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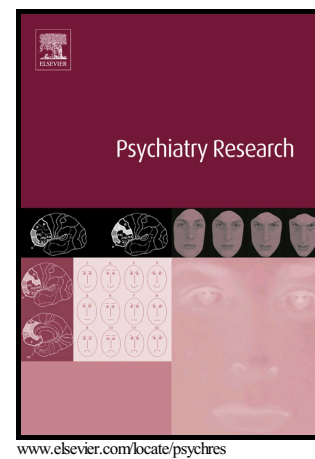
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Mortality in individuals with disruptive behavior disorders diagnosed by specialist services - a nationwide cohort study

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Abstract

Disruptive behavior disorders (DBDs), inclusive of oppositional defiant disorder (ODD) and conduct disorder (CD), are associated with outcomes likely to increase risk of mortality.

Using Danish National Registers, a total of 1.92 million individuals including 9495 individuals with DBDs diagnosed by specialist services were followed from their first birthday to 2013. Those with and without DBDs were compared using mortality rate ratios (MRRs) estimated using Poisson regression and adjusted for calendar period, age, sex, family history of psychiatric disorders, maternal age at time of birth, paternal age at time of birth, parental education status, and parental employment status. Over the course of follow up, which totalled 24.9 million person-years, 5580 cohort members died including 78 individuals with DBDs. The mortality rate per 10,000 person-years was 9.66 for individuals with DBDs compared to 2.22 for those with no diagnosis. This corresponded to a fully adjusted MRR of 2.57 (95% confidence interval 2.04-3.20). Comorbid substance use disorder and attention-deficit/hyperactivity disorder resulted in the highest MRR across all categories. These findings demonstrate the excess mortality associated with DBDs.

Keywords: disruptive behaviour disorders; conduct disorder; oppositional defiant disorder; mortality; deaths; registries; epidemiology

1. Introduction

Whilst many adult mental disorders have a demonstrated association with reduction in life expectancy (Hjorthoj et al., 2015; Saha et al., 2007), less is known of the increased mortality risk of mental disorders in childhood. Although childhood-onset mental disorders are not usually associated with fatal outcomes, these disorders may trigger a cascade of mental and physical comorbidity that accumulates over time and impacts upon life expectancy. For example, a nationwide cohort study of mortality associated with attention-deficit hyperactivity/disorder (ADHD) found those with ADHD and comorbid disruptive behavior disorders (DBDs; inclusive of oppositional defiant disorder [ODD] and conduct disorder [CD]) had an adjusted mortality rate ratio (MRR) of 2.17 (95% confidence intervals 1.33-3.31) (Dalsgaard et al., 2015). This was notably higher than those with ADHD only (1.50, 1.11-1.98), suggesting that DBDs are associated with an increased risk of mortality.

However, few studies have examined mortality associated with DBDs. Previous research has been restricted to special populations, e.g. offenders or inpatient samples, and/or relied on the use of symptom measures of DBDs rather than clinically defined disorders. For example, Neeleman and colleagues (1998) reported conduct problems at 16 years of age were associated with increased odds of suicide (odds ratio [OR]: 1.8, 1.3-2.5) and natural death (OR:1.2, 1.0-1.5) by age 50. Similarly, Zoccolillo and colleagues (1991) found that 7% of their sample of hospitalised girls with CD had died a violent death after four years compared with 0.03% of the age-matched general population. To our knowledge, no studies of mortality risk associated with DBDs have utilised a community representative sample with clinically defined diagnoses.

There are plausible reasons for these disorders to have an increased associated mortality.

DBDs are associated with a greater risk of substance abuse (Messer et al., 2006), comorbid

depression and anxiety disorders (Copeland et al., 2009, Erskine et al., 2016), comorbid schizophreniform psychosis (Maibing et al., 2015), psychiatric in-patient admissions (Dalsgaard et al., 2002), engagement in acts of aggression, violence, and risk taking (Nadaraja et al., 1997), and criminal convictions (Dalsgaard et al., 2013). These health and psychosocial problems are also likely to contribute to an increased risk of accidental deaths or suicide (von Stumm et al., 2011). DBDs and ADHD overlap substantially in terms of behavior and comorbidity (Angold et al., 1999), although differ considerably in terms of the possible mechanisms behind their respective symptomologies. This has been acknowledged in the restructuring of the latest version of the Diagnostic and Statistical Manual of Mental Disorders, DSM-5 (American Psychiatric Association, 2013), where ADHD is categorised under 'Neurodevelopmental Disorders' to reflect brain developmental correlates with the disorder. DBDs, including ODD and CD, have been categorised under the new 'Disruptive, Impulse-Control, and Conduct Disorders' classification. This reflects the emotional and behavioral self-control issues seen in this group of disorders as well as unique behavioural characteristics such as violating the rights of others and engaging in significant conflict with peers and authorities (American Psychiatric Association, 2013).

ADHD is associated with considerable and heterogeneous deficits in a broad range of cognitive functions, in particular executive functions involving impulse inhibition, working memory, and planning (Willcutt et al., 2005). By contrast, evidence of cognitive dysfunction is sparse when it comes to DBD cases and available studies are inconsistent in their findings or in controlling for ADHD. It seems that in DBD, cognitive deficits are more limited. These deficits have been related to the neurological reward system and a tendency for risky decision making and slower inhibitory responses (Hobson et al., 2011). These cognitive deficits in DBDs and/or ADHD may lead to risk taking behaviours or proneness to accidents which could result in injury or death. However, given the distinctions between these disorders, it is

important to examine the unique associations between the disorders and an increased risk of mortality.

We hypothesised that persons with DBDs would be at increased risk of mortality compared to those without the disorders. To the best of our knowledge, no large community representative study to date has examined mortality associated with DBDs. Utilising a nationwide cohort, we aimed to estimate excess all-cause mortality in children, adolescents, and adults with DBDs which had been diagnosed by specialist psychiatric or paediatric services. In addition, we aimed to examine the added effect of comorbid ADHD and substance use disorder (SUD) on mortality rates in individuals with DBDs.

2. Method

2.1. Study Population

The Danish Civil Registration System was established in 1968 (Pedersen et al., 2006) where all people alive and living in Denmark are registered. It includes the 10-digit personal identification number (PIN) and information on sex, date and place of birth, continuously updated information on vital status, and the parents' personal identifiers. The PIN is used in all national registers, enabling accurate linkage of data between registers at the level of the individual. Our study cohort included all children born in Denmark between January 1, 1981 and December 31, 2011 who were still alive and residing in Denmark at their 1st birthday or January 1, 1995, whichever came last.

2.2. Assessment of mental illness

Data from the Danish Psychiatric Central Research Register (DPCR) (Mors et al., 2011) and the Danish National Patient Register (DNPR) were used to obtain information on mental disorders in cohort members and their parents. The DPCR was computerized in 1969 and

contains data on all admissions to Danish psychiatric facilities. The DNPR was established in 1977 and contains data on all admissions to public hospitals in Denmark. In both registers, additional information on outpatient visits was included from 1995 onwards. The Danish modification of the International Classification of Diseases, 8th revision (ICD-8) was used between 1969 and 1993, and the International Classification of Diseases, 10th revision, Diagnostic Criteria for Research (ICD-10-DCR) was used from 1994 onwards. Diagnostic status of cohort members regarding DBDs was based on clinical diagnoses of ODD or CD extracted from the DPCR and the DNPR (ICD-8 code 308.03 and 308.04 and ICD-10-DCR codes F91.x and F90.1). From DPCR and DNPR, comorbid diagnoses of ADHD (ICD-8 code 308.01 and ICD-10-DCR codes F90.x or F98.8) and substance use disorder (SUD) (ICD-8 codes 291.x9, 294.39, 303.x9, 303.20, 303.28, 303.90, 304.x9 and ICD-10-DCR codes F10-F19) were obtained for all cohort members. Except for SUD, only contacts to departments of psychiatry, paediatrics, and neurology were included. Parents were classified as having a history of mental disorders if they had a contact with a public psychiatric hospital department with a psychiatric diagnosis (ICD-8 codes 290-315; ICD-10-DCR codes F00-F99). Date of onset was defined as the first day of the first contact (inpatient or outpatient) with the diagnosis in question.

2.3. Assessment of data on potential confounders

The Danish Medical Birth Register (DMBR) provided data on birth weight, gestational age, 5-minute Apgar score, and congenital malformations for all cohort members. Information on maternal and paternal age at time of birth was available from the civil registration system. Statistics Denmark provided data for highest parental education (categorised as basic school grades 8-10, upper secondary school, bachelor's degree, or postgraduate degree) and highest parental employment status (categorised as outside the labour force, unemployed, enrolled in

education, or employed) for the parents of all cohort members including those in the reference group.

2.4. Deaths

Information on date of death up to June 30, 2013 was available for almost 100% of all cohort members from the Danish Civil Registration System (Pedersen et al., 2006). The outcome was all cause mortality after the age of one or January 1, 1995 whichever came last. Cohort members were followed up until date of death, date of emigration from Denmark, or June 30, 2013, whichever came first.

2.5. Statistical Analysis

The mortality rate ratios (MRRs) were estimated by log-linear Poisson regression using with the GENMOD procedure in SAS (version 9.3) and compared the mortality rate in persons with and without DBDs. Crude MRRs were adjusted for calendar period, age, and the interaction with sex. In addition to the covariates in the crude model, the partially adjusted model adjusted for family history of psychiatric disorders and maternal and paternal age at time of birth. The fully adjusted model adjusted for covariates in the partially adjusted model as well as parental educational and employment status. We also examined the interaction with age at and time since DBD diagnosis and the effect of comorbid ADHD and SUD. The study was not powered to examine MRR due to suicides or other cause-specific relative risk of death.

A sensitivity analysis of MRRs was planned a priori with the cohort restricted to individuals with gestational age 37-44 weeks, birth weight over 2500 g, without congenital malformations, and with a 5-minute Apgar score of 10. Low birth weight, low Apgar score and congenital malformations are risk factors for DBDs and also associated with increased

mortality. Hence, to examine the robustness of the findings of increased mortality in DBDs, we estimated the MRR in individuals with DBDs, who had normal birth weight, a 5-minute Apgar score of 10 and had no congenital malformations.

Age, calendar period, and history of diseases in cohort members and their parents were treated as time-dependent variables (Clayton and Hills, 1993), whereas all other variables were treated as time independent. Calendar year and age were categorized in 2-year intervals. Maternal and paternal age was categorized in 5-year intervals with a separate category for unknown mother/father. Age at first diagnosis of DBD was divided into three groups; preschool children under 6 years, children aged 6 to 17, and adults aged 18 and above. We used the adjusted-score test to assess whether the regression models were subject to over-dispersion. P-values and 95% confidence intervals were based on likelihood ratio tests (Clayton and Hills, 1993).

2.6. Approvals

The study was approved by The Danish Data Protection Agency and The Danish Health and Medicines Authority. All personal information from the registers is anonymized when used for research purposes, and by Danish law, informed consent is not required for register-based studies.

3. Results

A total of 1,922,248 children were followed up to a maximum age of 32 years, from their 1st birthday or January 1, 1995 (whichever came last), until death, emigration from Denmark, or June 30, 2013 (whichever came first). This contributed a total of 24,907,560 person-years of observation. In 44,883 children and adolescents (2.3%), follow up was ended prior to the end of the study (June 30, 2013) because of emigration from Denmark (N=44 009) or loss to

follow-up (n=874). During follow-up, 5,580 cohort members died corresponding to a mortality rate of 2.24 per 10,000 person-years.

We identified 9,495 individuals who had been diagnosed with DBDs by specialist services within the cohort of which 7,303 were male (76.9%). Individuals with DBDs contributed a total of 80,757 person-years of observation. Mean age at DBD diagnosis was 10.8 years (standard deviation 5.0). Among individuals with DBDs, 5,417 (57.1%) had a comorbid diagnosis of ADHD and 1,729 (18.2%) had comorbid SUD.

During follow-up, 78 individuals with DBDs died. The all-cause mortality rate was 9.66 per 10,000 person-years compared to 2.22 per 10,000 person-years in persons without DBDs. This corresponded to a crude MRR for DBDs of 3.19 (2.53-3.96; $p < 0.00001$) and a fully adjusted MRR of 2.57 (2.04-3.20; $p < 0.00001$). Adjusting for parental history of psychiatric disorders most strongly accounted for the attenuation in the MRR. We found no interaction by gender ($p = 0.74$). Females with DBDs had a fully adjusted MRR of 2.82 (1.46-4.86) while males with DBDs had a fully adjusted MRR of 2.53 (1.97-3.20).

The distribution of age at time of death of the 78 persons with a DBD diagnosis who died during follow-up were as follows: age 9-13 years: n=4; age 14-17 years: n=19; age 18-29 years: n=55. Regarding causes of death, we had information about cause of death available for deaths in 2011 and earlier. Hence, among the 78 persons with DBD who died during follow-up, we have information on cause of death for 65. Of these 42 (64.6%) died from unnatural causes such as accidents, suicide and homicide.

Age at first diagnosis had a significant effect on the MRR among individuals with DBDs ($p = 0.002$). Children diagnosed with DBDs before the age of 12 had a fully adjusted MRR of 1.81 (1.28-2.47), those diagnosed between age 13 and 17 had an MRR of 3.28 (2.21-4.66),

and adults diagnosed with DBDs after the age of 18 had an MRR of 7.37 (4.14-11.97), compared to those with no diagnosis (Table 1).

The impact of comorbid disorders on the mortality of persons with DBDs is shown in Table 2. Those with DBDs and comorbid SUD had a significantly increased MRR (MRR 7.88, 4.84-12.02) while individuals with DBDs and both comorbid ADHD and SUD had the highest MRR (8.27, 4.84-13.05). The MRR for DBDs and comorbid ADHD (2.18, 1.34-3.32) was not significantly different to those with DBDs alone (1.75, 1.14-2.55).

Time since DBD diagnosis had no significant effect on MRRs ($p=0.21$). Within the first year of DBD diagnosis, the fully adjusted MRR was 5.00 (2.50-8.79). From 1-2 years, 3-4 years, 5-9 years, and more than 10 years after DBD diagnosis respectively, the fully adjusted MRRs were 2.48 (1.24-4.36), 3.34 (1.84-5.51), 2.41 (1.54-3.57), and 2.04 (1.31- 2.99) compared to those without DBDs. In the sensitivity analysis restricted to children born at term, with normal birth weight, 5-minute Apgar score of 10, and no congenital malformations, individuals with DBDs had a fully adjusted MRR of 2.76 (2.12-3.52) with significant differences according to age at diagnosis ($p=0.00014$) but not sex ($p=0.63$) (see Table 3).

4. Discussion

Using a nationally representative sample, we report for the first time the excess mortality in persons with DBDs diagnosed by specialist services. After adjusting for potential confounding factors, those diagnosed by psychiatrists or paediatricians with DBDs alone were almost twice as likely to die compared to individuals without these disorders.

Furthermore, the risk of excess mortality increased more than eight fold in those individuals with DBDs and comorbid SUD. This excess mortality is consistent with increased risk of premature death associated with other childhood (Dalsgaard et al., 2015) and adult mental disorders (Hjorthoj et al., 2015; Saha et al., 2007) and is likely explained by a combination of increased risk of suicide, accidents, engagement in criminal behaviour with associated misadventure, and physical health problems (Neeleman et al., 1998; Odgers et al., 2008; Steingrimsson et al., 2015; Zoccolillo and Rogers, 1991). This proposition was confirmed by the subgroup analysis (n=65) examining cause of mortality which revealed almost two thirds died from unnatural causes.

Although sex did not influence the MRR in those with DBDs, age at first diagnosis was found to be a significant factor. For example, mortality was increased in those diagnosed before 13 years of age (MRR and 95% CI: 1.81; 1.28-2.47) whilst those diagnosed after the age of 18 had an MRR of 7.37 (4.14-11.97). DBDs have varying developmental trajectories with some children having problems limited to childhood, others having adolescent-onset conduct problems, and a third group whose conduct problems persist from childhood through the adolescent years (Moffitt et al., 2008; Odgers et al., 2007). Historically, the developmental trajectory of DBDs was thought to be influenced by both environmental and genetic factors with the childhood-onset persistent subtype more likely to occur in those children who experience early adversity, have neurodevelopmental vulnerabilities, school and peer difficulties, and parents with antisocial behaviours (Moffitt et al., 2008). More recently, it has been proposed that genetic variants may have a very strong influence on the persistence of conduct problems (Pingault et al., 2015).

However, understanding the developmental trajectories of mental disorders has been further complicated by emerging evidence that disorders such as ADHD once considered to always

be present in childhood, may also arise de novo in adults (Moffitt et al., 2016). More research is needed to better understand the reasons for the differences in excess of mortality with age of diagnosis of DBDs in this cohort. However, the current literature suggests for the majority of young children, conduct problems are limited to childhood and longitudinal studies show no increased attributable health burden in adulthood (Moffitt et al., 2008; Odgers et al., 2007). This may explain why the MRR of children diagnosed before the age of thirteen was less compared to those first diagnosed when older. By contrast those with childhood-onset persistent, and to a lesser extent adolescent-onset, CD have been shown to have increased physical and mental health problems, economic concerns and engagement in serious violence (Odgers et al., 2007; Odgers et al., 2008), all of which likely contribute to the increased MRR in those diagnosed with DBDs in adolescence and young adulthood. It is possible that where the diagnosis of DBDs has been first made after the age of 18, the individuals have come to the attention of specialist services as a result of some other problem, for example substance use disorder or non-accidental self-injury. Therefore young adults diagnosed by specialist services with DBDs may be more likely than those with DBD who do not present for care to have other high risk behaviors which may have be the cause of the very high associated excess mortality.

These findings have important policy and clinical implications. CD is one of the leading global causes of disease burden in children (Erskine et al., 2014). However, in these reports of disease burden, no mortality was attributed to CD as no deaths were directly attributed to the disorder. Therefore, the overall disease burden estimates reported for CD are likely an underestimate. Recognising the mortality associated with CD and the wider DBD group is important to ensure policy makers are aware of the health and societal costs associated with these disorders (Erskine et al., 2015). Moreover, the excess mortality attributable to DBDs should encourage governments to implement strategies known to prevent or reduce conduct

problems in young children such as parent skills training (Furlong et al., 2013) and social and emotional competency in young children (Dodge et al., 2015).

This study examined the excess mortality associated with DBDs in a large Danish population based study. While the validity of the diagnoses of DBDs in the Danish health registers have not been examined, all assessments and diagnoses were provided by registered child and adolescent psychiatrists or pediatricians at specialised psychiatric and pediatric departments in public hospitals. There was relatively small attrition and the capture of mortality in the Danish Civil Registration System is almost 100% (Pedersen et al., 2006), limiting biases that might have otherwise arisen.

Like all research, this study had limitations. ODD and CD have been grouped together as there would be inadequate power to assess risk of a rare outcome such as mortality for either disorder alone. It is possible that there is a difference in the excess mortality between those with ODD and those with CD. Secondly, the database only includes those who attend hospital or outpatient clinics of pediatricians, psychiatrists or neurologists. In Denmark, most children with psychiatric disorders are assessed, diagnosed and treated by specialists of child and adolescent psychiatry (a few by specialists of pediatrics), the vast majority at departments at public hospitals and significantly fewer by such specialists in private practices. In addition, some children with symptoms of DBDs and their families receive support or parent management training from municipalities. The latter are not included in this study, as the Danish registers do not hold information on such data from municipalities. No study has estimated the population prevalence of DBDs in Denmark. However, it is likely that a significant proportion of children who meet diagnostic criteria for DBDs are not referred for specialist assessment and hence, the included sample may represent those with more severe and impairing symptoms of DBDs..

Third, although a strength of the paper was the ability to adjust for many potential confounding factors, there were other variables which were not included in the statistical models. For example, adjustment for other psychiatric diagnoses and neurodevelopmental disorders would potentially enable a more precise measure of the excess mortality due to DBDs alone. However, DBDs in childhood are associated with increased risk of anxiety and depression (Erskine et al., 2016) and adjusting for these may erroneously reduce the mortality attributable to DBDs.

Finally, we were unable to differentiate deaths due to suicide, accidents, or incidents of violence from those due to natural causes. We were also unable to assess if the provision of pharmacological or non-pharmacological intervention influenced the MRR associated with DBDs. Atypical antipsychotics are increasingly used for the treatment of these disorders (Toteja et al., 2014) and are associated with increased risk of metabolic and cardiovascular events in children and adolescents (McIntyre and Jerrell, 2008). However, it is unknown if there is an excess mortality associated with atypical antipsychotics in children and young people which would be of interest in future studies.

We show for the first time that DBDs as diagnosed by specialist services have an associated increased mortality which is significantly larger when accompanied by SUD and SUD and ADHD combined. Evidence-based interventions that prevent the onset and persistence of these disorders have been developed (Patel et al., 2015). The excess mortality associated with DBDs, in addition to the known high burden of physical and mental morbidity and adverse psychosocial sequelae, should galvanise governments to implement programmes that reduce the prevalence of DBDs in the population.

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Table 1 Mortality rate ratios (MMR) according to age at first diagnosis with DBDs compared to those without DBDs at same age[§]

Age at first DBD diagnosis	Number of deaths	Person-years	Mortality rate per 10,000 person-years	Crude model		Partially adjusted model		Fully adjusted model	
				MRR (95% CI) [#]	MRR (95% CI) [†]	MRR (95% CI) [‡]	MRR (95% CI) [§]		
1-12 years	36	59,961	6.00	2.25 (1.59-3.07)	1.91 (1.35-2.60)	1.81 (1.28-2.47)			
13-17 years	28	17,653	15.86	4.07 (2.74-5.78)	3.45 (2.32-4.90)	3.28 (2.21-4.66)			
≥18 years	14	3,143	44.54	9.18 (5.16-14.90)	7.74 (4.35-12.58)	7.37 (4.14-11.97)			
Never diagnosed with DBDs	5,502	24,826,802	2.22	1.00 (reference)	1.00 (reference)	1.00 (reference)			
Total Cohort	5,580	24,907,560	2.24						

[§] Cohort consisted of 1.92 million children born 1981-2011.

[#] Crude model adjusted for age, calendar year and gender.

[†] Partially adjusted model adjusted for age, calendar year, gender, parental history of psychiatric disorders, maternal and paternal age at time of birth.

[‡] Fully adjusted model adjusted for age, calendar time, gender, parental history of psychiatric disorders, maternal and paternal age at time of birth, parental education, and parental employment status.

DBDs: Disruptive behavior disorders; CI: confidence interval.

Table 2 Mortality rate ratios (MRR) in individuals with DBDs in combination with ADHD and/or SUD compared to individuals with none of these disorders in the total cohort

Diagnoses	Number of deaths	Person-years	Mortality rate per 10,000 person-years	Crude model MRR (95% CI)[#]	Fully adjusted model MRR (95% CI)[§]
Diagnosed with DBDs	24	41,026	5.85	2.14 (1.39-3.11)	1.75 (1.14-2.55)
Diagnosed with DBDs and ADHD	19	31,177	6.09	2.58 (1.58-3.92)	2.18 (1.34-3.32)
Diagnosed with DBDs and SUD	19	4,601	41.29	10.21 (6.27-15.54)	7.88 (4.84-12.02)
Diagnosed with DBDs, ADHD and SUD	16	3,953	40.47	10.34 (6.05-16.31)	8.27 (4.84-13.05)
Diagnosed with ADHD and/or SUD	501	432,485	11.58	3.66 (3.33-4.03)	3.26 (2.96-3.59)
Never diagnosed with DBDs, ADHD or SUD	5,001	24,394,318	2.05	1.00 (Reference)	1.00 (Reference)
Total cohort	5,580	24,907,560	2.24		

[§] Cohort consisted of 1.92 million children born between 1981-2011 .

[#] Crude model adjusted for age, calendar time, and gender.

[§] Fully adjusted model adjusted for age, calendar time, gender, parental history of psychiatric disorders, maternal and paternal age at time of birth, parental education, and parental employment status

DBDs: Disruptive behavior disorders; ADHD: Attention-deficit/hyperactivity disorder; SUD: Substance use disorder; CI: confidence intervals.

Table 3 Sensitivity analysis[§] showing mortality rate ratios according to age at first diagnosis with DBDs compared to those without DBDs at same age

Age at first DBD diagnosis	Number of deaths	Person-years	Mortality rate per 10,000 person-years	Crude model MRR (95% CI) [#]	Partially adjusted model MRR (95% CI) [†]	Fully adjusted model MRR (95% CI) [§]
1-12 years	26	46,562	5.58	2.23 (1.48-3.21)	1.90 (1.26-2.73)	1.80 (1.19-2.59)
13-17 years	24	14,395	16.67	4.56 (2.96-6.65)	3.84 (2.50-5.61)	3.65 (2.37-5.32)
≥18 years	12	2,585	46.42	10.35 (5.53-17.42)	8.70 (4.65-14.65)	8.26 (4.41-13.91)
Never diagnosed with DBDs	4,030	20,490,195	1.97	1.00 (reference)	1.00 (reference)	1.00 (reference)
Total cohort	4,092	20,553,738	1.99			

[§] The sensitivity analysis restricted the cohort to 1.57 million children born at term with birth weight > 2500 g, 5 minute Apgar score of 10, with no congenital malformations, and born between 1981-2011 .

[#] Crude model adjusted for age, calendar year, and gender.

[†] Partially adjusted model adjusted for age, calendar year, gender, parental history of psychiatric disorders, maternal and paternal age at time of birth.

[§] Fully adjusted model adjusted for age, calendar time, gender, parental history of psychiatric disorders, maternal and paternal age at time of birth, parental education, and parental employment status.

DBDs: Disruptive behavior disorders; CI: confidence interval

Highlights

- First national-level study reporting the association between DBDs and mortality.
- Individuals with DBDs had a two and half fold increased risk of mortality.
- Those with comorbid substance use disorder and ADHD had the highest mortality.