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Supplemental Table S1 Details on national and regional registers used in the current study

Register, coverage period	Summary of available information
The Swedish National Diabetes Register, 1996-	The Swedish National Diabetes Register (NDR) was launched in 1996, and integrate both hospitals and primary care clinics. Patient's data are either reported continuously via electronic medical records, through local extraction software or registered directly online. The NDR defines type 1 diabetes as receiving insulin treatment and diagnosis before or at age 30, which has been validated in 97% of cases [1]. Diabetes-related data, even those prior to the 1996, are retrieved from the patient by linking via the patient's personal identify number.
The Swediabkids Database, 2000-	The Swediabkids database was established in 2000 and collected information for more than 95% of Swedish children and adolescents with type 1 diabetes, which contains outpatient records from all pediatric diabetes centers in Sweden. Since 2007 the registry has included data on almost all (98%) children and adolescents with diabetes in Sweden, and since 2008 information on severe hypoglycemia is recorded [2]. Diabetes-related data, even those prior to 2000, are retrieved from the patient records by linking via the patient's personal identify number.
The National Patient Register, 1964-	The National Patient Register (NPR) provides information on inpatient (nationwide coverage since 1987) and outpatients (since 2001) specialist health care facilities. Diagnoses are coded using the International Classification of Diseases (ICD) 7-10 and given by a consultant physician at the time of discharge. The validity of many diagnoses has been evaluated and found to be 95-100% [3].
The Multi-Generation Register, 1932-	The Multi-Generation Register contains information that links Swedish residents to their parents [4].
The Total Population Register, 1961-	The Total population Register contains information on life events, including birth, death, marital status, migration for the Swedish population [5].
The Swedish Prescribed Drug Register, 2005-	The prescribed drug register has had complete coverage of prescriptions in Sweden since July 2005, coded according to the Anatomical Therapeutic Chemical (ATC) classification system [6].

Supplemental Table S2 Diagnosis criteria, the International Statistical Classification of Disease codes (ICD-codes), and Anatomical Therapeutic Chemical Classification System codes (ATC-codes) used to define the variables in the study

Variable	**Used register and corresponding diagnostic criteria**		
Exposure	**Swediabkids**	**The Swedish Diabetes Register**	
Type 1 diabetes	Being diagnosed with type 1 diabetes (ICD-10 code E10), which is recorded from all pediatric diabetes centers in Sweden.	Receiving insulin treatment and diagnosis before or at age 30. This criterion has been validated for 97% of the total patients.	
Outcomes			
Diagnoses	**National Patient Register, ICD-codes**		
	ICD-8 (1969-1986)	**ICD-9 (1987-1996)**	**ICD-10 (1997-)**
Depression	300.4	296B, 300E, 311	F32, F33, F34 (excluding F34.0), F38, F39
Anxiety disorders	300.00, 300.20, 307	300A, 300C, 300X, 308-309	F40, F41
Stress-related disorders	307	308-309	F43
Using prescribed medications	**Prescribed Drug Register, ATC-codes**		
Antidepressants	N06A		
Non-selective monoamine reuptake inhibitors	N06AA		
Selective serotonin reuptake inhibitors	N06AB, N06AE02		
Others	N06C, N06AF, N06AG, N06AX, N06AE06		
Anxiolytics	N05B, N05C		
Exclusion Criteria	**National Patient Register, ICD-codes**		
	ICD-8 (1969-1986)	**ICD-9 (1987-1996)**	**ICD-10 (1997-)**
Chromosomal abnormality	759.30-759.50,759.83,310.5, 311.50,312.50,313.50, 314.50,315.50	758	Q90-Q99

Supplemental Table S3 Characteristics and incidence of outcomes across sub-cohorts of relatives

	Parents	Full-siblings	Maternal half-siblings	Paternal half-siblings	Cousins
Unique individuals, n*	6,617,950	2,596,984	484,181	495,183	2,953,507
Unique relative pairs, n †	6,936,914	3,970,352	750,090	810,026	19,056,970
Unique individual diagnosed with type 1 diabetes, n (%) ‡	20,005 (0.3)	15,314 (0.6)	2821 (0.6)	2870 (0.6)	17,596 (0.6)
Any diagnosis of depression, anxiety, or stress-related disorders, n (%) §	525,241 (7.9)	174,450 (6.7)	55,718 (11.5)	52,330 (10.6)	215,041 (7.3)
Depression, n (%) §	307,106 (4.6)	100,141 (3.9)	31,504 (6.5)	29,522 (6.0)	123,177 (4.2)
Anxiety, n (%) §	256,182 (3.9)	98,202 (3.8)	31,774 (6.6)	29,783 (6.0)	121,142 (4.1)
Stress-related disorders, n (%) §	176,575 (2.7)	47,931 (1.8)	17,741 (3.7)	16,348 (3.3)	60,963 (2.1)
Using antidepressants or anxiolytics, n (%) §	552,821 (16.2)	391,829 (15.4)	105,991 (22.3)	102,065 (21.1)	486,450 (16.5)

* Unique individuals: as relative sub-cohorts comprised all possible relative-pairs, the index person A can appear in the sub-cohort with a relative person B, but can also with a relative person C. The 'count of unique individual' means to count the index person A only once.
† Number of unique relative pairs used in the statistical analysis, where index person A with relative person B could also be analyzed as index person B with relative A, if they fulfilled the requirement for each cohort.
‡ Number of unique individuals who contributed to that relative sub-cohort and being diagnosed with type 1 diabetes.
§ Number of unique individuals with outcomes in each relative sub-cohort; the percentage in parentheses is the incidence of each outcome for each relative type, except for using antidepressants or anxiolytics where the denominator was each relative type reminded to reside in Sweden since 2005.

Supplemental Table S4 Crude hazard ratio and 95% confidence interval of within-individual association and familial co-aggregation of childhood-onset type 1 diabetes with depression, anxiety, stress-related disorders and using antidepressants or anxiolytics

Outcome	Individuals	Parents	Full-siblings	Maternal half-siblings	Paternal half-siblings	Cousins
Any diagnosis of depression, anxiety and stress-related disorders						
Crude	1.73 (1.67, 1.80)	1.22 (1.17, 1.27)	1.20 (1.13, 1.26)	1.12 (1.01, 1.24)	1.14 (1.02, 1.28)	1.12 (1.09, 1.15)
Depression						
Crude	1.93 (1.84,2.02)	1.21 (1.14, 1.27)	1.20 (1.11, 1.29)	1.21 (1.05, 1.38)	1.14 (1.00, 1.29)	1.15 (1.11, 1.19)
Anxiety						
Crude	1.53 (1.44, 1.62)	1.23 (1.16, 1.31)	1.20 (1.11, 1.28)	1.14 (1.00, 1.36)	1.17 (1.01, 1.35)	1.12 (1.09, 1.16)
Stress-related disorders						
Crude	1.83 (1.70, 1.98)	1.27 (1.19, 1.36)	1.27 (1.15, 1.40)	0.98 (0.82, 1.17)	1.17 (0.96, 1.41)	1.05 (1.00, 1.10)
Using any of antidepressants or anxiolytics †						
Crude	1.39 (1.35, 1.44)	1.18 (1.16, 1.21)	1.14 (1.09, 1.18)	1.15 (1.06, 1.24)	1.28 (1.19, 1.38)	1.13 (1.11, 1.15)
Using antidepressants†						
Crude	1.48 (1.43, 1.54)	1.24 (1.21, 1.27)	1.12 (1.07, 1.18)	1.10 (1.00, 1.21)	1.25 (1.14, 1.37)	1.10 (1.07, 1.12)
Using anxiolytics†						
Crude	1.34 (1.29, 1.39)	1.16 (1.13, 1.19)	1.15 (1.10, 1.20)	1.10 (1.01, 1.20)	1.27 (1.17, 1.38)	1.14 (1.12, 1.17)

Supplemental Table S5 Within-individual associations and familial co-aggregations of type 1 diabetes with using specific types of antidepressants*

Outcome	Individuals	Parents	Full-siblings	Maternal half-siblings	Paternal half-siblings	Cousins
Non-selective monoamine reuptake inhibitors (Non-SSRI)						
Crude	1.63 (1.42, 1.88)	1.20 (1.13, 1.27)	1.00 (0.84, 1.19)	1.28 (0.94, 1.74)	1.54 (1.11, 2.13)	1.06 (0.98, 1.14)
Adjusted†	1.58 (1.37, 1.82)	1.18 (1.11, 1.26)	0.95 (0.80, 1.13)	1.21 (0.89, 1.64)	1.41 (1.02, 1.95)	0.99 (0.92, 1.07)
Selective serotonin reuptake inhibitors (SSRI)						
Crude	1.44 (1.38, 1.51)	1.27 (1.23, 1.31)	1.15 (1.10, 1.22)	1.08 (0.97, 1.20)	1.24 (1.12, 1.38)	1.11 (1.08, 1.13)
Adjusted†	1.36 (1.31, 1.43)	1.28 (1.24, 1.32)	1.08 (1.02, 1.13)	0.98 (0.88, 1.09)	1.09 (0.98, 1.21)	1.01 (0.98, 1.03)
Other types of antidepressants						
Crude	1.61 (1.47, 1.77)	1.18 (1.12, 1.25)	1.06 (0.94, 1.18)	1.08 (0.88, 1.33)	1.23 (1.01, 1.49)	1.06 (1.01, 1.11)
Adjusted†	1.54 (1.40, 1.69)	1.17 (1.11, 1.24)	1.01 (0.90, 1.13)	1.03 (0.84, 1.26)	1.13 (0.93, 1.38)	1.00 (0.95, 1.05)

*Analyzed in individuals who remained reside in Sweden since 2005.
†Adjusted for sex and birth cohort of the index individual and the relative.

Supplemental Table S6 Hazard ratios and 95% confidence interval of familial co-aggregation between type 1 diabetes and the outcomes estimated after adjusting for the presence of type 1 diabetes in the relatives

Outcome	Parents	Full-siblings	Maternal half-siblings	Paternal half-siblings	Cousins
Any diagnosis of depression, anxiety and stress-related disorders					
Adjusted*	1.20 (1.15, 1.25)	1.06 (1.01, 1.12)	1.01 (0.91, 1.12)	0.99 (0.89, 1.11)	1.01 (0.99, 1.04)
Depression					
Adjusted	1.18 (1.12, 1.25)	1.06 (0.98, 1.13)	1.09 (0.95, 1.25)	1.00 (0.86, 1.16)	1.04 (1.01, 1.08)
Anxiety					
Adjusted	1.21 (1.14, 1.29)	1.07 (1.00, 1.15)	1.02 (0.89, 1.17)	1.01 (0.87, 1.16)	1.01 (0.97, 1.04)
Stress-related disorders					
Adjusted	1.24 (1.16, 1.33)	1.14 (1.03, 1.25)	0.90 (0.75, 1.07)	1.05 (0.86, 1.27)	0.97 (0.93, 1.02)
Using antidepressants or anxiolytics †					
Adjusted	1.18 (1.15, 1.20)	1.03 (0.99, 1.07)	1.02 (0.94, 1.10)	1.10 (1.03, 1.19)	1.01 (0.99, 1.03)
Using antidepressants†					
Adjusted	1.23 (1.20, 1.26)	1.03 (0.98, 1.08)	1.00 (0.91, 1.10)	1.11 (1.01, 1.21)	1.00 (0.98, 1.03)
Using anxiolytics†					
Adjusted	1.15 (1.12, 1.18)	1.04 (0.99, 1.08)	0.97 (0.89, 1.06)	1.09 (1.00, 1.18)	1.09 (1.00, 1.18)

* Adjusted for sex and birth cohort of the index individual and the relative, and the presence of type 1 diabetes in relatives.
† Using antidepressants or anxiolytics were analysed in individuals who remained reside in Sweden since 2005.

Supplemental Table S7 Within-individual associations and familial co-aggregations of type 1 diabetes with depression, anxiety, stress-related disorders and using antidepressants or anxiolytics, stratified by sex *

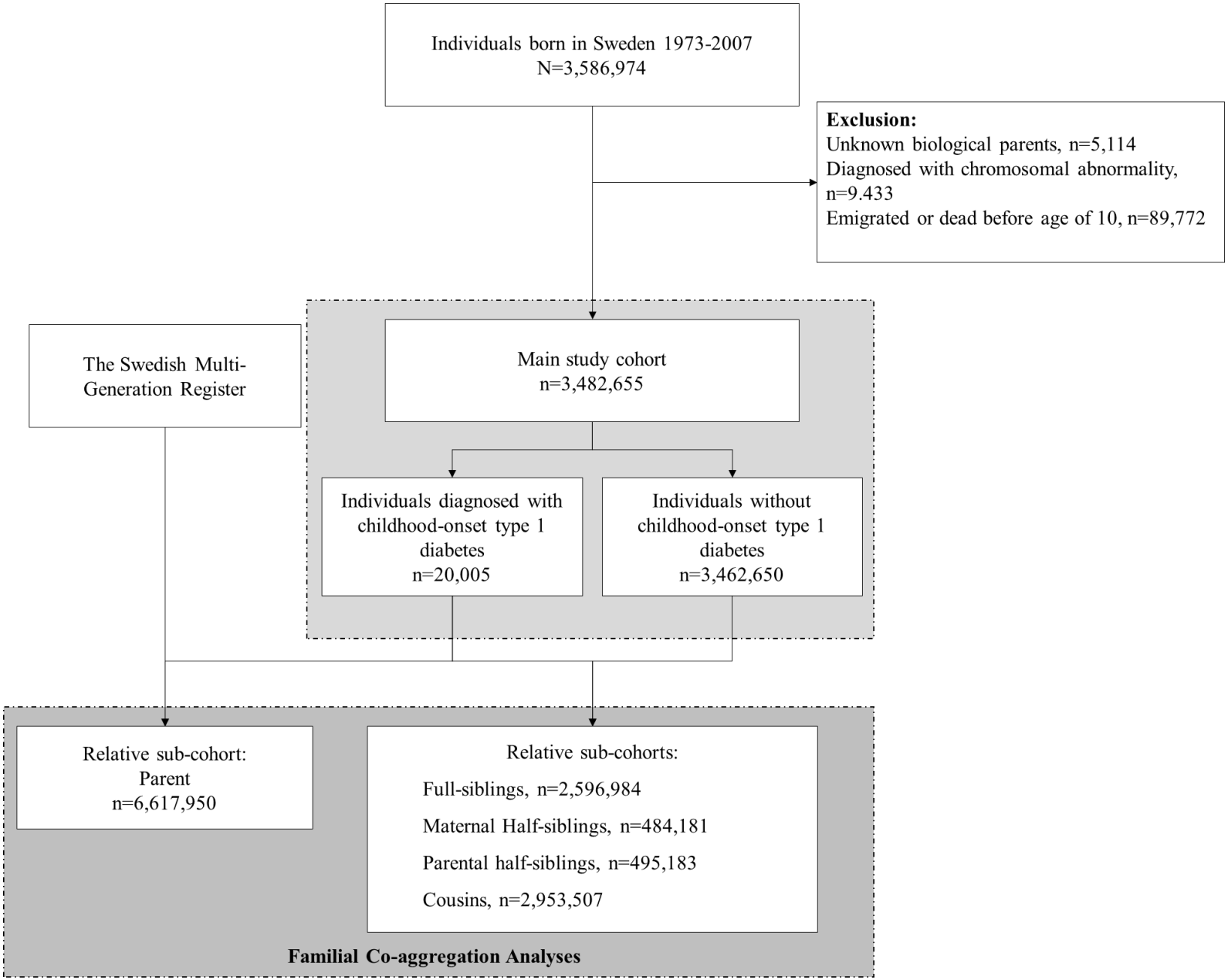
Outcome	Individuals	Parents	Full-siblings	Maternal half-siblings	Paternal half-siblings	Cousins
			Males			
	Males	**Fathers**	**Brothers**	**Maternal half-brothers**	**Paternal half-brothers**	**Male-cousins**
Any diagnosis of depression, anxiety and stress-related disorders						
Crude	1.76 (1.64, 1.88)	1.16 (1.08, 1.24)	1.11 (0.94, 1.31)	1.11 (0.94, 1.31)	1.08 (0.91, 1.29)	1.12 (1.07, 1.16)
Adjusted†	1.62 (1.51, 1.73)	1.15 (1.07, 1.23)	1.01 (0.86, 1.20)	1.01 (0.86, 1.20)	0.97 (0.81, 1.15)	1.02 (0.98, 1.06)
Depression						
Crude	1.92 (1.76, 2.10)	1.17 (1.07, 1.27)	1.10 (0.88, 1.37)	1.10 (0.88, 1.37)	1.03 (0.82, 1.31)	1.15 (1.09, 1.21)
Adjusted	1.77 (1.62, 1.93)	1.16 (1.07, 1.26)	1.02 (0.82, 1.27)	1.02 (0.82, 1.27)	0.93 (0.73, 1.17)	1.05 (1.00, 1.10)
Anxiety						
Crude	1.49 (1.35, 1.64)	1.19 (1.08, 1.32)	1.16 (0.94, 1.44)	1.16 (0.94, 1.44)	1.15 (0.92, 1.44)	1.11 (1.05, 1.17)
Adjusted	1.54 (1.23, 1.50)	1.19 (1.08, 1.31)	1.06 (0.86, 1.31)	1.06 (0.86, 1.31)	1.02 (0.82, 1.28)	1.00 (0.95, 1.06)
Stress-related disorders						
Crude	1.92 (1.69, 2.18)	1.21 (1.09, 1.35)	0.94 (0.69, 1.28)	0.94 (0.69, 1.28)	0.98 (0.71, 1.36)	1.04 (0.96, 1.12)
Adjusted	1.80 (1.58, 2.04)	1.20 (1.08, 1.34)	0.88 (0.64, 1.19)	0.88 (0.64, 1.19)	0.91 (0.66, 1.25)	0.97 (0.90, 1.05)
Using antidepressants or anxiolytics ‡						
Crude	1.42 (1.35, 1.49)	1.14 (1.11, 1.18)	1.13 (1.07, 1.20)	1.13 (1.01, 1.27)	1.21 (1.08, 1.36)	1.13 (1.10, 1.16)
Adjusted	1.30 (1.23, 1.36)	1.14 (1.10, 1.17)	1.04 (0.98, 1.10)	1.00 (0.89, 1.13)	1.05 (0.94, 1.17)	1.01 (0.98, 1.04)
Using antidepressants ‡						
Crude	1.53 (1.44, 1.63)	1.19 (1.14, 1.24)	1.12 (1.05, 1.21)	1.09 (0.94, 1.26)	1.20 (1.04, 1.38)	1.08 (1.04, 1.12)
Adjusted	1.42 (1.34, 1.51)	1.20 (1.15, 1.25)	1.05 (0.98, 1.13)	1.01 (0.87, 1.17)	1.09 (0.94, 1.26)	1.00 (0.96, 1.03)
Using anxiolytics‡						
Crude	1.35 (1.27, 1.43)	1.13 (1.09, 1.16)	1.15 (1.08, 1.23)	1.10 (0.96, 1.25)	1.22 (1.08, 1.38)	1.14 (1.10, 1.17)
Adjusted	1.22 (1.15, 1.3)	1.13 (1.09, 1.17)	1.06 (0.99, 1.13)	0.97 (0.85, 1.10)	1.05 (0.93, 1.19)	1.01 (0.98, 1.04)
			Females			
	Females	**Mothers**	**Sisters**	**Maternal half-sisters**	**Paternal half-Sisters**	Female-cousins
Any diagnosis of depression, anxiety and stress-related disorders						

Crude	1.79 (1.69, 1.90)	1.22 (1.15, 1.28)	1.11 (0.98, 1.27)	1.11 (0.98, 1.27)	1.17 (1.02, 1.34)	1.13 (1.09, 1.16)
Adjusted	1.65 (1.56, 1.75)	1.19 (1.13, 1.26)	1.02 (0.89, 1.16)	1.02 (0.89, 1.16)	1.02 (0.89, 1.18)	1.01 (0.98, 1.05)
Depression						
Crude	2.03 (1.90, 2.18)	1.19 (1.12, 1.27)	1.25 (1.07, 1.47)	1.25 (1.07, 1.47)	1.22 (1.02, 1.46)	1.16 (1.11, 1.20)
Adjusted	1.87 (1.75, 2.01)	1.17 (1.10, 1.25)	1.15 (0.98, 1.36)	1.15 (0.98, 1.36)	1.07 (0.89, 1.28)	1.04 (1.00, 1.09)
Anxiety						
Crude	1.60 (1.48, 1.73)	1.21 (1.12, 1.30)	1.11 (0.94, 1.32)	1.11 (0.94, 1.32)	1.17 (0.97, 1.40)	1.14 (1.09, 1.19)
Adjusted	1.45 (1.34, 1.57)	1.18 (1.10, 1.27)	1.00 (0.85, 1.19)	1.00 (0.85, 1.19)	1.00 (0.84, 1.20)	1.01 (0.97, 1.05)
Stress-related disorders						
Crude	1.84 (1.66, 2.03)	1.26 (1.16, 1.36)	0.98 (0.79, 1.23)	0.98 (0.79, 1.23)	1.25 (1.00, 1.58)	1.05 (0.99, 1.12)
Adjusted	1.72 (1.56, 1.90)	1.23 (1.13, 1.33)	0.92 (0.73, 1.14)	0.92 (0.73, 1.14)	1.13 (0.90, 1.43)	0.97 (0.92, 1.03)
Using antidepressants or anxiolytics ‡						
Crude	1.41 (1.35, 1.48)	1.18 (1.15, 1.21)	1.15 (1.09, 1.20)	1.14 (1.04, 1.26)	1.33 (1.21, 1.46)	1.13 (1.11, 1.16)
Adjusted	1.31 (1.25, 1.37)	1.15 (1.12, 1.17)	1.05 (1.00, 1.10)	1.03 (0.94, 1.14)	1.15 (1.05, 1.27)	1.02 (0.99, 1.04)
Using antidepressants ‡						
Crude	1.49 (1.42, 1.57)	1.22 (1.19, 1.26)	1.13 (1.07, 1.20)	1.09 (0.97, 1.22)	1.28 (1.14, 1.43)	1.11 (1.08, 1.14)
Adjusted	1.39 (1.32, 1.47)	1.20 (1.16, 1.23)	1.05 (0.99, 1.12)	1.01 (0.90, 1.13)	1.13 (1.01, 1.26)	1.01 (0.99, 1.04)
Using anxiolytics ‡						
Crude	1.37 (1.30, 1.44)	1.15 (1.12, 1.18)	1.15 (1.09, 1.22)	1.10 (0.98, 1.22)	1.30 (1.17, 1.45)	1.15 (1.12, 1.18)
Adjusted	1.26 (1.19, 1.32)	1.12 (1.09, 1.52)	1.05 (0.99, 1.11)	0.98 (0.88, 1.10)	1.12 (1.01, 1.24)	1.02 (1.00, 1.05)

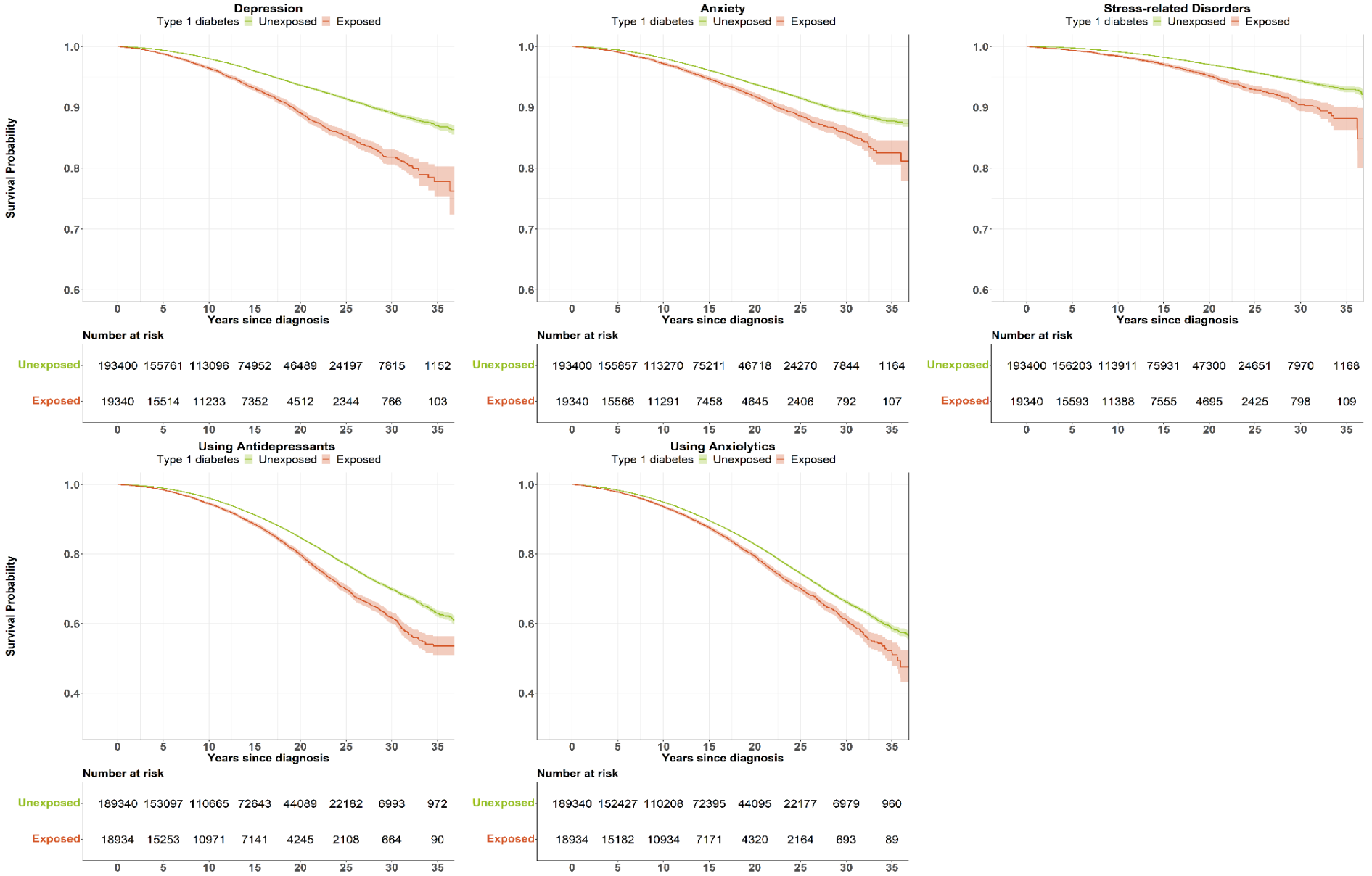
* Analyses were stratified by the sex of the outcome person, i.e. males vs. females with/without type 1 diabetes, mothers vs. fathers of individual with/without type 1 diabetes or brothers vs. sisters of individuals with/without type 1 diabetes.
†Adjusted for sex and birth cohort of the index individual and the relative.
‡ Number of unique individuals who contributed to that relative sub-cohort and being diagnosed with type 1 diabetes.

Supplemental Table S8 Comorbid depression, anxiety and stress-related disorders in individuals with and without type 1 diabetes in the main study cohort

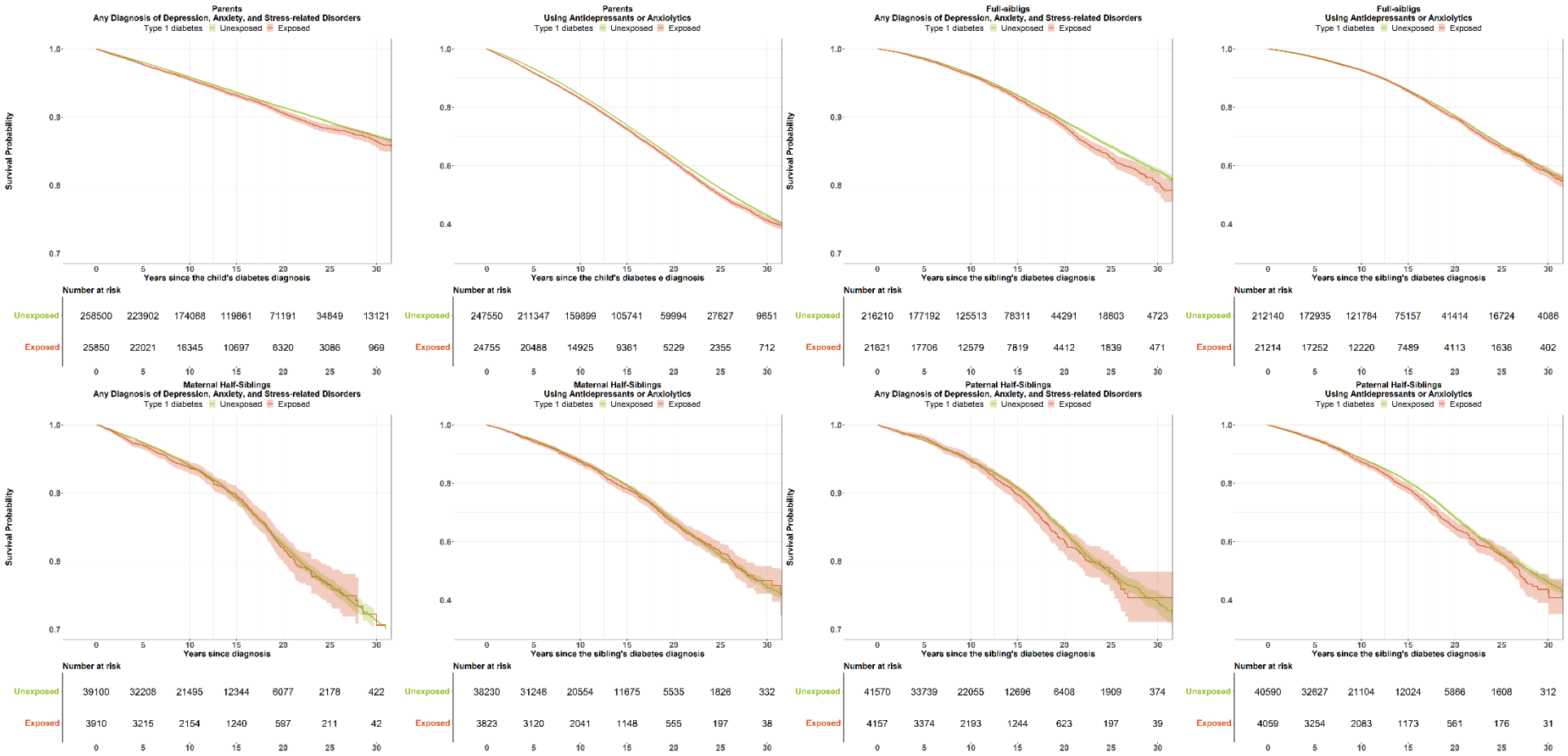
Comorbid diagnoses of depression, anxiety or stress-related disorders, n (%)	Type 1 diabetes	No type 1 diabetes
All three	176 (0.9)	17,000 (0.5)
Depression and anxiety	390 (2.0)	42,309 (1.2)
Depression and stress-related disorders	137 (0.7)	13,059 (0.4)
Anxiety and stress-related disorders	68 (0.3)	9990 (0.3)



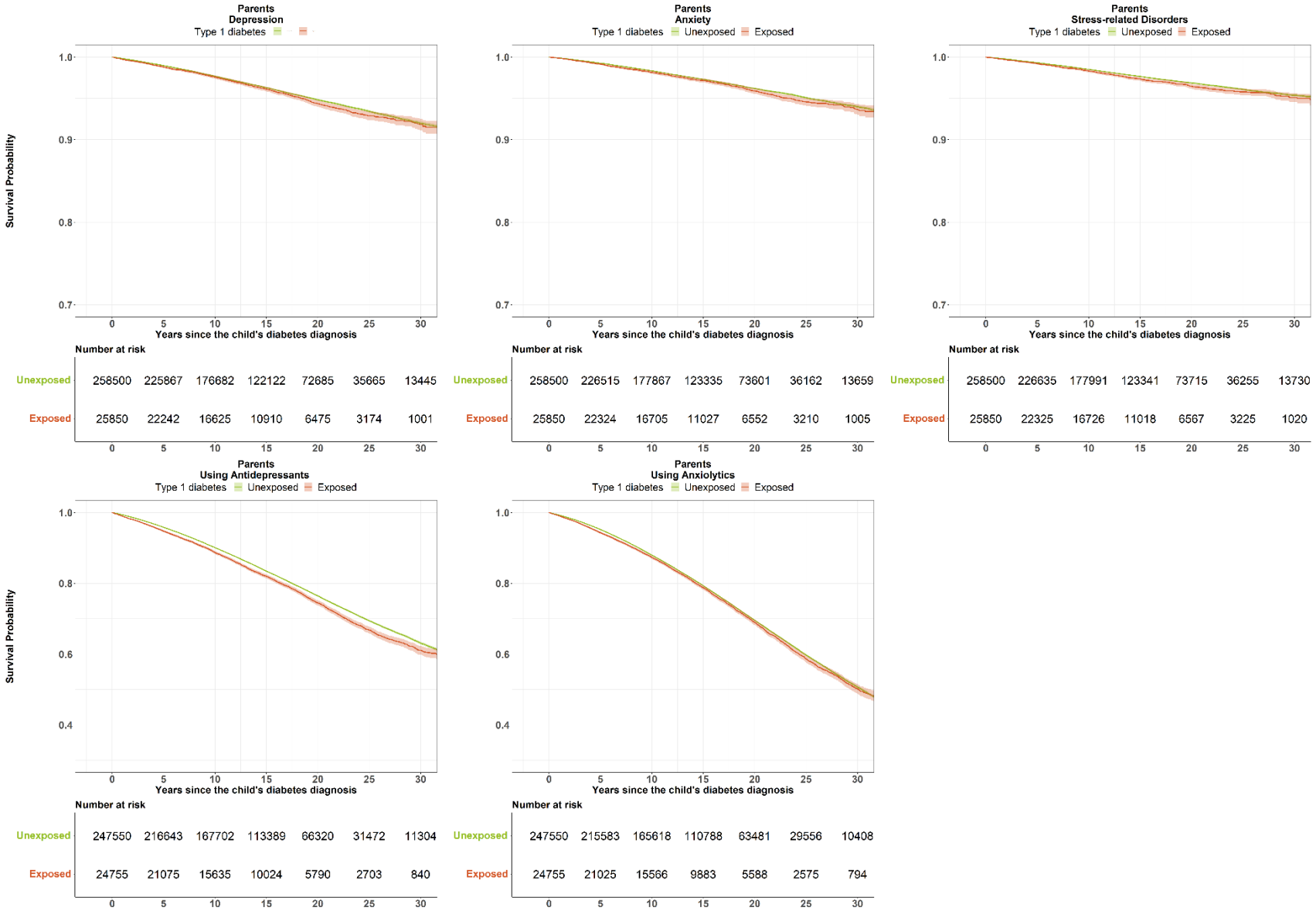
Supplemental Figure S1 Flow-chart of study cohort construction



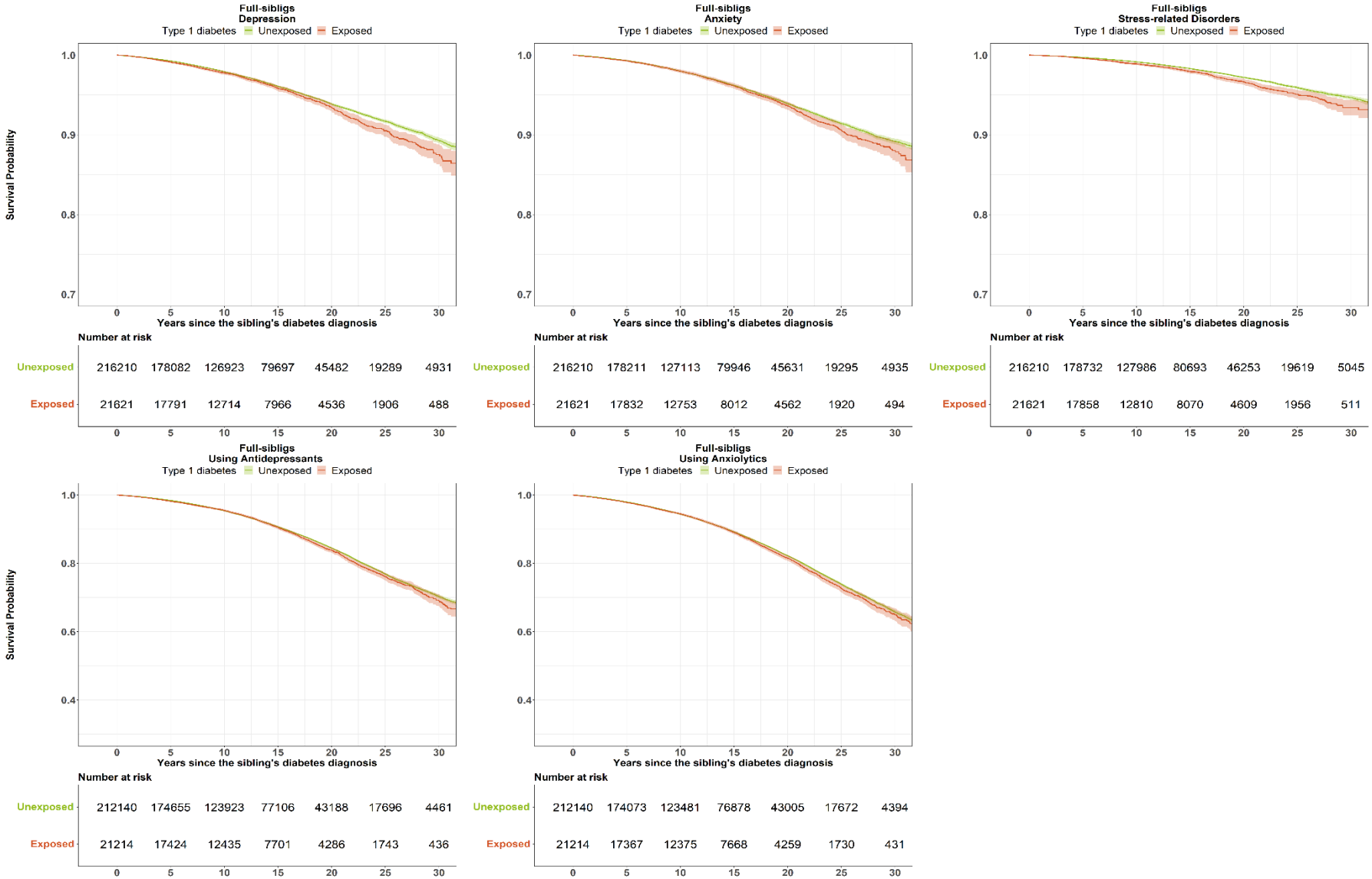
Supplemental Figure S2 Survival curve of receiving specific diagnosis of depression, anxiety, or stress-related disorders and using antidepressants or using anxiolytics in individuals diagnosed with childhood-onset type 1 diabetes compared to the matched reference individuals.



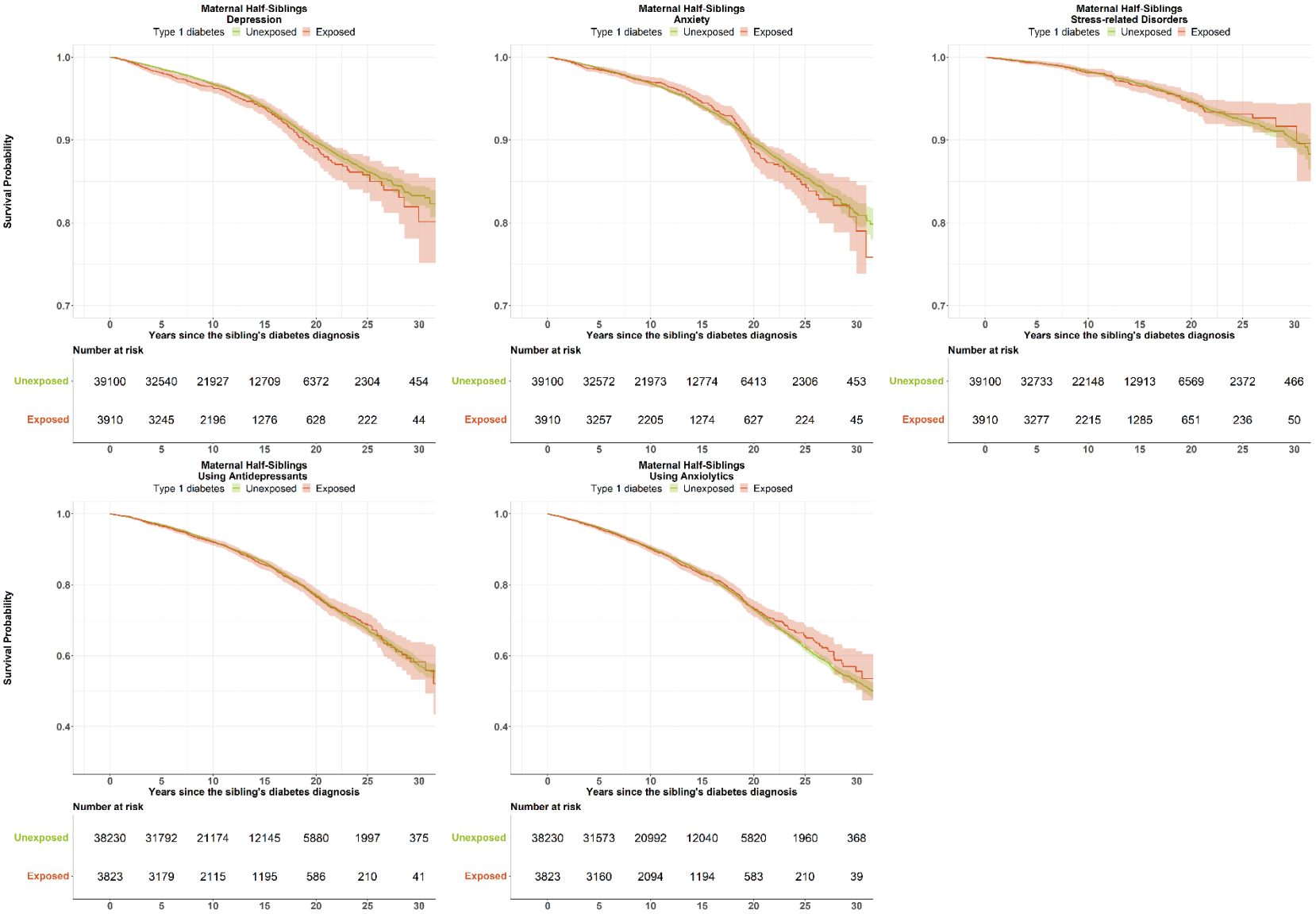
Supplemental Figure S3 Survival curve of receiving any diagnosis of depression, anxiety, or stress-related disorders and using antidepressants and anxiolytics in relatives of individuals diagnosed with childhood-onset type 1 diabetes compared to the matched relatives of individuals without childhood-onset type 1 diabetes * * Survival curves of specific diagnoses of each type of relatives are shown in **Supplemental Figure 4-7**



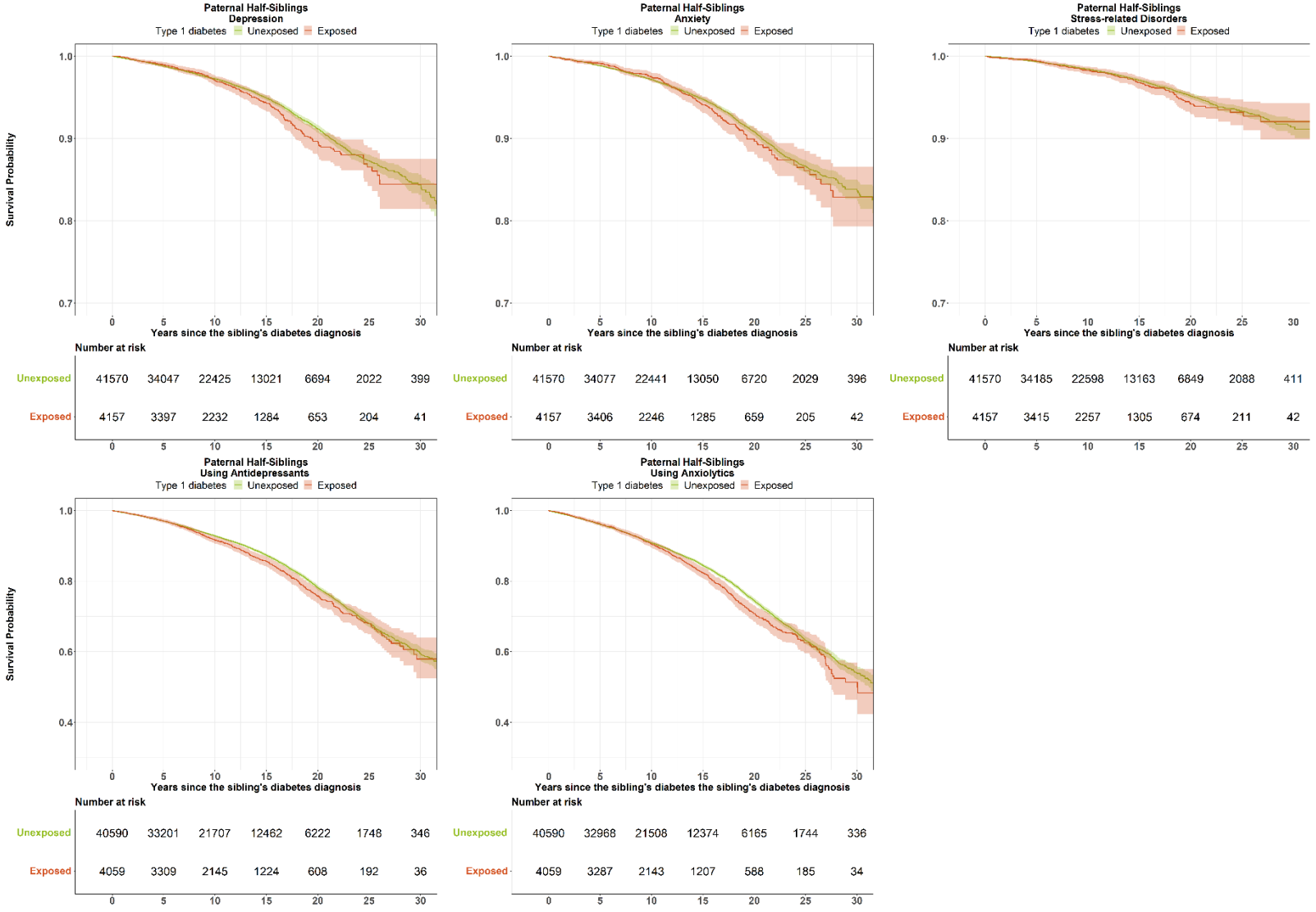
Supplemental Figure S4 Survival curve of receiving specific diagnosis of depression, anxiety, or stress-related disorders, using antidepressants, and using anxiolytics in parents of individuals diagnosed with childhood-onset type 1 diabetes compared to the matched paremts of individuals without childhood-onset type 1 diabetes



Supplemental Figure S5 Survival curve of receiving specific diagnosis of depression, anxiety, or stress-related disorders, using antidepressants, and using anxiolytics in full-siblings of individuals diagnosed with childhood-onset type 1 diabetes compared to the matched full-siblings of individuals without childhood-onset type 1 diabetes



Supplemental Figure S6 Survival curve of receiving specific diagnosis of depression, anxiety, or stress-related disorders, using antidepressants, and using anxiolytics in maternal half-siblings of individuals diagnosed with childhood-onset type 1 diabetes compared to the matched maternal half-siblings of individuals without childhood-onset type 1 diabetes.



Supplemental Figure S7 Survival curve of receiving specific diagnosis of depression, anxiety, or stress-related disorders, using antidepressants, and using anxiolytics in paternal half-siblings of individuals diagnosed with childhood-onset type 1 diabetes compared to the matched paternal half-siblings of individuals without childhood-onset type 1 diabetes.

Supplemental File 1 Description of construction process of matched sub-samples from each relative sub-cohorts

From each relative sub-cohorts, a matched sub-sample was constructed for plotting Kaplan-Meier curves and estimating the absolute proportions with outcomes in the exposed and unexposed. We first identified individuals diagnosed with type 1 diabetes (Group A) and all their relatives (Group B) and identified individuals who were not diagnosed with type 1 diabetes (Group A') and all their relatives (Group B'). Anyone included in Group B did not appear in Group B', as they at least had one relative being diagnosed with type 1 diabetes. For each individual from Group B, who were considered as exposed, we randomly selected five individuals (unexposed) from Group B', matched on sex and birth-year.

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