diabetes and eating disorders but weak, and not statistically significant, familial associations (17). However, our previous study grouped all eating disorders together and only examined full siblings of patients with type 1 diabetes in the familial analysis. Given that Scandinavia has one of the highest rates of type 1 diabetes (18), it would be of interest to use both Swedish and Danish population data to create well-powered samples for analyses in order to closely examine the familial relationship between type 1 diabetes and eating disorders by subtypes.

In sum, findings from a large familial coaggregation study could provide support for the theory of an intricate combination of shared environmental and genetic factors that contribute to the development of type 1 diabetes and eating disorders. Accordingly, we aimed to conduct a family study examining the comorbidity between type 1 diabetes before age 18 and eating disorders in both the Swedish and the Danish populations.

RESEARCH DESIGN AND METHODS

Study Population

Sweden

We included individuals born in Sweden between 1 January 1977 and 31 December 2003 who had a personal identity number and biological parents who could be identified through the registers (2,690,665 individuals). We excluded individuals who had a congenital malformation (110,801), died before their sixth birthday (11,680), or emigrated before their sixth birthday (50,912), leading to a sample size of 2,517,277 individuals. No individuals were lost to follow-up. Twins (79,676) and double cousins (9,243), i.e., cousins sharing both sets of grandparents, were removed from sibling and cousin analyses, respectively.

Denmark

We included individuals born in Denmark between 1 January 1976 and 31 December 2006 who had a personal identity number and biological parents who could be identified through the registers (1,906,870 individuals). We excluded individuals who had a congenital malformation (2,998), died before their sixth birthday (10,824), emigrated before their sixth birthday (16,672), or were lost to follow-up (455), leading to a sample size of 1,825,920 individuals. Twins (24,467) and double cousins (404) were also removed from sibling and cousin analyses, respectively.

Using the Swedish Multi-Generation Register and Danish Civil Registration System, we identified biological within-generation relatives within the respective study populations to represent varying levels of shared genetic and environmental relatedness. These were full siblings (not twin pairs or higher multiples), half siblings, cousins, and half cousins (Fig. 1).

Data Sources

Sweden

Data were obtained from multiple Swedish registers linked through a personal identification number (19). These registers were the Medical Birth Register (20), which identified our cohort, and the Multi-Generation Register (21), which provided information on family members. The Migration and Death Registers were used to determine migration and death. Diagnostic information on eating disorders came from the nationwide National Patient Register, which contains diagnostic information on the basis of ICD-9 and ICD-10 from all inpatient and most outpatient specialist care (22). Further refinement of the diagnostic information came from the Swedish National Quality Assurances Register for Specialized Eating Disorder Treatment (Riksät) (23) along with the Stepwise database (24); these registers are based on the DSM-IV, Text Revision (DSM-IV-TR). Diagnostic information for type 1 diabetes was taken from the National Patient Register (25,26) and the quality registers Swediabkids and the National Diabetes Register (27).

Denmark

The Civil Registration System (28) was used to attain information on sex, birth year, familial information, and mortality. Similar to the Swedish sample, personal identification numbers were used to link all Danish national registers. Diagnostic information on eating disorders came from The Danish National Patient Register (DNPR) (29) and the Psychiatric Central Research Register (30). Diagnostic information for type 1 diabetes came from the DNPR. Inpatient contacts have been registered in the DNPR since 1977 and in the Psychiatric Central Research Register since 1969. Both registers have included outpatient contacts since 1995. The ICD-10 has been the diagnostic system used in

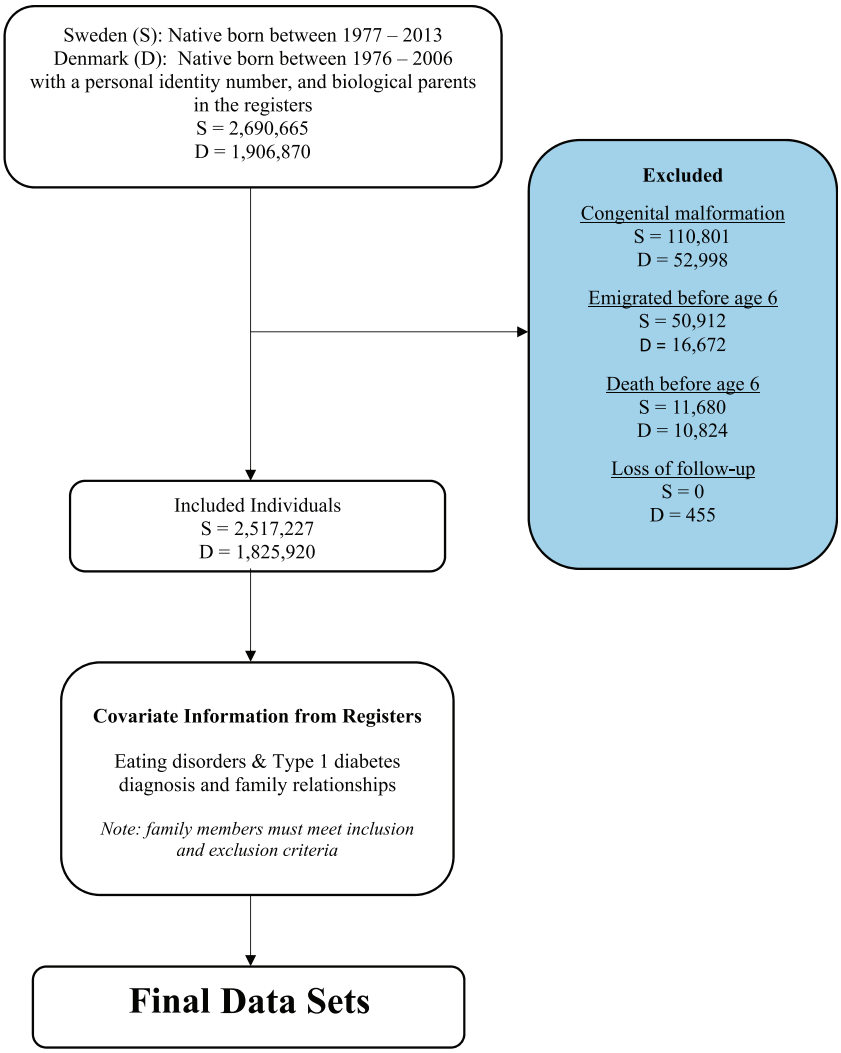

Figure 1—Flowchart of data set creation.

Denmark since January 1994. Prior to that, the ICD-8 was used.

Type 1 Diabetes

Sweden

Type 1 diabetes was defined as receiving a diagnosis between ages 1 and 18 years in Swediabkids or in the National Patient Register (ICD-8 codes 250.00–250.09, ICD-9 codes 250.1–250.9, ICD-10 code E10). Although ICD-8 and ICD-9 do not have distinct codes for type 1 diabetes and type 2 diabetes, the code is still commonly used by researchers (17) and is considered to have a high positive predictive value because type 2 diabetes was uncommon in young populations in the 1970s and 80s (31).

Denmark

Type 1 diabetes was defined as receiving an ICD diagnosis in the DNPR (ICD-8 codes 250.00–250.09, ICD-10 code E10) between ages 1 and 18 years. ICD-9 was not included because it was never introduced in Denmark.

Eating Disorders

Eating disorder diagnoses were derived using ICD codes and DSM-IV-TR from register data and were broken down into two categories: AN and other eating disorder (OED). Both ICD and DSM-IV-TR definitions of atypical AN and AN made up the AN grouping, and OED consisted of bulimia nervosa, atypical bulimia nervosa, or eating disorder not otherwise specified; all diagnostic codes for eating disorders are listed in Table 1. The categories were not mutually exclusive, meaning that both categories were recorded if an individual received both diagnoses. On the basis of these two categories, we created a combined category: any eating disorder (AED). Eating disorders diagnosed after age 6 years were considered valid.

The study was approved by the Regional Ethics Committee in Stockholm, Sweden (Dnr 2013/862-31/5). In Sweden, no informed consent was needed because study participants were not identifiable on the basis of our study question. According to Danish law, informed consent is not required for register-based studies. The Danish Data Protection Agency (AU DT ID: 2015-57-0002; AU LBNR: 565) and the Danish Health Data Authority (SDS FSE ID: 98) approved the current study.

Analysis

Data management was conducted using SAS software, and R/Stata software was used for further analysis. Regrettably, we were unable to combine Swedish and Danish samples; thus, the data sets were analyzed separately. The birth years in both countries varied on the basis of the availability of register data for our exposure and outcomes. For all analyses, a cluster-robust sandwich estimator was used for SEs and CIs to account for dependencies between individuals in the same family (32). Given that eating disorders are primarily diagnosed in women (33), we fit Cox regression models stratified on sex in each analysis. Ethnicity information was not available in either sample.

Sweden

Birth years were separated into five cohorts (1977–1981, 1982–1986, 1987–1991, 1992–1996, 1997–2003).

Denmark

Birth years were separated into six cohorts (1976–1980, 1981–1985, 1986–1991, 1991–1995, 1996–2000, 2001–2006).

Association Between Type 1 Diabetes and Eating Disorders

To analyze the risk of receiving an eating disorder diagnosis in the exposed group (i.e., patients with type 1 diabetes) compared with the unexposed group, we estimated hazard ratios (HRs) with 95% CIs by performing survival analyses using Cox regression, with age as underlying time scale. For each included eating disorder category, we considered

Table 1—ICD codes and DSM-IV-TR diagnoses used to determine eating disorder diagnoses for the AN and OED outcome groups

	ICD-8	ICD-9*	ICD-10	DSM-IV-TR
Sweden				
AN				
AN	—	307B	F50.0	307.1
Atypical AN	—	—	F50.1	307.50, criteria 1 and 2
OED				
Bulimia nervosa	—	—	F50.2	307.51
Atypical bulimia nervosa	—	—	F50.3	307.50, criterion 3
Eating disorder not otherwise specified	—	307F	F50.9	—
Denmark				
AN				
AN	306.50	—	F50.0	—
Atypical AN	—	—	F50.1	—
OED				
Bulimia nervosa	—	—	F50.2	—
Atypical bulimia nervosa	—	—	F50.3	—
Eating disorder not otherwise specified	306.58 and 306.59	—	F50.8† and F50.9	—

*ICD-9 was never adopted in Denmark. †Added to Danish analysis after consultation with Danish clinicians.

type 1 diabetes as a time-varying exposure; individuals were treated as unexposed before a type 1 diabetes diagnosis and as exposed after. Individuals were at risk for eating disorders from their sixth birthday until death, emigration, eating disorder diagnosis, or the end of the follow-up period (31 December 2013 in Sweden, 31 December 2016 in Denmark), whichever came first.

We additionally meta-analyzed the association across the two countries. Since the data sets had to be analyzed separately, we combined the estimates using an inverse variance–weighted meta-analytic approach.

Familial Coaggregation Analysis

First, we identified all possible pairs of full and half siblings/cousins. Because of power considerations, we were not able to examine maternal and paternal relationships separately. We used survival analysis with time-varying exposure to determine the familial coaggregation of type 1 diabetes and eating disorders; individuals were considered unexposed before the date of observed type 1 diabetes in their relative and exposed thereafter. This analysis was completed for each of our outcomes: AED, AN, and OED. Because the familial coaggregation analysis results systematically differed between the countries, we did not meta-analyze them.

Sensitivity Analysis

Because the ICD-8 and ICD-9 used the same diagnostic code for type 1 and type 2 diabetes, we repeated the full sibling analysis in the Swedish sample, including only type 1 diabetes diagnoses using ICD-10. To estimate the aggregated effect of the increased risk for eating disorders on an absolute scale, rather than relative, we created Kaplan-Meier survival curves in the Swedish data. We followed each individual exposed to a type 1 diabetes diagnosis from the date of diagnosis until outcome or censoring. We then matched 10 individuals without type 1 diabetes on sex and birth year to each exposed individual and followed them from the same date until outcome or censoring.

RESULTS

Descriptive Statistics

Sweden

A total of 2,517,260 individuals (17 removed because of miscoded sex) were included in the analysis. Our sample included 15,923 individuals (0.63%, 45.79% female) diagnosed with type 1 diabetes and 27,333 (1.09%, 93.60% female) diagnosed with AED.

Denmark

The data set contained 1,825,920 individuals, with 6,575 diagnosed with type 1 diabetes (0.35%, 46.87% female) and 18,683 (1.02%, 93.03% female) diagnosed with AED. The incidence of type 1 diabetes and AED was slightly lower than in Sweden. Table 2 contains full demographic information from both countries for individuals diagnosed with type 1 diabetes and the unexposed group.

Association Between Type 1 Diabetes and Eating Disorders

Table 3 includes the results for the within-individual analyses. Swedish individuals who had a type 1 diabetes diagnosis had a greater risk of also receiving an eating disorder diagnosis in all categories (HR [95% CI]: AED 2.02 [1.80–2.27], AN 1.63 [1.36–1.96], OED 2.34 [2.07–2.63]). Likewise, Danish individuals diagnosed with type 1 diabetes had a greater risk for all eating disorder categories (AED 2.19 [1.84–2.61], AN 1.78 [1.36–2.33], OED 2.65 [2.20–3.21]). The absolute risk for Sweden (1.98%) was lower than in Demark (2.25%). The results of the meta-analyses of the within-individual estimates showed an HR (fixed effect) of 2.07 (1.88–2.28) for AED, 1.68 (1.44–1.95) for AN, and 2.44 (2.17–2.72) for OED.

Familial Coaggregation Analysis

Table 3 presents results for the familial coaggregation analyses.

Sweden

Full siblings of individuals with type 1 diabetes had a higher risk of being diagnosed with an eating disorder for all categories (HR [95% CI]: AED 1.25 [1.07–1.46], AN 1.28 [1.04–1.57], OED

Table 2—Diagnosis of type 1 diabetes from age 1 to 18 years and lifetime eating disorders

	Sweden			Denmark	
	Type 1 diabetes diagnosis	No type 1 diabetes diagnosis		Type 1 diabetes diagnosis	No type 1 diabetes diagnosis
Total	15,923 (0.63)	2,501,337 (99.37)		6,575 (0.36)	1,819,345 (99.64)
Sex (female)	7,292 (45.79)	1,221,775 (48.84)		3,082 (46.87)	890,984 (48.97)
Birth cohorts					
1977–1981	2,170 (13.63)	435,041 (17.39)	1976–1980	949 (14.43)	292,593 (16.08)
1982–1986	2,392 (15.02)	437,026 (17.47)	1981–1985	763 (11.60)	250,405 (13.76)
1987–1991	3,512 (22.06)	536,825 (21.46)	1986–1990	999 (15.19)	282,859 (15.55)
1992–1996	3,886 (24.40)	505,103 (20.19)	1991–1995	1,412 (21.48)	327,680 (18.01)
1997–2003	3,963 (24.89)	587,341 (23.48)	1996–2000	1,359 (20.67)	313,191 (17.21)
			2001–2006	1,093 (16.62)	352,617 (19.38)
AED	316 (1.98)	27,017 (1.08)		148 (2.25)	18,870 (1.04)
AN	121 (0.76)	12,647 (0.51)		64 (0.97)	9,360 (0.51)
OED	283 (1.78)	21,046 (0.84)		121 (1.84)	12,998 (0.71)

Data are *n* (%).

1.28 [1.07–1.52]). Increased HRs were found for half siblings (AED 1.05 [0.80–1.39], AN 1.15 [0.75–1.77], OED 0.99 [0.73–1.35]) and full cousins (AED 1.10 [1.00–1.20], AN 1.08 [0.98–1.19], OED 1.12 [0.99–1.27]), with an exception for OED in half siblings, although all CIs contained 1. Half cousins had HRs <1 for AED (0.97 [0.79–1.20]) and AN (0.81 [0.57–1.16]) and >1 for OED (1.05 [0.85–1.32]); however, all CIs included 1.

Denmark

All familial analyses for each eating disorder category had CIs that contained 1. The directions of these results were mixed for full siblings (HR [95% CI]: AED 1.01 [0.78–1.32], AN 1.14 [0.80–1.62], OED 0.98 [0.71–1.36]), half siblings (AED 0.74 [0.44–1.25], AN 1.07 [0.56–2.07], OED 0.84 [0.48–1.49]), and full cousins (AED 0.97 [0.83–1.13], AN 1.04 [0.85–1.29], OED 0.92 [0.76–1.11]). The half cousin analysis between type 1 diabetes and all eating disorders yielded HRs <1, although these were not statistically significant (AED 0.64 [0.33–1.23], AN 0.90 [0.41–1.94], OED 0.67 [0.31–1.46]).

Sensitivity Analysis

In Swedish data, a reduced, but statistically significant, positive association between full siblings of individuals with type 1 diabetes and all eating disorder categories remained when only those in the diabetes quality register or with an ICD-10 type 1 diabetes diagnosis were considered (HR [95% CI]: AED 1.24 [1.06–1.44], AN 1.28 [1.04–1.56], OED 1.26 [1.06–1.50]).

In Supplementary Fig. 1, we present the Kaplan-Meier plots of the survival function for those exposed to a type 1 diabetes diagnosis compared with the matched unexposed individuals in Swedish data. For AED, AN, and OED, a difference of the proportion free of outcome between the exposed and unexposed to a type 1 diabetes diagnosis was seen already after 2–3 years. The divergence of this proportion increased steadily over time; at 30 years of follow-up, 97.8% of the unexposed group had not received an AED diagnosis compared with 95.8% of those exposed to type 1 diabetes (results for AED, AN, and OED available in Supplementary Fig. 1).

CONCLUSIONS

Findings in Relation to Other Studies

Although the analyses were completed separately, our study consisted of a combined total of 4.3 million individuals, with 22,498 individuals diagnosed with type 1 diabetes between our two samples. To our knowledge, this study is the largest to explore the familial association between type 1 diabetes and eating disorders. The results of this study provide support for previous research in smaller sample sizes, showing an increased risk for ED in patients with type 1 diabetes (11,34). Additionally, studies that have examined this comorbidity using familial or heritability analysis have only done so in the context of a subanalysis for broader scope studies in single-country samples (16,17). However, our study, which sought to provide closer consideration with increased power, upheld their findings and did not find unequivocal support for a familial coaggregation for this comorbidity. Thus, our study adds robust support to previous findings and provides more insight into the association between type 1 diabetes and the various subtypes of eating disorders.

In both cohorts, the within-individual analysis, or co-occurrence, found that patients with type 1 diabetes had twice as high a risk of being diagnosed with AED than those without a type 1 diabetes diagnosis. Moreover, the CIs for each eating disorder category for the within-individual analysis contained the estimate of the other country between the Danish and Swedish samples (with the only exception being the Danish estimate of OED), which indicates that the strength of the associations are similar across countries. This finding was supported by the additional meta-analysis of the within-individual findings for both countries.

The positive association between type 1 diabetes and eating disorders supports current literature linking the two disorders (17,35). In this analysis, the HR of OED appears to be higher than AN. This slight elevation in our results could reflect the use of insulin restriction or omission for weight loss, a compensatory behavior more akin to bulimia nervosa that is unique to patients with

Table 3—Co-occurrence and familial coaggregation between type 1 diabetes exposure and subsequent eating disorders

	All individuals, *n*	Individuals with type 1 diabetes, *n* (%)	Pairs of relatives†, *n* (%)	AED, HR* (95% CI)	AN, HR* (95% CI)	OED, HR* (95% CI)
Sweden						
Within individual (co-occurrence)	2,517,260	15,923 (0.63)	NA	2.02 (1.80–2.27)‡	1.63 (1.36–1.96)‡	2.34 (2.07–2.63)‡
n (%)				26,840 (1.07)	12,573 (0.50)	20,911 (0.83)
Full siblings	1,789,806	11,473 (0.64)	1,336,734	1.25 (1.07–1.46)‡	1.28 (1.04–1.57)‡	1.28 (1.07–1.52)‡
n (%)				20,092 (1.12)	9,581 (0.54)	15,552 (0.87)
Half siblings	492,133	3,041 (0.62)	453,863	1.05 (0.80–1.39)	1.15 (0.75–1.77)	0.99 (0.73–1.35)
n (%)				5,681 (1.15)	2,367 (0.48)	4,630 (0.94)
Full cousins	1,952,785	12,748 (0.65)	4,761,929	1.10 (1.00–1.20)	1.08 (0.98–1.19)	1.12 (0.98–1.27)
n (%)				21,694 (1.11)	10,347 (0.53)	16,810 (0.86)
Half cousins	510,050	3,313 (0.65)	947,500	0.97 (0.79–1.20)	0.81 (0.57–1.16)	1.05 (0.85–1.32)
n (%)				5,558 (1.09)	2,430 (0.48)	4,469 (0.88)
Denmark						
Within individual (co-occurrence)	1,825,920	6,559 (0.36)	NA	2.19 (1.84–2.61)‡	1.78 (1.36–2.33)‡	2.65 (2.20–3.21)‡
n (%)				18,683 (1.02)	9,271 (0.51)	12,875 (0.71)
Full siblings	1,300,833	4,771 (0.37)	934,967	1.01 (0.78–1.32)	1.14 (0.80–1.62)	0.98 (0.71–1.36)
n (%)				13,437 (1.03)	6,825 (0.52)	9,127 (0.70)
Half siblings	375,026	1,297 (0.35)	340,033	0.74 (0.44–1.25)	1.07 (0.56–2.07)	0.84 (0.48–1.49)
n (%)				4,462 (1.19)	2,049 (0.55)	3,227 (0.86)
Full cousins	1,214,978	4,566 (0.38)	2,958,609	0.97 (0.83–1.13)	1.04 (0.85–1.29)	0.92 (0.76–1.11)
n (%)				12,472 (1.03)	6,439 (0.53)	8,404 (0.69)
Half cousins	226,105	824 (0.36)	390,693	0.64 (0.33–1.23)	0.90 (0.41–1.94)	0.67 (0.31–1.46)
n (%)				2,191 (0.97)	1,081 (0.48)	1,526 (0.67)
Meta-analysis						
Within individual (co-occurrence)	4,343,180	22,482 (0.51)	NA	2.07 (1.88–2.28)‡	1.68 (1.44–1.95)‡	2.44 (2.17–2.72)‡

The absolute number of people included in each analysis and diagnostic information varies from the numbers presented in Table 2. Participants with missing variables and were automatically excluded from analysis. Additionally, we only took the first eating disorder diagnosis per individual, thus excluding additional eating disorder diagnoses. NA, not applicable. *Adjusted for sex and birth year of index individual and relative (when applicable). †Number of unique pairs. ‡CI does not contain 1.

diabetes (8,11). A previous study found that 15% of pediatric patients with type 1 diabetes reported insulin omission for the specific purpose of weight loss rather than other factors. The prevalence of this behavior in the context of the severity of the complications that they entail indicates the need for standardized interventions and screening (36). Future research should examine the prevalence of bulimia nervosa in individuals with type 1 diabetes.

In our familial coaggregation analysis, the HR declined with decreasing relatedness; only full siblings in Sweden had CIs that did not contain 1. Although the CIs overlapped, the HRs between relatives were consistently lower for the Danish group. This could potentially be due to the higher incidence of type 1 diabetes in Sweden or perhaps the inclusion of the more detailed Swedish quality registers in the analysis. The AN effect size across each familial coaggregation analysis was consistently higher than OED in both samples, with an exception of the Swedish full sibling analysis. This trend deviates from other familial coaggregation eating disorder studies (e.g., schizophrenia, death by suicide), which typically have shown stronger associations between OED and the disease in question for each relationship (24,37). Thus, restrictive eating habits appear to be more common than other eating disorder behaviors, such as binge eating. However, given the low power and since the results for AN and OED had overlapping CIs, caution in interpretation is warranted.

The majority of eating disorder cases occurred after a type 1 diabetes diagnosis; this could be due to slightly differing, but overlapping ages of onset. The average age of onset for type 1 diabetes is ~10–14 years (38), with eating disorders being mid- to late teens (with a notable exception of adulthood for binge eating disorder) (33,39). Additionally, diagnostic bias could contribute to this finding because the lag between symptom onset and diagnosis may be longer in eating disorders than in type 1 diabetes. The survival curves showed that the differences between exposed and unexposed in proportions of those without an eating disorder diagnosis increases over time, suggesting that the risk increase is present long after the initial type 1 diabetes diagnosis. These results reiterate that eating disorders can develop at any age, and clinicians must watch for eating disorder symptoms in patients of all ages.

Finally, because statistically significant familial coaggregation was only consistently seen among the Swedish full siblings, it is possible that the familial overlap is mainly driven by disease effect rather than by shared genetics between the disorders. For example, living with a sibling with type 1 diabetes could lead to increased vigilance from caregivers around eating behavior and weight in general, accelerating detection and referral of other family members.

Strengths and Limitations

The greatest strength of this study is the multinational population-based design with prospectively collected information on disease diagnoses. Moreover, the results and diagnostic information can be considered representative for the general population because all individuals have access to publicly funded health care and are automatically included in the national registers (19). However, even with a considerable sample size of >4 million individuals, we still did not have adequate power to explore the extent of the contribution of shared factors through comparing paternal and maternal half sibling (40). Furthermore, we were too underpowered to examine bulimia nervosa and binge eating disorder as distinct categories, and understanding these associations could have important implications for prevention interventions. We have demonstrated shared factors for type 1 diabetes and all eating disorders and encourage future studies using alternative methodologies (e.g., genetic designs) to further explore the mechanisms underlying this association.

Clinical Implications

Our findings further support existing evidence that patients with type 1 diabetes are at higher risk of subsequent eating disorders. Because a majority of the eating disorder cases occurred after the onset of type 1 diabetes, it is critical to ensure that any of the psychoeducation and support materials developed for youth with type 1 diabetes do not unintentionally encourage disordered eating behavior. For example, heightened vigilance toward eating and weight can predispose individuals to disordered eating behavior. Likewise, any weight gain associated with type 1 diabetes management or, alternatively, social praise for weight loss can also influence the risk of engaging in behaviors that could precipitate eating disorders.

Diabetes care teams should be vigilant for the signs of impending eating disorders in their young patients with type 1 diabetes and ensure that eating disorders remain on their radar for early detection and intervention to avoid the potential long-term adverse effects of comorbid type 1 diabetes and eating disorders. Potential warning signs include evidence of consistent insulin restriction or omission, refusal to take medications that might cause weight gain, or specific asks for medications with side effects that include appetite suppression or weight loss, such as amylin analog (8,41). Standardized use of screening measures already designed for patients with type 1 diabetes would also help with identification of eating disorder symptoms.

Moreover, specialists within patients' diabetes care teams would benefit from additional education on warning signs of disordered eating behavior and clear referral pathways for specialist eating disorders services. Comprehensive communication across care teams is critical for the best health outcomes of the patient and may be needed to identify subtle onset of eating disorder symptoms.

Finally, educational programs related to eating behavior should be available for patients with type 1 diabetes and their caregivers. Once symptoms of an eating disorder are identified, the diabetes care team should work closely with the eating disorder care team assembled. Future studies, such as familial studies on bulimia nervosa and binge eating disorder in relation to type 1 diabetes, are warranted to better understand the etiology behind the co-occurrence.

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