Incidence Rates of Treated Mental Disorders in Childhood and Adolescence in a Complete Nationwide Birth Cohort

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ABSTRACT

Objective: To investigate incidences, cumulative incidence rates, and risk factors of diagnosed mental disorders in a complete nationwide birth cohort across the entire period of childhood and adolescence.

Methods: Based on nationwide Danish registries, the entire cohort of all children born in 1995 was followed up to December 31, 2013. Data for children who migrated during the period were censored in the time analyses, and death before age 18 years was considered a competing risk. Incidence rates and cumulative incidence rates for any first-time–diagnosed mental disorder and 10 major categories of mental disorders according to *ICD-10* criteria were calculated for 68,982 individuals. In addition, the effects of age, sex, and further child- and family-related risk factors on mental disorders were analyzed.

Results: The incidences of any mental disorder, substance use disorders, depression, and anxiety disorders showed an increase in adolescence, whereas those for autism spectrum disorders, attention-deficit/hyperactivity disorder, conduct disorder, and tic disorder increased during childhood and decreased thereafter. Males had higher incidence rates of any mental disorders, substance use disorders, autism spectrum disorders, ADHD, conduct disorder, and tic disorder. Females had higher risks for depressive, anxiety, obsessive-compulsive, and eating disorders. Several other risk and protective factors for any mental disorder were identified. The cumulative incidence rate at age 18 years amounted to 11.02% for any mental disorder.

Conclusions: These findings provide the most comprehensive estimates of the development, incidence rates, and contributing risk factors of registered mental disorders for the entire period of childhood and adolescence that have been calculated so far.

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There is strong evidence of specific developmental vulnerabilities for mental disorders in childhood and adolescence given that a sizable proportion of lifetime mental disorders originate during this period of life. Two major studies came to rather similar findings: half of all lifetime cases in the US National Comorbidity Survey replication study[1] started by age 14 years, and among adult cases of the representative birth cohort studied longitudinally in Dunedin (New Zealand),[2] 50% had received a diagnosis before 15 years of age, and 74% before age 18 years.

Similarly, there is converging evidence from prevalence estimation studies showing that a sizeable proportion of young people suffer from mental disorders, as shown, for instance, in an analysis[3] of the size and burden of mental disorders in Europe 2010. A recent meta-analysis[4] of the worldwide prevalence of mental disorders in children and adolescents calculated that 13.4% (95% CI, 11.3%–15.9%) were diagnosed with a mental disorder. Within the extended time period from 0 to 18 years, the risk of falling ill with a mental disorder is particularly high among adolescents.[5,6]

Whereas point prevalence estimations may be inflated due to the inclusion of mild and transient cases, lifetime prevalence calculations may be additionally jeopardized by a response call bias when participants are asked to report lifetime mental disorders in retrospect. Worldwide, only a few studies have spanned longer time periods via repeated longitudinal assessments (eg, Kim-Cohen et al,[2] Copeland et al[7]), and even among those studies there was rarely an entire lifetime perspective based on all ages among all participants. This deficit may be better controlled for by incidence studies covering large populations over extended time periods.

Scandinavian countries are able to provide these data by using their public mental health service system and registries of all citizens, which is very useful for both health service planning and research. Recently, a follow-up study[8] of all Danish residents who received their first lifetime treatment in a psychiatric setting for any mental disorder from January 1, 2000, through December 31, 2012, revealed that during the course of life, 37.66% of females and 32.05% of males received their first treatment. In that study, no attempt was made to calculate lifetime risks of mental disorders separately for children, adolescents, and adults, and neither the observation time nor the included diagnoses covered the entirety of childhood and adolescence for all participants.

Numerous risk factors related to childhood adversities have an impact on both typical development and the development of mental disorders in children and adolescents.[9–11] Child- and family-related factors relate to age, sex, and various childhood adversities including parental mental illness[12] and death.[13]

Clinical Points

- Incidences of registered mental disorders in a complete nationwide birth cohort increased substantially by adolescence for any mental disorder, substance use disorders, depression, and anxiety disorders.
- Sex effects were apparent with higher incidence rates for depression, anxiety disorders, obsessive-compulsive disorders, and eating disorders in females, whereas there was a male preponderance for substance use disorders, autism spectrum disorders, attention-deficit/hyperactivity disorder, conduct disorder, and tic disorder.
- The cumulative incidence rate of any registered mental disorder at age 18 years was 11% in this cohort, implying that childhood and adolescence are highly vulnerable periods for the development of mental disorders. A sizable number of risk factors were identified, underscoring the detrimental effects of childhood adversities on the development of mental disorders in youth.

Society-related factors are represented by various indicators of socioeconomic status[14] and degree of urbanization.[15]

The present study aims to calculate the total number of all first occurrences of all major types of diagnosed mental disorders emerging in childhood and adolescence in a complete nationwide birth cohort with a follow-up covering the total period of childhood and adolescence in all registered individuals. Furthermore, it attempts to analyze the impact of various risk factors on incidences.

METHODS

Description of the Dataset

Public health care is free of charge in Denmark and available regardless of income. Furthermore, mental health care by psychiatric institutions is accessible for all citizens either directly or via transfer by general practitioners who are not responsible for the care of individuals with mental disorders. Mental disorders in children and adolescents are assessed and treated in specialized Child and Adolescent Psychiatric Services only.

The dataset of the present study contained the total cohort of all children born between January 1, 1995, and December 31, 1995, in Denmark. A total of 68,982 individuals including 35,470 males and 33,512 females were identified through the Danish Civil Registration System (DCR). Only children with information in the DCR on both parents were included; 449 individuals were not included in this sample due to missing information on the father. This sample was followed up until December 31, 2013, or until death, emigration, or otherwise inactive Civil Registration System (CPR) number, whichever came first. A total of 431 (250 males and 181 females) had died before age 18 according to data from the cause of death registry and 1,152 (531 males and 621 females) had migrated to another country before age 18 as documented in the DCR registry. In 52 (27 males and 25 females), the dataset was incomplete before age 18 due to other reasons. Thus, for a total of 67,347 children, the entire period of childhood and adolescence until age 18 was covered. However, the data were included until time of death or censoring due to other reasons, ie, data of 68,982 children were used in the analyses. Only a small number of register variables were unavailable for a small number of participants.

The CPR numbers of the sample were linked to the National Patient Registry, which contains data on all individuals entering the public health system. Since 1995, the registry has included data based on World Health Organization *ICD-10*[16] diagnoses for both inpatient and outpatient admissions. In total, 7,903 participants representing 1,207,470.1 person years had a first-time diagnosis. Besides any mental disorder defined as any Fx.xx diagnosis from the *ICD-10*, the following diagnoses were considered: substance use disorders (F1), schizophrenia (F20), depression (F32–F33, F34.1), anxiety disorders (F40, F41, F93.0–F93.2), obsessive-compulsive disorder (F42), eating disorders (F50), autism spectrum disorders (F84), attention-deficit/hyperactivity disorder (ADHD; F90), conduct disorder (F90.1, F91, F92), and tic disorder (F95). The following diagnoses were excluded from the analyses due to low frequencies: organic mental disorders (F0; n = 61), bipolar disorders (F30–31; n = 55), posttraumatic stress disorder (F43.1; n = 46), and selective mutism (F94.0; n = 19).

In addition to age and sex, the following variables were considered as risk factors and data on them were extracted from various registries, including the DCR (national patient register), birth register, student register, register of family incomes, register of population information, cause-of-death register, and register of placements outside the home: perinatal risks (birth weight < 2,500 or ≥ 2,500 g, duration of pregnancy < 37 vs ≥ 37 weeks, Apgar score < 8 vs ≥ 8, mother smokes yes vs no, age of mother < 35 vs ≥ 35 years, age of father < 35 vs ≥ 35 years), education of the parents (assessed as highest during the observation time), socioeconomic status of the parents (assessed as highest during the observation time), disposable family income below national mean for the years 2000–2005, urbanization (municipalities above 100,000 inhabitants), at least 1 move to another municipality, divorce of the parents before the child turns 15, any maternal or paternal mental illness present before the diagnosis of the child's illness, maternal or paternal death, and placement of the child outside of the home. All data reside with Denmark Statistics; access to the data will be provided only by special permission from this national agency.

Statistical Analyses

First, the total and the sex- and age-specific incidence rates per 1,000 person years for any first occurrence of any mental disorder and the various diagnostic categories were calculated. Next, the cumulative incidences in terms of the probability that a person was diagnosed with a given disorder before age 18 were identified. In addition, both incidence rates and cumulative incidence functions were plotted in figures showing curves for any mental disorder and the various diagnoses for the total cohort and separately for the two sexes.

The incidence rate at age 2 years included the children who received any diagnosis after age 1 up to and including age 2. The same held for each age group from 1 to 19 years; the 19-year-old group includes only ages from 18 up to but not including 19 since none of the children turned 19 before the end of study. The cumulative incidence function from competing risk regression was used for the calculation of cumulative incidences. Competing risk analysis was used because death is a competing risk to the event of getting a diagnosis. If a person left the country or his or her CPR number became inactive, that individual's data were censored at the time of this event. The cumulative incidence functions from the competing risk analysis were compared for males versus females to analyze for sex effects.

In addition, age effects on incidence rates were addressed for the 2 age groups age 0 up to and including 13 and age above 13, reflecting the distinction between childhood and adolescence. The age effects were studied using piecewise linear regression that estimated a linear regression model for the incidence rates of each of the 2 age groups and then compared the intercepts and slopes for the 2 age groups. To check the model fit and, hence, the reliability of the age effects, the residuals were plotted and inspected along with the coefficient of determination. If the coefficient of determination is close to 1 and the residuals are random, the model fit is considered to be good.

For cumulative incidences, only sex effects were analyzed, since the cumulative incidence function itself is a function of time and, hence, of age. Sex and further risk effects on any mental disorder were studied by competing risk regression analyses with the calculation of subhazard ratios (SHRs). The model included both categorical and time-dependent variables. All analyses were performed in the statistical software programs Stata version 14.1 (StataCorp LP, College Station, Texas) and R version 3.2.3 (R Foundation).

Ethical Standards

The use of anonymized data was approved by the Danish Data Protection Agency. No further institutional review board approval was needed for the present study.

RESULTS

Overall Incidence

Findings regarding incidence rates of any mental disorder and the 10 diagnostic categories separate for the total sample, the 2 sexes, and for age ≤13 and age >13 years are shown in Supplementary Table 1. The confidence intervals for incidence rates of disorders in males versus females did not overlap for almost all of the 10 diagnostic categories, indicating that the 2 sexes were likely to have different incidence rates. The curves on incidence rates, as shown in Figure 1, also indicate that for males the increase of incidence rates was not strictly linear but had peaks at several ages for some diagnoses. The curve of incidence rates for males with autism spectrum disorders had a peak at ages 6 and 15 years and for males with ADHD at ages 9 and 14 years. For males with conduct disorder, there was a wavy upwards trend until age 16 years, with a rapid decline afterward, whereas females indicated a peak only around age 16 years.

Age and Sex Effects

The test findings on the age effects on incidence rates are collected in Table 1. The model fit according to the coefficient of determination was good for the majority of the models. However, some of the residual plots indicated less reliable models despite having a relatively large R^2 value. Therefore, the associated diagnoses are not mentioned among the results, and neither are tic disorder for females and autism spectrum disorders for males due to the rather low R^2 values for these models. Although the coefficient of determination was good for the schizophrenia models, there were only 3 children with schizophrenia before age 13 years, which is not enough for a reliable analysis. The disorders with a higher increase in the incidence rate after age 13 years (ie, a positive coefficient for comparisons of slopes, $P < .05$, and a reliable model) were any mental disorder (total and females), substance use disorders (total), depression (total), and anxiety disorders (total). For autism spectrum disorders (total), ADHD (total and males), conduct disorder (total and males), and tic disorder (total), the incidence rates increased until age 13 years and then decreased (the coefficient for comparisons of slopes was negative and $P < .05$). For obsessive-compulsive disorder, there was a trend for an increase in the incidence rates in adolescent males ($P = .057$), but the difference was so close to zero (−0.04) that the possible age effect had no real meaning. For eating disorders, there was a tendency toward an increase in the incidence rates in adolescent females ($P = .058$).

Cumulative Incidences

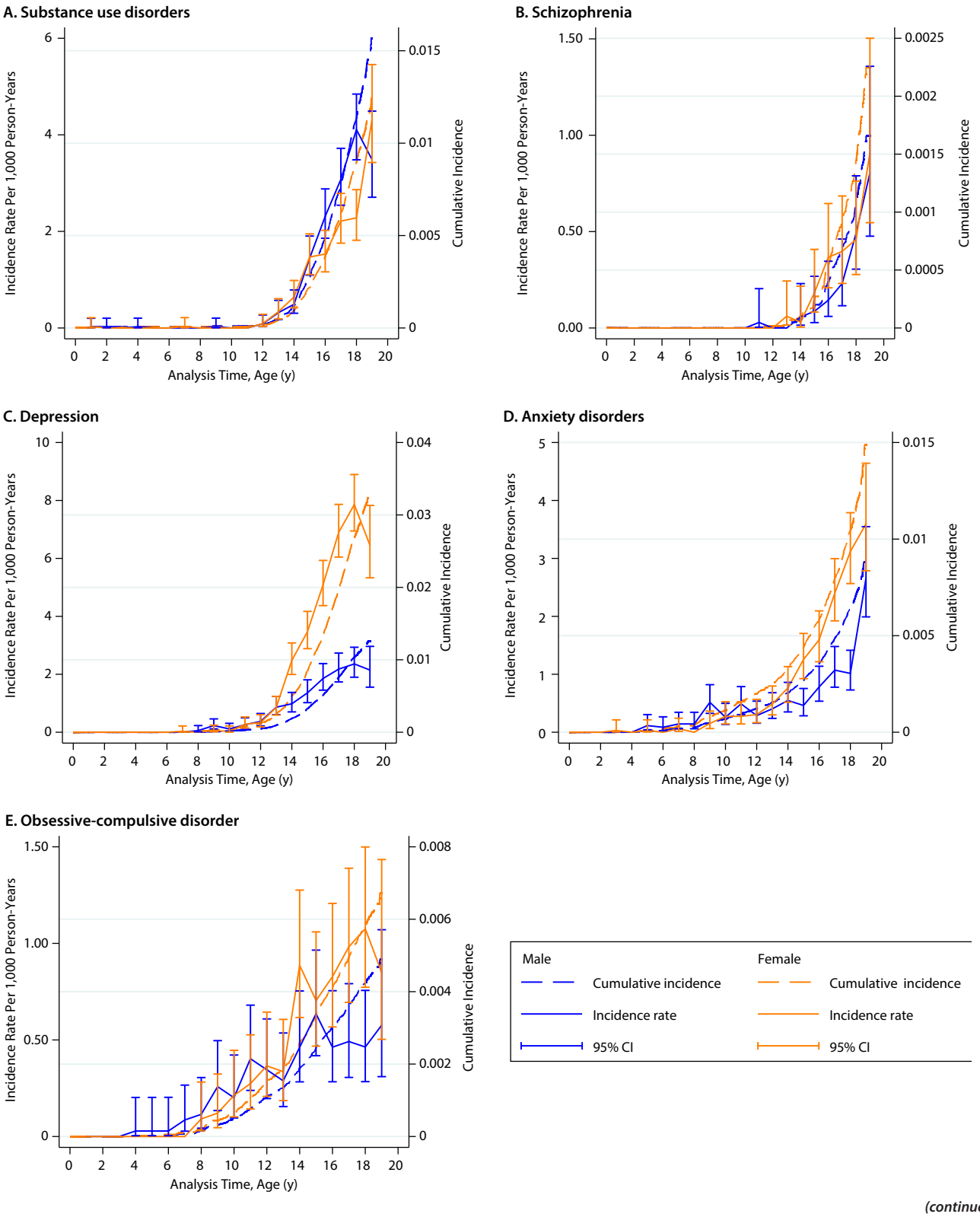
The cumulative incidences for any mental disorder and the 10 diagnostic categories are shown in Table 2. The cumulative incidence rates at age 18 years was 11.02% for any mental disorder; the highest rate found for an individual disorder was for ADHD (2.51%), followed by depression (1.84%), autism spectrum disorders (1.79%), conduct disorder (1.32%), and substance use disorders (1.02%), with all other diagnostic categories below 1%.

Furthermore, the sex effects on the cumulative incidences are shown in Table 3. Findings based on competing risk regression analyses revealed that there were sex differences for any mental disorder and all 10 diagnostic categories except schizophrenia. Considering the subhazard ratios in the total sample, males had a higher risk for any mental disorder, substance use disorders, autism spectrum disorders, ADHD, conduct disorder, and tic disorder, whereas females had a higher risk for depression, anxiety disorders, obsessive-compulsive disorder, and eating disorders.

Risk Factors

In addition to sex and age, a more complex risk model was analyzed including a larger list of potential risk factors and any mental disorder as the outcome. The findings in Table 4 indicated both protective and risk factors. Protective factors

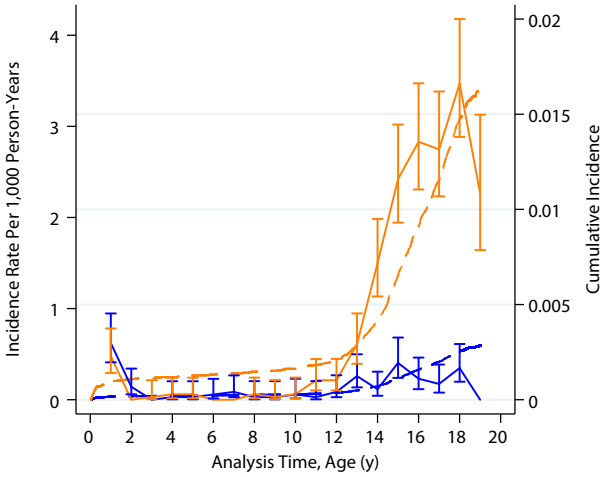
Figure 1. Age- and Sex-Specific Incidence Rates and Cumulative Incidences for 10 Major Mental Disorders in Childhood and Adolescence[a]



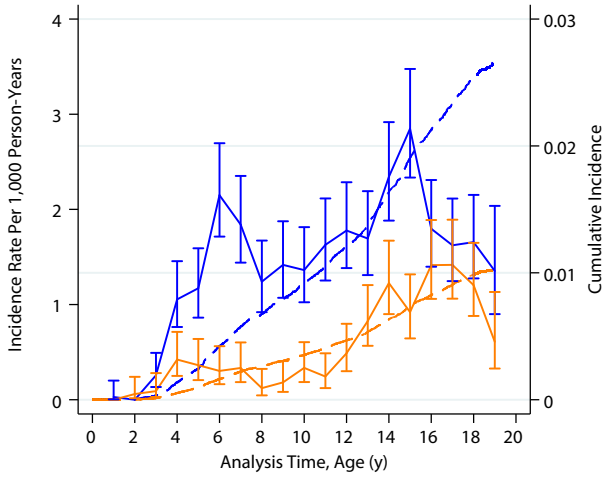
(continued)

Figure 1 (cont.).

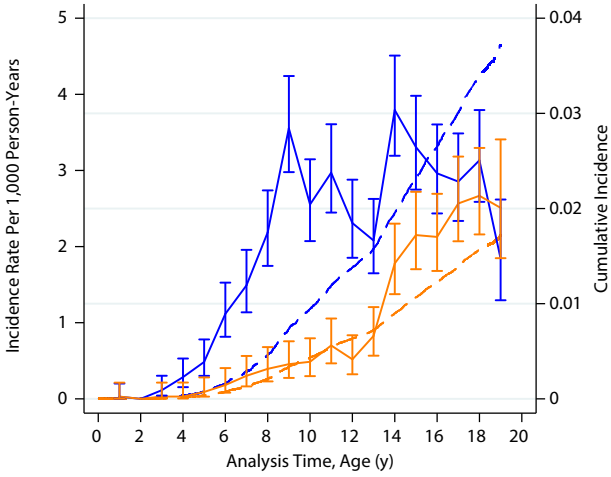
F. Eating disorders



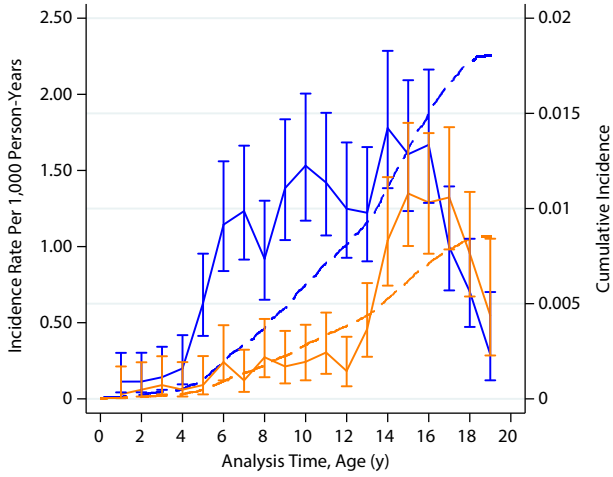
G. Autism spectrum disorders



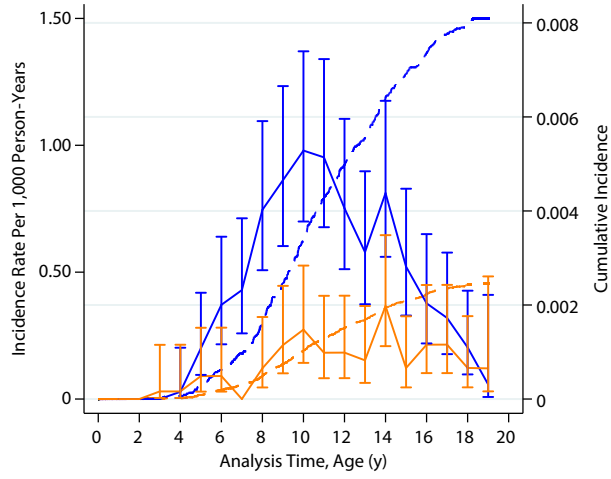
H. Attention-deficit/hyperactivity disorder

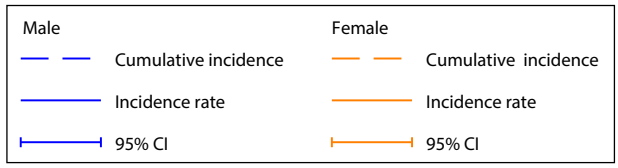


I. Conduct disorder



J. Tic disorder





[a]For the purpose of better visibility, different scalings were used in the figure parts.

Table 1. Piecewise Linear Regression Comparing the Intercepts and Slopes of the Linear Regression Models of the Incidence Rates of 2 Age Groups (≤ 13 Years vs > 13 Years) and the Coefficient of Determination as an Indicator of the Model Fit

	Comparison of Intercepts				Comparisons of Slopes				Coefficient of
Diagnosis	Coefficient	SE	*P*	95% CI	Coefficient	SE	*P*	95% CI	Determination (R^2)
Any mental disorder									
Total	3.82	0.72	.000	2.35 to 5.30	0.48	0.19	.016	0.09 to 0.86	0.95
Males	−0.26	0.90	.774	−2.09 to 1.57	−0.26	0.23	.281	−0.73 to 0.22	0.83
Females	8.00	0.97	<.001	6.02 to 9.98	1.23	0.25	<.001	0.72 to 1.75	0.96
Substance use disorders									
Total	0.37	0.08	<.001	0.21 to 0.52	0.65	0.02	<.001	0.61 to 0.69	0.99
Males	0.43	0.16	.012	0.10 to 0.76	0.71	0.04	<.001	0.63 to 0.80	0.97
Females	0.30	0.22	.185	−0.15 to 0.76	0.59	0.06	<.001	0.47 to 0.71	0.93
Schizophrenia									
Total	−0.07	0.05	.133	−0.17 to 0.02	0.15	0.01	<.001	0.12 to 0.17	0.91
Males	−0.11	0.05	.055	−0.22 to 0.00	0.15	0.01	<.001	0.12 to 0.18	0.88
Females	−0.03	0.06	.592	−0.16 to 0.09	0.14	0.02	<.001	0.11 to 0.17	0.87
Depression									
Total	1.37	0.25	<.001	0.87 to 1.87	0.58	0.06	<.001	0.45 to 0.71	0.96
Males	0.70	0.18	<.001	0.34 to 1.07	0.16	0.05	.001	0.07 to 0.26	0.91
Females	2.08	0.38	<.001	1.30 to 2.86	1.02	0.10	<.001	0.82 to 1.22	0.96
Anxiety disorders									
Total	−0.24	0.19	.224	−0.63 to 0.15	0.50	0.05	<.001	0.40 to 0.61	0.91
Males	−0.41	0.21	.060	−0.84 to 0.02	0.35	0.05	<.001	0.24 to 0.46	0.80
Females	−0.06	0.23	.814	−0.53 to 0.42	0.66	0.06	<.001	0.54 to 0.79	0.93
Obsessive-compulsive disorder									
Total	0.30	0.05	<.001	0.20 to 0.40	−0.01	0.01	.284	−0.04 to 0.01	0.94
Males	0.16	0.08	.045	0.00 to 0.31	−0.04	0.02	.057	−0.08 to 0.00	0.79
Females	0.45	0.09	<.001	0.27 to 0.63	0.01	0.02	.633	−0.04 to 0.06	0.91
Eating disorders									
Total	1.01	0.18	<.001	0.65 to 1.38	0.06	0.05	.180	−0.03 to 0.16	0.83
Males	0.25	0.12	.045	0.01 to 0.50	−0.01	0.03	.751	−0.07 to 0.05	0.13
Females	1.82	0.28	<.001	1.25 to 2.40	0.14	0.07	.058	0.00 to 0.29	0.89
Autism spectrum disorders									
Total	0.61	0.21	.005	0.19 to 1.03	−0.24	0.05	<.001	−0.35 to −0.13	0.73
Males	0.49	0.34	.159	−0.20 to 1.19	−0.39	0.09	<.001	−0.57 to −0.21	0.60
Females	0.74	0.17	<.001	0.40 to 1.08	−0.09	0.04	.044	−0.18 to 0.00	0.76
Attention-deficit/hyperactivity disorder									
Total	0.81	0.23	.001	0.34 to 1.27	−0.25	0.06	<.001	−0.37 to −0.13	0.90
Males	0.52	0.40	.196	−0.28 to 1.33	−0.58	0.10	<.001	−0.78 to −0.37	0.81
Females	1.11	0.19	<.001	0.73 to 1.49	0.09	0.05	.074	−0.01 to 0.19	0.93
Conduct disorder									
Total	0.67	0.13	<.001	0.42 to 0.93	−0.30	0.03	<.001	−0.37 to −0.23	0.85
Males	0.32	0.19	.092	−0.06 to 0.70	−0.44	0.05	<.001	−0.54 to −0.35	0.80
Females	1.04	0.15	<.001	0.74 to 1.34	−0.15	0.04	<.001	−0.23 to −0.07	0.82
Tic disorder									
Total	−0.11	0.09	.238	−0.29 to 0.07	−0.14	0.02	<.001	−0.19 to −0.10	0.69
Males	−0.27	0.14	.063	−0.56 to 0.02	−0.22	0.04	<.001	−0.30 to −0.15	0.70
Females	0.07	0.06	.280	−0.06 to 0.19	−0.06	0.02	.001	−0.09 to −0.03	0.45

included female sex, advanced education of the parents, higher socioeconomic status as indicated by self-employment or CEO position, and disposable family income above the national mean. Risk factors predicting any mental disorder were perinatal risks, social position as youth, being a student or pensioner, divorce of the parents, maternal and paternal mental illness prior to diagnosis of the child, paternal death, and the child's being placed outside the home.

DISCUSSION

The findings of the present study were based on a complete national birth cohort with coverage of all diagnosed mental disorders during the entire period of childhood and adolescence. Not only did these cases fulfill diagnostic criteria for various major mental disorders according to *ICD-10* criteria, but the disorders also had been severe enough to be referred to mental health specialists. Given the public nature of the mental health system, with only a very small number of specialists working in private outpatient practices, there were no financial factors influencing the referrals and the registry data.

In general, the approach of studying cumulative incidences in a total national birth cohort covering the total period of childhood and adolescence not only is novel but also provides a very solid calculation of the disease burden in the population that is not accomplished with cross-sectional population studies of diverse age groups or longitudinal studies of selected samples, which are the most frequently used types of studies in developmental psychopathology. In fact, preceding prevalence studies[4,5] were mostly based on rather small sample sizes and often had unknown representativeness, small number of diagnostic subgroups, heterogeneous age compositions, and mostly rather short and

Table 2. Cumulative Incidences at Age 18 for Each Diagnosis in the Cohort by Sex

	Total			Males			Females		
Diagnosis	n	Cumulative Incidence, %	95% CI	n	Cumulative Incidence, %	95% CI	n	Cumulative Incidence, %	95% CI
Any mental disorder	7,903	11.02	10.78–11.25	4,219	11.58	11.25–11.92	3,684	10.43	10.10–10.76
Substance use disorders	825	1.02	0.95–1.10	472	1.18	1.07–1.29	353	0.85	0.75–0.95
Schizophrenia	114	0.13	0.10–0.15	50	0.10	0.07–0.14	64	0.15	0.11–0.19
Depression	1,392	1.84	1.74–1.95	404	1.05	0.94–1.16	988	2.69	2.51–2.86
Anxiety disorders	674	0.84	0.77–0.91	265	0.63	0.54–0.71	409	1.06	0.95–1.17
Obsessive-compulsive disorder	365	0.50	0.45–0.56	159	0.43	0.36–0.49	206	0.58	0.50–0.67
Eating disorders	613	0.85	0.78–0.92	95	0.27	0.22–0.32	518	1.46	1.33–1.59
Autism spectrum disorders	1,248	1.79	1.69–1.88	913	2.54	2.37–2.70	335	0.99	0.88–1.09
Attention-deficit/hyperactivity disorder	1,776	2.51	2.39–2.62	1,235	3.44	3.25–3.63	541	1.51	1.38–1.65
Conduct disorder	909	1.32	1.23–1.40	628	1.78	1.64–1.92	281	0.83	0.73–0.92
Tic disorder	364	0.53	0.48–0.59	283	0.80	0.71–0.90	81	0.24	0.19–0.29

discontinuous follow-up periods. Furthermore, a previous Danish register-based study[8] did not cover all diagnoses and had no complete follow-up of the entire period of childhood and adolescence for each individual enrolled in the analyses. Both community and register studies, including the present study, share the same shortcoming that the exact age at onset of the disorder cannot be determined because community studies have to rely on retrospective accounts and register studies are subject to more or less delayed referrals.

The incidence rates of the present study cannot be directly compared to prevalence rates as obtained in community studies. The advantage of the latter may be the high quality of diagnostic information and also the coverage of subclinical cases, which, however, are differentiated from clinical cases in need of treatment by deficits in psychosocial functioning. Unfortunately, the latter criterion has not been sufficiently assessed in all community studies concerned with child and adolescent mental health.[4,5] Despite these differences in study design, the major findings of the present study converge with those on the developmental patterns of mental health disorders in childhood and adolescence obtained in previous prevalence studies. These similarities pertain first to the rank order of the cumulative incidences with the exception of the rather high incidences of autism spectrum disorders in the present study. However, according to some recent time-trend analyses by the senior author's research group,[15] there is clear evidence that in Denmark the recognition of autism spectrum disorders has increased significantly in the recent past. Furthermore, the similarities between the present study and preceding prevalence studies are also reflected on other levels, namely, the age- and sex-specific patterns of first occurrences of mental disorders in childhood and adolescence and the cumulative incidence rate at age 18 years.

Regarding the age effects, there are 2 major types of curves, namely one type with an early onset, various peaks during childhood, and a decline of incidences during adolescence and another type with low frequencies during childhood but a rapid increase in incidences starting above age 13 years. The early-onset type is represented by autism spectrum disorders, ADHD, conduct disorder, and tic disorder. The incidences in this group with varying peaks in childhood may be due to various factors of influence.

Table 3. Competing Risk Regression Models Measuring the Effect of Sex on Each of the Defined Disorders With a Unique Model for Each Pair of Rows (Males vs Females) and Death as the Competing Risk (N = 68,982)

Diagnosis	Subhazard Ratio	SE	*P*	95% CI
Any mental disorder				
Males	1.00			Reference
Females	0.90	0.02	.000	0.86–0.94
Substance use disorders				
Males	1.00			Reference
Females	0.79	0.06	.001	0.69–0.91
Schizophrenia				
Males	1.00			Reference
Females	1.36	0.26	.105	0.94–1.97
Depression				
Males	1.00			Reference
Females	2.62	0.15	.000	2.33–2.94
Anxiety disorders				
Males	1.00			Reference
Females	1.64	0.13	.000	1.40–1.91
Obsessive-compulsive disorder				
Males	1.00			Reference
Females	1.37	0.15	.003	1.12–1.69
Eating disorders				
Males	1.00			Reference
Females	5.82	0.65	.000	4.67–7.24
Autism spectrum disorders				
Males	1.00			Reference
Females	0.39	0.02	.000	0.34–0.44
Attention-deficit/hyperactivity disorder				
Males	1.00			Reference
Females	0.46	0.02	.000	0.41–0.51
Conduct disorder				
Males	1.00			Reference
Females	0.47	0.03	.000	0.41–0.54
Tic disorder				
Males	1.00			Reference
Females	0.30	0.04	.000	0.24–0.39

For instance, the curve of autism spectrum disorders may reflect a clinically well-known and quite frequently delayed recognition or referral of childhood autism with a steady increase of incidences until school entry at age 6 years, while the peak at age 15 years may be mostly represented by young adolescents with Asperger syndrome encountering increasing problems in coping with their social disability.[17] Furthermore, the rather high cumulative incidence rate of 1.79% for autism spectrum disorders at age 18 reflects the sizable increase of incidences observed in Denmark over a

Table 4. Findings From Competing Risk Regression With Any Mental Disorder in the Cohort as Outcome and Death as a Competing Risk (n = 66,730)

Variable	Subhazard Ratio	SE	*P* Values	95% CI
Sex				
Male (n = 34,229)	(Reference)			
Female (n = 32,501)	0.89	0.02	<.001	0.85–0.94
Perinatal risks				
No (n = 32,496)	(Reference)			
Yes (n = 34,234)	1.22	0.03	<.001	1.16–1.27
Highest education of the parents[a]				
Primary school (n = 6,456)	(Reference)			
Gymnasium or gymnasium with vocational qualification (n = 1,882)	0.79	0.06	.002	0.68–0.92
Vocational traineeship (n = 30,206)	0.86	0.03	<.001	0.80–0.92
Higher education (n = 28,186)	0.70	0.03	<.001	0.65–0.76
Highest socioeconomic status of the parents[a]				
Supported by public sector[b] (n = 5,029)	(Reference)			
Self-employed or employee for spouse (n = 5,208)	0.77	0.05	<.001	0.68–0.87
CEO in company, organization or the public sector (n = 2,407)	0.79	0.07	.006	0.67–0.94
Wage earner (n = 53,573)	0.99	0.04	.854	0.91–1.08
Youth, student, or pensioner (n = 513)	1.23	0.12	.040	1.01–1.49
Disposable income for the families for the years 2000–2005[a]				
Mean income less than 243,626 DKK (n = 12,729)	(Reference)			
Mean income higher than or equal to 243,626 DKK (n = 54,001)[c]	0.81	0.03	<.001	0.76–0.86
Urbanization[a]				
Municipalities with more than 100,000 inhabitants (n = 12,155)	(Reference)			
Municipalities with less than 100,000 inhabitants (n = 54,575)	1.02	0.03	.604	0.96–1.08
Moves to another municipality before age 15				
No (n = 19,585)	(Reference)			
Once or more (n = 47,145)	1.16	0.03	<.001	1.10–1.22
Divorce of parents before child turns 15[a]				
No (n = 48,741)	(Reference)			
Yes (n = 17,989)	1.36	0.03	<.001	1.30–1.43
Time-dependent covariates:				
Any maternal mental diagnosis (n = 7,955)	1.45	0.06	<.001	1.34–1.58
Any paternal mental diagnosis (n = 6,743)	1.35	0.06	<.001	1.23–1.48
Maternal death (n = 814)	0.91	0.12	.442	0.71–1.16
Paternal death (n = 1,867)	1.30	0.10	<.001	1.13–1.50
Child placed outside the home (n = 2,226)	2.73	0.17	<.001	2.41–3.08

[a]The variable has missing values for at least 1 observation.
[b]Unemployed at least 6 months annually, receiver of unemployment benefit, early retirement pensioner, voluntarily retired person receiving a special pensioner, or receiver of Social Security benefits.
[c]243,626 DKK is approximately equivalent to $37,052 USD.

time period of 16 years due to an increasing awareness of these disorders both among professionals and in the public.[18]

The incident peaks for ADHD at ages 9 and 14 years might well map onto changes in the educational demands and responsibilities of children in the Danish school system that are leading to greater number of referrals since these events are associated with increased symptom disruption.[19] The conduct disorder curve fits well to the distinction of an early-onset type during childhood and an adolescent-onset type.[20] Finally, the curve for increasing incidences until age 10 years and then declining incidences for tic disorder may reflect underlying brain maturation effects, since these disorders are considered to be strongly affected by neurobiological substrate factors.[21]

The second type of cumulative incidences with a marked increase above age 13 years is manifested by the curves for substance use disorders, depression, and anxiety disorders and by the same trend also for eating disorders in females. This phenomenon of rising incidences in adolescence has been linked to the major changes in the neural systems that subserve the multitude of higher cognitive functions, reasoning, interpersonal interactions, cognitive control of emotions, risk-vs-reward appraisal, and motivation, and it has been concluded that these challenges may increase the risk of cognitive, affective, and addictive disorders.[22] However, much is still to be learned about why these effects unfold particularly with some disorders and not with others.

Furthermore, the apparent sex effects on mental disorders unfolding particularly in adolescence need a better understanding in terms of their causal processes concerned with psychopathology.[23] According to the present study's findings, these effects were relevant for depression, anxiety disorders, obsessive-compulsive disorders, and eating disorders in females. For schizophrenia and for affective and anxiety disorders, marked changes in hormones and hormonal receptors (particularly in the areas of the amygdala and the hippocampus), increased emotional responses to social stimuli, and rapid alterations in motivation and reward systems during adolescence have been hypothetically linked to these processes.[22]

At the same time, psychosocial factors are operant, including the increasing social demands on both sexes that may be associated with the cognition of failure and, thus, a higher chance of developing emotional problems. In contrast, the preponderance of males with substance use disorders has been linked to personality traits, including

high novelty seeking and low harm avoidance.[24] The strong female preponderance in eating disorders with its peak of anorexia nervosa in adolescence traditionally has been associated with the changes occurring in puberty, which are more pronounced for females. However, it should be noted that recent time trend analyses based on the Danish registries across 16 years indicate that better recognition of the still relatively rare cases of male eating disorders may point also to a change in male vulnerability.[25]

Other diagnoses, including neurodevelopmental disorders such as autism spectrum disorders, ADHD, and tic disorder and the very common and youth-specific conduct disorder, show both a distribution with a strong male preponderance[23] and multiple age peaks. Whereas some[26] argue that females with autism spectrum disorders could present with a phenotype different from that of males, there is also evidence from time-trend analyses of Danish register data that females with autism spectrum disorders might have been insufficiently recognized in clinical practice in the past.[18] In contrast, males and females with ADHD are more similar than different with regard to the core symptoms except more frequently described inattentiveness in girls and small sex differences in comorbidity, with more internalizing problems in girls and more externalizing behavior in boys.[27] Although females were still less likely to be referred for treatment, the gender gap has decreased more recently as evidenced by further recent Danish time-trend analyses.[28] Similarly, conduct disorder has long been considered a male-specific disorder, as reflected in the early and continuous occurrences throughout childhood in the present analysis, but recent studies[29,30] and the present study indicate that, mostly due to better recognition, conduct disorder is on the rise, particularly among female adolescents.

Furthermore, the cumulative incidence rate of 11.02% for any mental disorder at age 18 years in the present study is remarkably close to the worldwide prevalence of 13.4% for ages 0–18 years.[3] However, there are substantial differences between these two types of studies. The worldwide prevalence rate of 13.4% is derived from a very small set of clinically assessed diagnoses compared with the administrative claims data from Denmark that relies on the unassessed "best practices" of community clinicians. Moreover, the varying time frames of the prevalence estimation across studies was not considered in the review on prevalence studies,[3] and the reported worldwide prevalence rate may be slightly inflated in that it was calculated only preferentially and not entirely by selecting estimates associated with the presence of functional impairment, so that there was no clear indication for treatment in all of these individuals.[4] In contrast, due to their referral to mental health specialists, the children and adolescents of the present study did not have subclinical problems and were definitely impaired, insomuch that they all received assessment and treatment.

Finally, the model of various contributing protective and risk factors to any mental disorder underscores the protective factors of female sex when considering the whole period of youth, which, however, changes with adolescence as shown in the preceding analyses. The additional risk factors comprising perinatal risks, low parental education, low socioeconomic status, below-average income of the family, parental divorce and illness, paternal death (perhaps due to consequent financial constraints more relevant than maternal death in the present study), and placement of the child outside of the family all support the findings of studies showing the detrimental effects of early childhood adversities on developing mental disorders in youth.[9] Whereas the present study, like most register-based studies, may have definite limitations for a proposed research agenda addressing the mechanisms explaining how adversities transform into psychopathology,[11] future registry-based studies may well contribute to the analysis of cumulative risks as outlined in a theoretical frame.[10]

In addition to the aforementioned limitations of all incidence studies, a concern has been raised repeatedly regarding the possible insufficiency of register diagnoses since they come from a large group of different clinicians without application of standardized interviews. However, for the Danish registries, various studies have consistently shown sufficient validity for major psychiatric diagnoses, including schizophrenia,[31,32] affective disorders,[33] autism spectrum disorders,[34] and ADHD.[35] Obviously, the high quality of specialty training for mental health professionals in the country and the strengths of the clinical assessment with detailed information from various sources have contributed to these very positive findings.

CONCLUSIONS

This study of a complete nationwide birth cohort assessed the registered incidence rates of mental disorders in childhood and adolescence and demonstrated that the incidences increased substantially by adolescence for any mental disorder, substance use disorders, depression, and anxiety disorders. Furthermore, sex effects were apparent with higher incidence rates for depression, anxiety disorders, obsessive-compulsive disorder, and eating disorders in females, whereas there was a male preponderance for substance use disorders, autism spectrum disorders, ADHD, conduct disorder, and tic disorders. At the end of adolescence before turning into adulthood, 11 in 100 individuals had been diagnosed with a mental disorder in this cohort.

These findings of the diverse developmental patterns of various mental disorders throughout childhood and adolescence and the sizable number of disorders at the time of transition into adulthood underscore the fact that childhood and adolescence are highly vulnerable periods for the development of mental disorders. The findings are relevant for mental health planning activities, as the approach used in the present study provides a very solid basis for calculating the needs in youth. Providing the age-appropriate treatment facilities for the various disorders at all developmental stages and defining the mental problems deserving continuous care at the time of nearing adulthood represent major challenges for all developed mental health systems.

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Supplementary Material

Article Title: Incidence Rates of Treated Mental Disorders in Childhood and Adolescence in a Complete Nationwide Birth Cohort

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List of Supplementary Material for the article

1. Table 1 Incidence rates for each diagnosis in the cohort by sex and age

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Supplementary Table 1 Incidence rates for each diagnosis in the cohort by sex and age

		Total				Males				Females			
	Age	Person years	Number of cases with the defined diagnosis	Incidence rate per 1000 Person years	95% CI	Person years	Number of cases with the defined diagnosis	Incidence rate per 1000 Person years	95% CI	Person years	Number of cases with the defined diagnosis	Incidence rate per 1000 Person years	95% CI
Any mental disorder [1]	0-13	866713.97	3468	4.00	3.87-4.14	442120.86	2465	5.58	5.36-5.80	424593.10	1003	2.36	2.22-2.51
	>13	340756.17	4425	12.99	12.61-13.37	172735.36	1748	10.12	9.66-10.61	168020.81	2677	15.93	15.34-16.55
Substance use disorders [2]	0-13	884311.63	34	0.04	0.03-0.05	454688.75	18	0.04	0.02-0.06	429622.88	16	0.04	0.02-0.06
	>13	369399.93	790	2.14	1.99-2.29	189932.49	454	2.39	2.18-2.62	179467.44	336	1.87	1.68-2.08
Schizophrenia	0-13	884396.02	3	0.00	0.00-0.01	454735.01	<3	0.00	0.00-0.02	429661.01	<3	0.00	0.00-0.02
	>13	370967.82	111	0.30	0.25-0.36	190840.75	49	0.26	0.19-0.34	180127.07	62	0.34	0.27-0.44
Depression	0-13	884215.54	118	0.13	0.11-0.16	454624.73	66	0.15	0.11-0.18	429590.81	52	0.12	0.09-0.16
	>13	367658.61	1274	3.47	3.28-3.66	189760.80	338	1.78	1.60-1.98	177897.82	936	5.26	4.93-5.61
Anxiety disorders	0-13	883972.54	138	0.16	0.13-0.18	454441.28	85	0.19	0.15-0.23	429531.26	53	0.12	0.09-0.16
	>13	369345.32	536	1.45	1.33-1.58	190093.03	180	0.95	0.82-1.10	179252.29	356	1.99	1.79-2.20
Obsessive compulsive disorders	0-13	884105.04	108	0.12	0.10-0.15	454546.99	62	0.14	0.11-0.17	429558.04	46	0.11	0.08-0.14
	>13	369890.75	257	0.69	0.61-0.79	190312.18	97	0.51	0.42-0.62	179578.56	160	0.89	0.76-1.04
Eating disorders	0-13	883686.55	111	0.13	0.10-0.15	454335.45	51	0.11	0.09-0.15	429351.10	60	0.14	0.11-0.18
	>13	369298.80	502	1.36	1.25-1.48	190522.33	44	0.23	0.17-0.31	178776.47	458	2.56	2.34-2.81
Autism spectrum disorders	0-13	881188.98	665	0.75	0.70-0.81	452100.15	541	1.20	1.10-1.30	429088.83	124	0.29	0.24-0.34
	>13	365849.03	583	1.59	1.47-1.73	186849.08	372	1.99	1.80-2.20	178999.96	211	1.18	1.03-1.35
Attention deficit hyperactivity	0-13	881329.05	795	0.90	0.84-0.97	452134.64	662	1.46	1.36-1.58	429194.42	133	0.31	0.26-0.37

disorders [3]													
	>13	364071.84	980	2.69	2.53-2.87	185584.77	573	3.09	2.84-3.35	178487.06	407	2.28	2.07-2.51
Conduct disorders	0-13	882290.54	470	0.53	0.49-0.58	452971.15	392	0.87	0.78-0.96	429319.39	78	0.18	0.15-0.23
	>13	367213.69	439	1.20	1.09-1.31	187982.41	236	1.26	1.11-1.43	179231.28	203	1.13	0.99-1.30
Tic disorders	0-13	883427.17	250	0.28	0.25-0.32	453945.56	205	0.45	0.39-0.52	429481.61	45	0.10	0.08-0.14
	>13	369405.47	114	0.31	0.26-0.37	189513.73	78	0.41	0.33-0.51	179891.73	36	0.20	0.14-0.28

[1] 10 persons were excluded due to registration errors. [2] 1 person was excluded due to a registration error. [3] 1 person was excluded due to a registration error.