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## Incidence of mental health hospitalizations, treated self-harm, and emergency room visits following new anxiety disorder diagnoses in privately insured US children

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### Abstract

**Background.**—Anxiety disorders are one of the most common mental illnesses in children and associated with high healthcare utilization. We aimed to estimate two-year cumulative incidence of mental health related hospitalizations, treated self-harm, and emergency room (ER) visits in children newly diagnosed with anxiety disorders and, for context, in children without anxiety disorders.

**Methods.**—We identified commercially-insured treatment naïve children (3–17 years) with a new office-based anxiety disorder diagnosis (ICD-9-CM) from 2005–2014 in the MarketScan claims database. We followed children for up to two years after diagnosis for the first of each event: mental health-related hospitalization, inpatient treated self-harm, and ER visits (any, anxiety-related, injury-related). Children without anxiety diagnoses were included as comparators, matched on age, sex, date, and region. We estimated cumulative incidence of each event using Kaplan-Meier analysis.

**Results.**—From 2005–2014 we identified 198,450 children with a new anxiety diagnosis. One-year after anxiety diagnosis, 2.0% of children had a mental health related hospitalization, 0.08%

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inpatient treated self-harm, 1.4% anxiety-related ER visit, and 20% any ER visit; incidence was highest in older children with baseline comorbid depression. One-year cumulative incidence of each event was lower in the comparison cohort without anxiety (ex. mental health-related hospitalizations=0.5%, treated self-harm=0.01%, ER visits=13%).

**Conclusions.**—Given the prevalence of anxiety disorders, two-year incidence estimates translate to a significant number of children experiencing each event. Our findings offer caregivers, providers, and patients information to better understand the burden of anxiety disorders and can help anticipate healthcare utilization and inform efforts to prevent these serious events.

### Keywords

Child; healthcare utilization; self-injurious behavior; incidence; emergency service; hospitalization; anxiety disorders

## BACKGROUND

Anxiety disorders are common in children and adolescents with current worldwide prevalence estimates of 2% (Global Burden of Disease Pediatrics Collaboration, 2016) to 7%. (Baxter AJ, Scott KM, Vos T, & Whiteford HA, 2013) In the United States (US), a third of individuals have an anxiety disorder by age 75. (Kessler RC, Berglund P, et al., 2005) Often beginning in childhood, (Kessler RC, Berglund P, et al., 2005; Merikangas KR et al., 2010) anxiety disorders are considered a gateway disorder, predicting subsequent anxiety disorders, depression, and substance use, (Beesdo K, Pine DS, Lieb R, & Wittchen HU, 2010; Birmaher B et al., 2007; Connolly SD, Bernstein GA, & Work Group on Quality Issues, 2007; Dahne J, Banducci AN, Kurdziel G, & MacPherson L, 2014; Pine DS, Cohen P, Gurley D, Brook J, & Ma Y, 1998; Zimmermann P et al., 2003) highlighting the importance of diagnosing and managing pediatric anxiety disorders.

Anxiety disorders are associated with a high utilization of healthcare services, with pediatric anxiety commonly seen in emergency rooms (ER) and hospitals. (Dark T, Flynn HA, Rust G, Kinsell H, & Harman JS, 2017; Deacon, Lickel, & Abramowitz, 2008; McLaughlin TP, Khandker RK, Kruzikas DT, & Tummala R, 2006; Ramsawh HJ, Chavira DA, & Stein MB, 2010) Out of 150 conditions, anxiety disorders were recently ranked twentieth in conditions with the largest personal health care spending in the US for children and adolescents, totaling 3.4 billion dollars. (Bui AL et al., 2017) The high costs related to anxiety disorders draw focus on understanding and reducing healthcare utilization due to serious events.

ER visits, mental health related hospitalizations, and self-harm place a significant burden on patients, caregivers, and the healthcare system. (Deacon et al., 2008; Howell EM & Teich J, 2008; Newton AS, Rosychuk RJ, Niu X, Radomski AD, & McGrath PJ, 2016; Sinclair JM, Gray A, Rivero-Arias O, Saunders KE, & Hawton K, 2011; Zima BT et al., 2016) Suicide is the third leading cause of death in children aged 5–14 years and second in adolescents 15–24 years. (CDC/NCHS) Mental health related hospitalizations are relatively common in children with mental health diagnoses and costly. (Howell EM & Teich J, 2008; Torio CM, Encinosa W, Berdahl T, McCormick MC, & Simpson LA, 2015) Anxiety ranked sixth (of 531) in most common chronic condition in pediatric acute-care hospitalizations, (Berry JG et al.,

2017) and accounted for a growing proportion of pediatric hospitalizations from 2005 to 2014.(Zima BT et al., 2016) Annually, almost one in five US children have an ER visit, with injury being a common cause,(National Center for Health Statistics, 2013) and over one million ER visits occurred with anxiety the primary reason for the visit, 7% of which occurred in children.(Dark T et al., 2017) Previous work provided important insights into how many children with mental health diagnoses experience ER visits and hospitalizations in a year(Howell EM & Teich J, 2008) and how often anxiety is the reason for pediatric ER visits and hospitalizations.(Dark T et al., 2017; Newton AS et al., 2016; Torio CM et al., 2015; Zima BT et al., 2016) However, it is less clear how many children diagnosed with anxiety go on to experience each event, rather than how many events are attributable to anxiety.

Using longitudinal data to determine the incidence of ER visits, mental health hospitalizations, and treated self-harm in children newly diagnosed with an anxiety disorder extends the existing literature. Cumulative incidence estimates of these serious, impactful events can increase clinician, caregiver, and patient awareness at diagnosis, a time when information may be particularly sought-after. This information can contribute to the clinician's larger discussion with caregivers and patients on the importance of managing symptoms, when to seek additional care, and the impact of comorbid psychiatric conditions. Further, event estimates can help policymakers predict healthcare utilization and inform prevention efforts.

In a cohort of commercially insured children newly diagnosed with an anxiety disorder in an office setting, we aimed to estimate the two-year cumulative incidence of mental health related hospitalizations, inpatient treated self-harm, and ER visits. Additionally, we estimated the two-year cumulative incidence of these events in a similar population of commercially insured children without a diagnosed anxiety disorder to provide context and better understand baseline event incidence in absence of anxiety disorder diagnoses.

## METHODS

### Data Source & study population

We used Truven Health Analytics' MarketScan Commercial Claims and Encounters database,(Hansen LG & Chang S, 2011) which contains health plan data for individuals covered by employer-sponsored private health insurance across the US. We utilized data on inpatient admissions and services, outpatient services, outpatient dispensed prescriptions, and enrollment files from January 1, 2004 to December 31, 2014. We identified children (3–17 years) newly diagnosed with an anxiety disorder from 2005 to 2014. An anxiety diagnosis was defined as an ICD-9-CM code (293.84, 300.0x, 300.2x, 300.3x, 309.21, 309.81, 313.23) corresponding to anxiety disorders in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V),(American Psychiatric Association, 2013) along with post-traumatic stress disorder (PTSD), or obsessive compulsive disorder (OCD), which were previously grouped under anxiety disorders in the DSM-IV. We required children to have at least one year of insurance enrollment (with prescription and mental health services coverage) prior to the first recorded anxiety disorder diagnosis (eFigure 1) to increase the likelihood that we identified a new diagnosis. We excluded children with a prior

year diagnosis of bipolar disorder (296.0x, 296.4x-.8x), personality disorder (301.x), schizophrenia (295.x), and autistic disorder (299.00) given more complex history and treatment regimens.

We restricted the cohort to children naïve to anxiety treatment during the year before their anxiety disorder diagnosis, including psychotherapy (based on recorded CPT codes) or dispensed SSRI prescriptions, benzodiazepines (alprazolam, chlordiazepoxide, clobazam, clonazepam, clorazepate, diazepam, halazepam, lorazepam, oxazepam, prazepam), buspirone, other antidepressants, hydroxyzine, or antipsychotics. We allowed baseline prescriptions for medications that are sometimes used to treat anxiety (ex. beta-blockers, anticonvulsants, clonidine/guanfacine) since these medications are rarely the initial anti-anxiety pharmacotherapy (Bushnell GA et al., 2017) and have primary non-anxiety indications. Finally, we restricted the cohort to children with their new anxiety diagnosis in an office setting (83%) to create a more similar, clinically relevant cohort. In preliminary analyses, cumulative incidences were higher during follow-up when allowing new anxiety diagnoses from all settings; however, children diagnosed with anxiety outside an office (i.e. inpatient, ER, urgent care) likely had a different trajectory leading to their diagnosis.

### Incident event definitions

Events were identified beginning the day after the new anxiety disorder diagnosis for up to 2 years. A mental health related hospitalization was defined as an inpatient admission with a recorded psychiatric diagnosis (ICD-9-CM=290–319); a secondary definition required a psychiatric diagnosis in the primary diagnostic position. An inpatient, treated self-harm event was defined as an inpatient record for suicide and self-inflicted injury (ICD-9-CM=E950-E958). (Centers for Disease Control and Prevention, 2011) We also examined recorded suicide ideation (ICD-9-CM=V62.84). ER visits included claims with ER designated as the category of service. (Truven Health Analytics Inc., 2011) Anxiety-related ER visits required a diagnostic code for anxiety [cohort inclusion anxiety disorder codes, adjustment disorder with anxiety (ICD-9-CM=309.24, 309.28), or acute stress disorder (ICD-9-CM=308.x)]. Injury-related ER visits required an ICD-9-CM diagnostic code 800–999 or E800–999 (excluding late effects=905–909, E929, E959, E969, E977, E989, E999 and place of injury=E849).

### Comparison cohort

A comparison cohort was created to estimate event incidence in children with the same restrictions as the anxiety cohort (except for an anxiety diagnosis) and identical event definitions. To create the comparison cohort, we selected all children in the dataset that matched with a child in the anxiety cohort on age, sex, date, and geographical region (North Central, Northeast, South, West) (eFigure 1). For the match on date, we required eligible matches to have a diagnostic code recorded on the exact date a child was diagnosed with anxiety, termed “match date”. From the 15 million children who matched with at least one child on those four criteria, we applied the same baseline inclusion criteria used for the anxiety cohort, resulting in 8 million children who matched with at least one child in the anxiety cohort (eFigure 1). From that pool of eligible matches we randomly selected 10 per child in the anxiety cohort; a child in the comparison cohort could match once. All children

in the database were eligible as potentially matches. As we ignored future claims when selecting the cohort, (Lund JL et al., 2017) a small subset (3%) of children in the comparison cohort were also in the anxiety cohort. Covariate and event definitions were consistent with the anxiety cohort.

### Primary patient covariates

For each child, age, sex, year of first anxiety diagnosis (or match date), provider type of anxiety diagnosis (or match date diagnoses), and, for the anxiety cohort, specific anxiety disorder diagnosis were included. In the year prior to a child's new anxiety diagnosis (or match date), we created indicators for psychiatric and non-psychiatric comorbidities, inpatient and outpatient visits, ER visits, and medication use. A primary stratification variable was psychiatric conditions in the prior year, defined as 1) no psychiatric comorbidity diagnosis, 2) comorbid depression diagnosis (ICD-9-CM=296.2x, 296.3x, 300.4x, 309.1x, or 311.xx), and 3) other psychiatric comorbidity (ICD-9-CM=290–319, excluding anxiety disorder and depression diagnoses and excluded baseline comorbidities=bipolar disorder, personality disorder, schizophrenia, autistic disorder). As the study cohort was restricted to treatment naïve children, a proportion of children previously treated for psychiatric comorbidities were, by default, excluded.

### Statistical analysis

We described the anxiety and comparison cohorts. We used Kaplan Meier estimator to estimate two-year cumulative incidence and associated 95% confidence intervals (CI) of each incident event (log-log transformation). When calculating cumulative incidence of each event, children were followed until that event occurred or were censored at insurance disenrollment, end of data (12/31/2014), or 2 years after their anxiety diagnosis (or match date), whichever occurred first. We stratified results by most common initial anxiety disorder diagnoses, age group, and psychiatric comorbidity; in the comparison cohort, we present stratification results for children with no baseline psychiatric comorbidities to represent event incidence in children without any recorded psychiatric diagnosis. The analysis for recorded suicide ideation was restricted to children diagnosed with anxiety (or match date) in 2006 or later, based on ICD-9-CM code availability. For a sensitivity analysis, we stratified results by the presence of a follow-up anxiety disorder diagnosis within 90 days of the first diagnosis; a single diagnostic code may not represent a true diagnosis. In an additional sensitivity analysis, cumulative incidence was estimated after excluding children with prior psychiatric-related inpatient admission or recorded suicidal ideation or self-harm, events are strong predictors of some events under consideration. Analyses were completed with SAS version 9.4, Cary, NC. The University of North Carolina Institutional Review Board approved this study.

## RESULTS

The cohort included 198,450 children with a new office-based anxiety disorder diagnosis; the median age was 12 years (interquartile range=8–15 years) and 45% were male (Table 1). The majority had a new anxiety diagnosis for unspecified anxiety disorder (53%), followed by generalized anxiety disorder (25%), OCD (5%), and PTSD (4%). A psychiatrist or

psychologist/therapist diagnosed 46% of children with anxiety followed by 21% diagnosed by a pediatrician. Six-percent of children had a baseline depression diagnosis, of whom 86% had depression diagnosed at least 30 days prior to the anxiety diagnosis.

Ten matches were identified for >99% children in the anxiety cohort to create the comparison cohort (N=1,980,082). The comparison cohort had a lower baseline prevalence of recorded psychiatric comorbidities, medication utilization, outpatient visits, and certain non-psychiatric comorbidities (Table 1). Among the most common (top 70%) ICD-9-CM diagnoses recorded on the match date in the comparison cohort, 37% were related to a vaccination or routine visit, 32% general acute concern (ex. fever, ear infection), 8% injury/pain-related, 3% psychiatric diagnoses, 11% conditions likely requiring repeat visits (ex. acne, chronic rhinitis), and 9% potentially more severe, chronic conditions (ex. asthma, obesity, unspecified chest pain). Eighty-percent of children with anxiety and 85% of the comparison cohort had at least 6 months of follow-up (1-year=61% and 73%, respectively).

### **Cumulative incidence, anxiety cohort**

Table 2 displays cumulative incidence of each event at 1, 6, 12, and 24 months following a new anxiety disorder diagnosis. Within 1 year, 2.0% of children had a mental health related hospitalization; 1.7% (95% CI=1.6–1.8) when restricting to hospitalizations with a primary mental health diagnosis. Around 0.08% children had an inpatient, treated self-harm event 1 year after a new anxiety disorder diagnosis and 1.0% had a recorded suicide ideation claim. ER visits were common; 20% of children had an ER visit, 9% an injury-related ER visit, and 1.4% an anxiety-related ER visit within 1 year after a new anxiety disorder diagnosis. The two-year incidence of each event was similar in children with an unspecified anxiety or GAD diagnosis and higher in children with a PTSD diagnosis (eTable 2).

### **Cumulative incidence, comparison cohort**

The two-year cumulative incidence of each event was lower in the comparison cohort compared to the anxiety cohort (Table 2). One year after the match date, 0.5% of children had a mental health related hospitalization (0.4% with a primary mental health diagnosis), 0.01% an inpatient, treated self-harm event, 13% an ER visit, and 7% an injury-related ER visit.

### **Age and psychiatric comorbidity stratification**

In children with newly diagnosed anxiety, the two-year cumulative incidence of each event varied by age at diagnosis and baseline psychiatric comorbidities (Figure 1; Table 3). The cumulative incidence of mental health related hospitalizations (6-months=5.1%, 95% CI:4.6–5.6), inpatient, treated self-harm (6-months=0.43%, 95% CI:0.30–0.60), and anxiety-related ER visits (6-months=2.2%, 95% CI:1.9–2.6) following a new anxiety diagnosis occurred more frequently in children 14–17 years with comorbid depression compared to other age and comorbidity groups (Figure 1). Of note, CIs are slightly wider in stratified analyses given smaller sample per strata (Table 3).

Restricting the comparison cohort to children without baseline psychiatric diagnoses (N=1,805,682, 91%), the one-year cumulative incidence estimates remained lower than in



children with anxiety disorders and no psychiatric comorbidity (Table 3). For example, 2.7% of children 14–17 years in the anxiety cohort with no psychiatric comorbidity had a mental health related hospitalization and 0.12% an inpatient, treated self-harm event within one year, compared to 0.6% and 0.02%, respectively, in the comparison cohort with no psychiatric diagnosis.

### Sensitivity analyses

In children with a follow-up anxiety disorder diagnosis within 90 days ( $n=113,437$ , 57%), one-year incidence of ER visits overall and injury-related ER visits were similar to children without a follow-up diagnosis ( $n=85,013$ ). The cumulative incidence of inpatient, treated self-harm, mental health related hospitalizations, and anxiety-related ER visits were higher in children with a follow-up anxiety diagnosis (eTable 1). After excluding 0.5% ( $n=968$ ) of the anxiety cohort and 0.1% ( $n=2,073$ ) of the comparison cohort with baseline psychiatric hospitalizations or recorded suicidality, results, not shown, were consistent (ex. 1-year incidence of mental health hospitalizations: 1.91%=anxiety cohort, 0.47%=comparison cohort vs. 1.95% and 0.47%, respectively, in full cohorts).

## DISCUSSION

In this cohort of privately-insured children, many experienced a serious healthcare related event in the two years following their new anxiety diagnosis; incidence of each event was lower in children without anxiety disorders. With 54 million children worldwide estimated to have an anxiety disorder,(Global Burden of Disease Pediatrics Collaboration, 2016) incidence estimates translate to a significant number of children with anxiety experiencing each event and a sizable burden on the healthcare system. Our findings offer caregivers, providers, and patients a better understanding on the impact of anxiety disorders which can inform care decisions. Further, findings underscore research efforts to prevent these serious events.

The event incidence in children with anxiety and context provided by the comparison cohort, suggest many children with anxiety disorders need improved care. Despite impairments, many children with mental health problems do not receive professional care.(Rickwood DJ, Deane FP, & Wilson CJ, 2007) A third or less of adolescents with anxiety disorders reported receiving care; lower than adolescents with depression and ADHD.(Chavira DA, Stein MB, Bailey K, & Stein MT, 2004; Merikangas KR et al., 2011; Merikangas et al., 2010) For children with mild anxiety, education and support may help manage symptoms, but anxiety should be monitored at follow-up visits.(Ramsawh HJ et al., 2010) We observed higher incidence of psychiatric-related events in children with follow-up anxiety diagnoses, possibly a consequence of children with more severe anxiety receiving follow-up diagnoses. Since pediatric anxiety disorders can be chronic and persistent(Wehry AM, Beesdo-Baum K, Hennelly MM, Connolly SD, & Strawn JR, 2015) and management of anxiety disorders can positively impact health outcomes and economic production,(Chisholm D et al., 2016) future research should examine when and how to optimize care to reduce event occurrence.

Consistent with prior findings, we observed higher incidence in older children. The rate of ER visits for anxiety or stress disorders increases substantially across childhood,(Newton AS

et al., 2016) as does the national suicide rate.(Centers for Disease Control and Prevention, 2013) We observed higher incidence in children with diagnosed depression; higher medical costs were reported for individuals with anxiety and depression compared to only anxiety. (Marciniak MD et al., 2005; McLaughlin TP et al., 2006; Stein MB, Cantrell CR, Sokol MC, Eaddy MT, & Shah MB, 2006) Depression, which is highly prevalent in individuals with anxiety disorders,(Kessler RC, Chiu WT, Demler O, & Walters E, 2005) is strongly associated with suicidal behavior;(Cash SJ & Bridge JA, 2009) therefore, monitoring suicide risk in children with anxiety and comorbid depression is recommended.(Connolly SD et al., 2007) Given our baseline restrictions (e.g. treatment naïve), examination of children with new anxiety disorder diagnoses, and later onset of depression than pediatric anxiety disorders,(Merikangas KR et al., 2010) only 6% of our cohort had diagnosed depression. Understanding if, and when, depression symptoms developed following an anxiety diagnosis would further inform results.

Our self-harm definition required a claim with an external cause of injury code, which often have low sensitivity but high specificity in identifying suicide attempts.(Kim HM et al., 2012; Lu CY et al., 2014; Walkup JT, Townsend L, Crystal S, & Olfson M, 2012) Relatedly, suicide ideation and the corresponding diagnostic code are typically missing from patient records.(Anderson HD et al., 2015; Kempland RS, Gasgarth R, Johnson B, Patil M, & Houry D, 2008) Therefore, our observed inpatient, treated self-harm and suicide ideation incidences represent a fraction of all events and can be viewed as a lower limit of the true two-year incidence.

Prior studies found adults with anxiety disorders to have higher mental-health related inpatient admissions, inpatient visits, and ER visits than controls, including adults with anxiety and no depression,(Marciniak M, Lage MJ, Landbloom RP, Dunayevich E, & Bowman L, 2004; McLaughlin TP et al., 2006) and adults with PTSD had an increased incidence of suicide than controls.(Gradus JL et al., 2015) We additionally observed a higher incidence of injury-related ER visits in children with anxiety disorders than the comparison cohort, our event least directly related to anxiety disorders. Over-anxious disorder symptoms predicted unintentional injuries in children;(Rowe R, Simonoff E, & Silberg JL, 2007) potential explanations included parents of anxious children may be more likely to report injuries (in our case this could be related to going to the ER) and children with anxiety may react more strongly to less severe injuries.(Rowe R et al., 2007) However, further research is needed to explore potential causality. In children without a baseline psychiatric diagnosis, two-year cumulative incidence of each event remained higher in children with anxiety than the comparison cohort, which may be particularly useful for clinicians and parents to understand and anticipate risks in children with anxiety alone.

The comparison cohort provided context for incidence estimates found in the anxiety cohort, with estimates from the same datasource and with consistent baseline restrictions and event definitions. The comparison cohort is not meant to represent the general population and differences in cumulative incidences between anxiety and comparison cohorts should not be interpreted causally. There are often higher comorbidities reported in individuals with anxiety disorders than control groups.(Gradus JL et al., 2015; Marciniak M et al., 2004; McLaughlin TP et al., 2006) The higher healthcare utilization and comorbidity diagnoses we



observed could be related to anxiety symptoms before diagnosis, such as somatic symptoms which are common in pediatric anxiety.(Crawley SA et al., 2014; Ginsburg, Riddle, & Davies, 2006; Ramsawh HJ et al., 2010) Observed differences in two-year cumulative incidence between anxiety and comparison cohorts may be due to baseline differences, which are part of the full picture when estimating event occurrence in individuals with and without anxiety disorders.

Our study population represents a subset of all US children with anxiety disorders. Research in US children covered by Medicaid and uninsured children would complement our findings. Further, the median age in our sample was 12 years, whereas the median age of onset for adolescences with anxiety disorders was 6 years.(Merikangas KR et al., 2010) The major distinction is that our cohort restricts to children with recorded anxiety disorder diagnoses from a healthcare provider. Delays in seeking care are common, among adults the median delay in initial treatment contact for anxiety disorders was 9 to 23 years.(Wang PS et al., 2005) Relatedly, the higher incidence we observe in older children could partially be attributed to children with longer periods of untreated, unrecognized anxiety.

The research can be applied to help providers inform and prepare caregivers and patients on risks, monitoring symptoms, and when to seek additional care to prevent serious events. As parents commonly report unmet needs for care coordination in pediatric anxiety,(Brown NM, Green JC, Desai MM, Weitzman CC, & Rosenthal MS, 2014) efforts are needed to help practitioners facilitate patient mental health care. Implications of the research on the healthcare system include anticipation of healthcare needs in children with anxiety and encouragement of facilities to be aware of anxiety disorders in pediatric admissions. Given children with anxiety often receive care outside mental health specialists,(Anderson LE, Chen ML, Perrin JM, & Van Cleave J, 2015) educating emergency medicine practitioners and practitioners of pediatrics and family practice in optimal management of pediatric mental illness is essential.(Dolan MA, Fein JA, & Committee on Pediatric Emergency Medicine, 2011) For example, integration of mental health specialist in ERs and primary care could help reduce repeated anxiety-related ER visits.(Dark T et al., 2017) Finally, estimates provide a benchmark to evaluate improvements in pediatric anxiety care.

Limitations of the work should be considered. We lack date of anxiety symptom onset and cannot be certain we identified the date anxiety was first diagnosed by a provider. Relatedly, children in the comparison cohort could have undiagnosed anxiety. We lack clinically derived data that could make findings more rigorous, including clinical diagnostic criteria and anxiety severity measures. While outside the scope of this manuscript, future research with greater clinical details could evaluate whether initial care or treatment can prevent events. Given inclusion criteria, estimates in children with psychiatric comorbidities should consider that those strata mostly include newly diagnosed or untreated children. We miss events that resulted in death if the child was not first admitted to the hospital; given cohort age, death does not account for substantial loss to follow-up and competing risk of death would minimally influence estimates. Differences in recorded suicide ideation between anxiety and comparison cohorts could be related to reporting opportunities, which, for example, may be more frequent in children receiving psychotherapy. Our injury-related ER visit definition is broad and allows an injury-related code in any diagnostic position. This

study focused on the clinically relevant subset of children diagnosed with anxiety in an office setting; however, children with new anxiety diagnoses in inpatient or ER settings are important to describe further as they may have more severe symptoms with delays in obtaining care. It is possible that due to inclusion requirements or study design, the comparison cohort represented a sicker or healthier comparison than intended.

Within two-years following a new anxiety disorder diagnosis, a significant proportion of children have a mental health related hospitalization, inpatient treated self-harm event, or ER visit, which translates to a sizable number of children given the prevalence of anxiety disorders. Describing the two-year cumulative incidence of each event adds to understanding the impact and burden of pediatric anxiety disorders. This information can encourage proper management of anxiety disorders, help anticipate healthcare utilization, and focus research efforts within pediatric anxiety to prevent these serious events.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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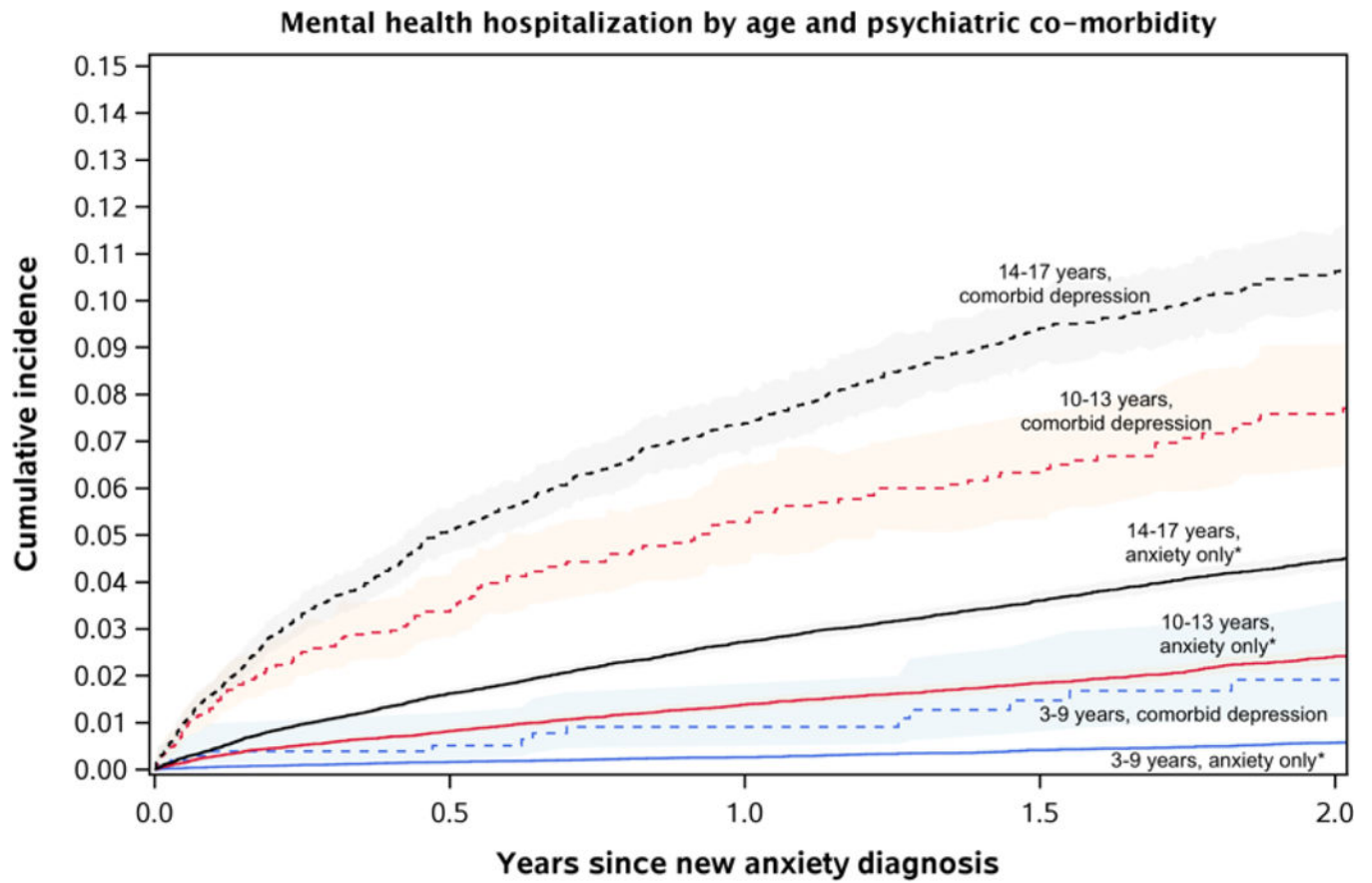
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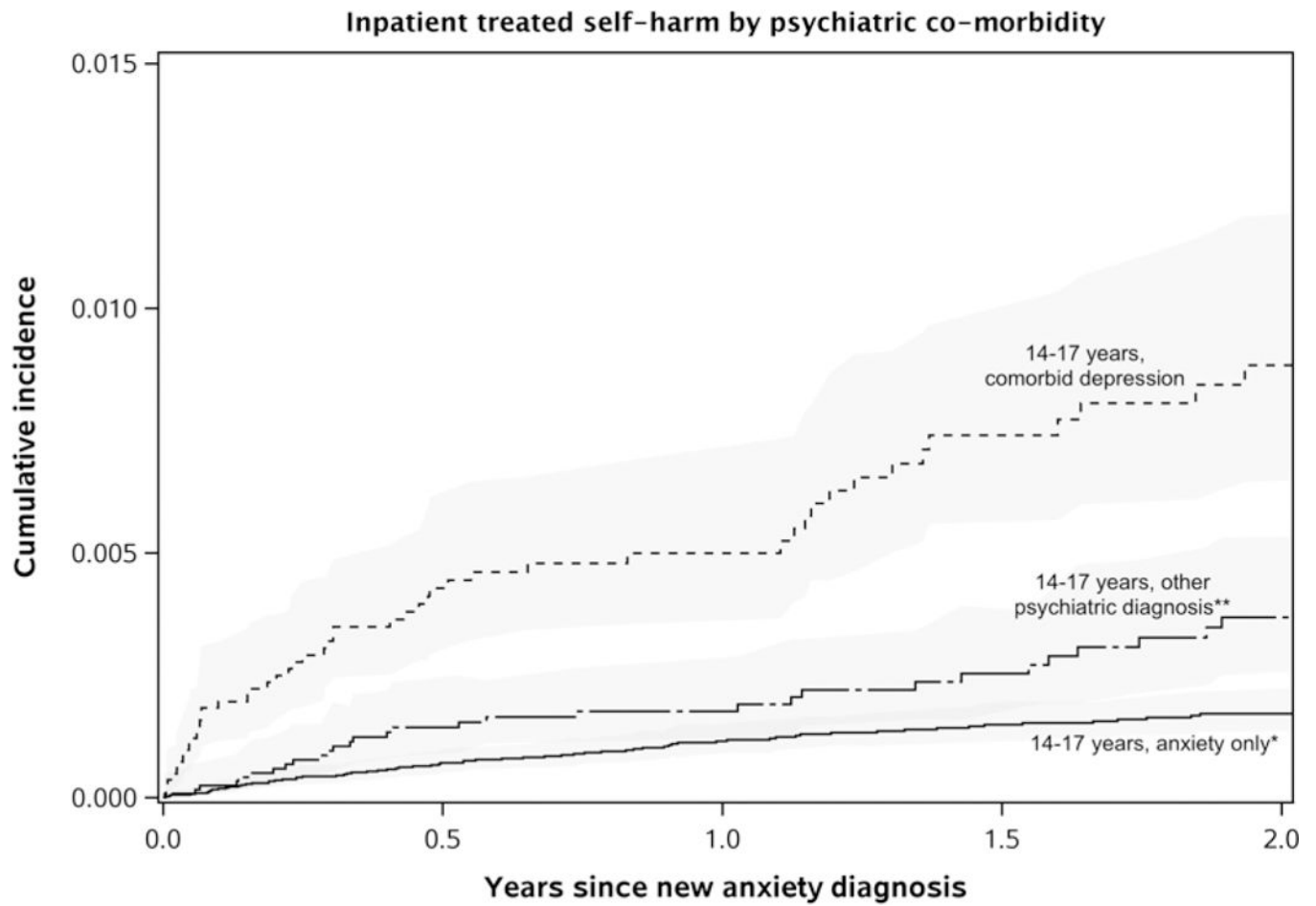
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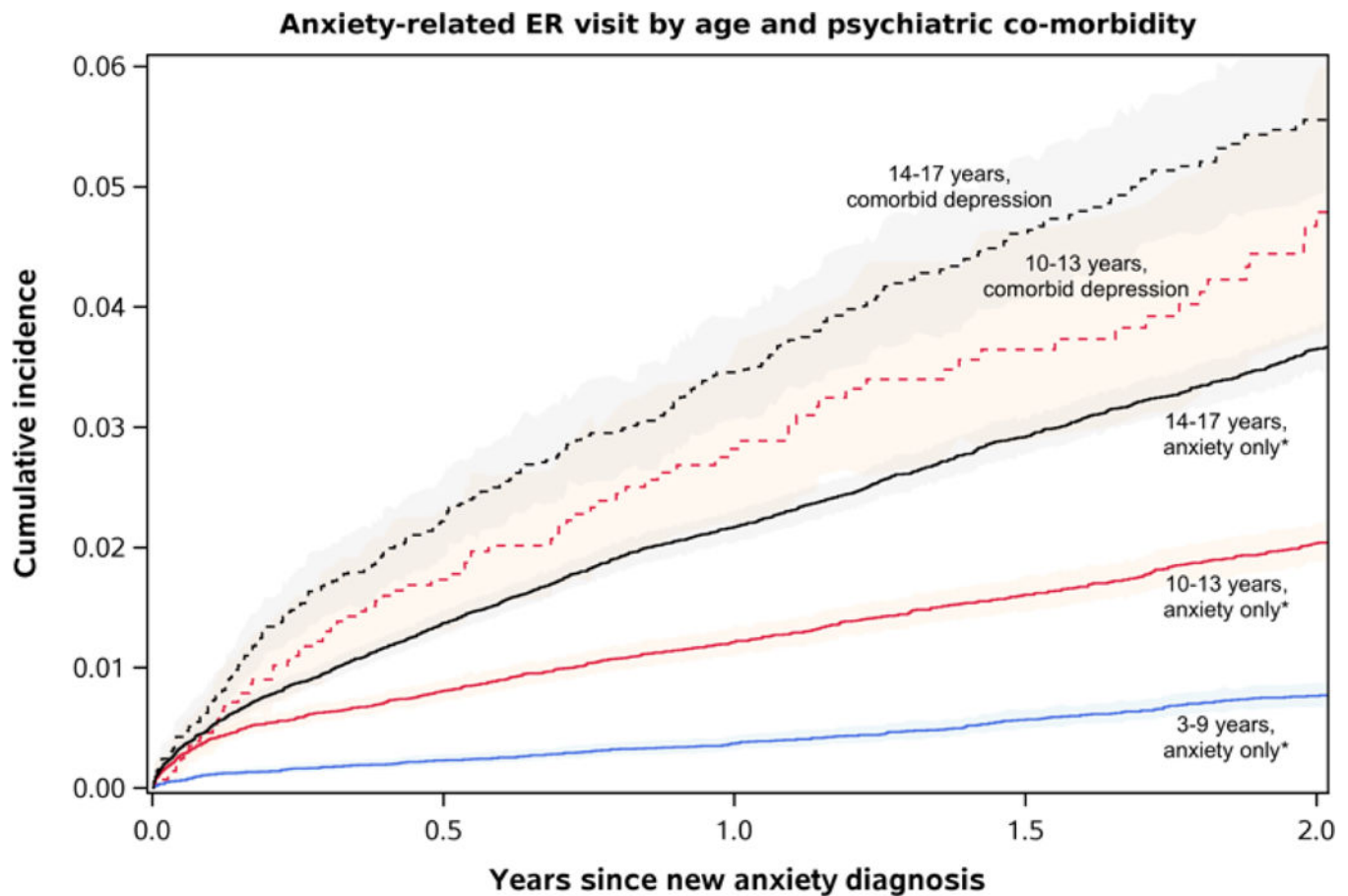
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**Figure 1.**

Cumulative incidence in anxiety cohort of a) mental health related hospitalizations, b) treated inpatient self-harm, and c) anxiety-related ER visits following a new anxiety diagnosis by age at anxiety diagnosis and psychiatric comorbidity (diagnosed at baseline)

A) Mental health related hospitalizations

\*No psychiatric comorbidity diagnosed at baseline

Not displayed = children with another diagnosed psychiatric comorbidity (included N=156,781)

B) Inpatient, treated self-harm in children 14–17 years at anxiety diagnosis

\*No psychiatric comorbidity diagnosed at baseline

\*\*Other psychiatric comorbidity: this excludes children with a baseline diagnosis of depression, bipolar disorder, personality disorder, schizophrenia, and autistic disorder  
Restricted to children aged 14–17 years at new anxiety diagnosis (included N=76,936)

C) Anxiety-related ER visits

\*No psychiatric comorbidity diagnosed at baseline

Not displayed = children with another diagnosed psychiatric comorbidity and, due to low event count, children 3–9 with comorbid depression (included N=155,725)

**Table 1.**

Patient characteristics of children newly diagnosed with anxiety and children in the comparison cohort

	Children with new anxiety diagnosis (n=198,450)		Comparison cohort (n=1,980,082)	
	No.	%	No.	%
<b>Matching factors<sup>a</sup></b>				
Male	89,341	45%	891,444	45%
Age, Median (IQR)	12 (8–15)		12 (8–15)	
3–9 years	65,052	33%	648,983	33%
10–13 years	56,462	28%	563,197	28%
14–17 years	76,936	39%	767,902	39%
<b>Child characteristics</b>				
New anxiety disorder diagnosis				
Unspecific anxiety	104,838	53%	-	
Generalized anxiety disorder	50,433	25%	-	
OCD	9,816	5%	-	
PTSD	8,066	4%	-	
Panic disorder	6,861	3%	-	
Separation anxiety disorder	5,674	3%	-	
Other, multiple <sup>b</sup>	12,762	6%	-	
Provider type, anxiety diagnosis/match date				
Psychiatry; Psychologist, therapist	91,539	46%	39,781	2%
Pediatrics; Family practice	62,942	32%	969,079	49%
Other types	33,627	17%	722,931	37%
Unknown; Multiple	10,342	5%	248,291	13%
Anxiety-related symptoms, prior 90 days <sup>c</sup>	28,339	14%	140,823	7%
Psychiatric diagnosed comorbidities				
Any non-anxiety diagnosis <sup>d</sup>	53,963	27%	174,400	9%
ADHD	23,895	12%	95,854	5%
Depression	12,294	6%	16,270	1%
Adjustment disorder	6,619	3%	26,423	1%
Sleep disorder	5,917	3%	14,255	1%
Disruptive behavior, conduct disorder	5,428	3%	10,136	1%
Self-harm	124	<1%	144	<1%
Suicide ideation	488	<1%	708	<1%
Medication use in prior year				
Count, therapeutic subgroups, Median (IQR)	2 (1–3)		1 (0–3)	
0–1	92,765	47%	1,034,653	52%
2–4	82,995	42%	793,672	40%
5+	22,690	11%	151,757	8%

	Children with new anxiety diagnosis (n=198,450)		Comparison cohort (n=1,980,082)	
	No.	%	No.	%
<b>Matching factors<sup>a</sup></b>				
ADHD medication	19,895	10%	106,283	5%
Opioid	16,759	8%	164,418	8%
Non-psychiatric diagnosed comorbidities				
Allergic rhinitis	24,822	13%	195,983	10%
Asthma	18,603	9%	154,189	8%
Acne	14,870	7%	145,646	7%
Fainting, dizziness	6,865	3%	33,827	2%
Gastro-esophageal reflux disease	5,480	3%	19,576	1%
Cardiac disorder	3,188	2%	17,629	1%
Migraine, chronic headache	4,042	2%	22,211	1%
Diabetes	1,067	1%	10,345	1%
Epilepsy, convulsions	2,461	1%	15,583	1%
Injury				
Fracture, sprain	25,280	13%	290,402	15%
Head injury	6,169	3%	54,348	3%
Other	37,935	19%	358,908	18%
Well visit	115,380	58%	1,221,235	62%
Outpatient, problem-oriented visit, Median (IQR)	3 (1–5)		2 (1–4)	
0–1	50,283	25%	653,417	33%
2–5	101,050	51%	1,011,636	51%
6+	47,117	24%	315,029	16%
Inpatient admissions <sup>e</sup>				
Psychiatric diagnosis	546	<1%	1,519	<1%
No-psychiatric diagnosis	2,733	1%	24,063	1%
Emergency room visit				
None	160,212	81%	1,652,013	83%
1 visit	29,433	15%	264,833	13%
2+ visits	8,805	4%	63,236	3%
Average length of follow-up (insurance enrollment), Median days (IQR)	558 (233–1164)		658 (337–1213)	

IQR: interquartile range; PTSD: post-traumatic stress disorder; OCD: obsessive-compulsive disorder; ADHD: attention-deficit/hyperactivity disorder

<sup>a</sup>Cohorts were balanced on two additional matching factors, year and region: Region distribution: North Central=27%, Northeast=21%, South=31%, West=20%, Unknown=1%; Year distribution: 2005–2006 (8%), 2007–2009 (19%), 2010–2012 (39%), 2013–2014 (34%)

<sup>b</sup>Anxiety cohort: agoraphobia 0.4%; anxiety due to medical condition 0.5%; social phobia 1.8%; other, specific phobia 1.5%; other anxiety 1.1%; selective mutism 0.5%; multiple specific anxiety diagnoses 0.7%

<sup>c</sup>ICD-9-CM code for abdominal pain, unspecified chest pain, headache, hyperventilation, malaise/fatigue, nausea, palpitations, or weight loss

<sup>d</sup>Children with a baseline diagnosis of bipolar disorder, personality disorder, schizophrenia, and autistic disorder were excluded from both cohorts

<sup>e</sup>Inpatient admission: psychiatric=inpatient admission associated with ICD-9-CM diagnosis 290–319

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Table 2.

Cumulative incidence of serious events in children following a new anxiety diagnosis (N=198,450) and in the comparison cohort (N=1,980,082)

	1 month		6 months		1 year		2 years	
	No. events	Incidence (95% CI)	No. events	Incidence (95% CI)	No. events	Incidence (95% CI)	No. events	Incidence (95% CI)
<i>Mental health related hospitalization<sup>a</sup></i>								
Children with anxiety	642	0.3% (0.3–0.4)	2,189	1.2% (1.2–1.3)	3,248	2.0% (1.9–2.0)	4,515	3.2% (3.1–3.3)
Comparison cohort	1,168	0.1% (0.1–0.1)	4,827	0.3% (0.3–0.3)	8,318	0.5% (0.5–0.5)	13,597	0.9% (0.9–1.0)
<i>Inpatient, treated self-harm</i>								
Children with anxiety	31	0.02% (0.01–0.02)	101	0.06% (0.05–0.07)	131	0.08% (0.06–0.09)	187	0.13% (0.11–0.15)
Comparison cohort	20	0.00% (0.00–0.00)	126	0.01% (0.01–0.01)	230	0.01% (0.01–0.02)	420	0.03% (0.03–0.03)
<i>Anxiety-related ER visit</i>								
Children with anxiety	599	0.3% (0.3–0.3)	1,620	0.9% (0.8–0.9)	2,371	1.4% (1.4–1.5)	3,386	2.4% (2.3–2.5)
Comparison cohort	590	0.0% (0.0–0.0)	2,645	0.1% (0.1–0.2)	4,657	0.3% (0.3–0.3)	7,864	0.6% (0.5–0.6)
<i>ER visit (any)</i>								
Children with anxiety	5,198	2.7% (2.6–2.7)	21,173	11.7% (11.6–11.9)	32,518	19.8% (19.6–20.0)	44,893	31.9% (31.6–32.1)
Comparison cohort	34,573	1.8% (1.8–1.8)	145,612	7.9% (7.9–7.9)	233,108	13.5% (13.4–13.5)	328,818	21.8% (21.7–21.9)
<i>Injury-related ER visit</i>								
Children with anxiety	1,764	0.9% (0.9–0.9)	9,148	5.1% (5.0–5.2)	15,186	9.4% (9.3–9.5)	22,619	16.7% (16.5–16.9)
Comparison cohort	12,932	0.7% (0.6–0.7)	67,485	3.7% (3.7–3.7)	113,483	6.6% (6.6–6.7)	168,996	11.4% (11.4–11.5)
<i>Recorded suicide ideation<sup>b</sup></i>								
Children with anxiety	312	0.2% (0.1–0.2)	1,080	0.6% (0.6–0.7)	1,626	1.0% (1.0–1.1)	2,246	1.7% (1.6–1.7)
Comparison cohort	435	0.0% (0.0–0.0)	2,021	0.1% (0.1–0.1)	3,597	0.2% (0.2–0.2)	6,062	0.4% (0.4–0.5)

<sup>a</sup>Secondary definition requiring a mental health diagnosis to be in the primary diagnostic position: 1-year incidence, anxiety cohort: 1.7% (95% CI: 1.6–1.8), comparison cohort: 0.4% (95% CI: 0.4–0.4%)

<sup>b</sup>Children diagnosed with anxiety (or match date) in 2005 excluded from analysis. Included N=191,454 anxiety cohort, N=1,910,519 comparison cohort



One-year cumulative incidence of serious events in children after a new anxiety diagnosis stratified by age at anxiety diagnosis and comorbid psychiatric conditions

Table 3.

Total No.	Mental health related hospitalization			Inpatient treated self-harm			Anxiety-related ER visit			ER visit			Injury-related ER visit		
	No. events	Incidence (95% CI)	No. events	No. events	Incidence (95% CI)	No. events	No. events	Incidence (95% CI)	No. events	No. events	Incidence (95% CI)	No. events	No. events	Incidence (95% CI)	No. events
Age at anxiety diagnosis															
3–9 years	65,052	229	0.4% (0.4–0.5)	*	-	233	0.4% (0.4–0.5)	8,988	17% (16–17)	4,198	8% (8–8)				
10–13 years	56,462	789	1.7% (1.6–1.8)	22	0.04% (0.03–0.07)	621	1.3% (1.2–1.4)	8,388	18% (18–18)	4,348	9% (9–10)				
14–17 years	76,936	2,230	3.5% (3.3–3.6)	109	0.17% (0.14–0.20)	1,571	2.3% (2.2–2.5)	15,142	24% (23–24)	6,640	11% (10–11)				
Psychiatric comorbidity <sup>a</sup>															
Depression	12,294	630	6.3% (5.8–6.8)	46	0.43% (0.32–0.57)	301	3.1% (2.7–3.4)	2,629	27% (26–28)	1,187	13% (12–13)				
3–9 years	1,056	*	-	*	-	*	-	159	19% (16–22)	80	10% (8–12)				
10–13 years	2,903	125	5.3% (4.4–6.3)	10	0.39% (0.20–0.70)	65	2.8% (2.2–3.6)	558	24% (22–26)	275	12% (11–14)				
14–17 years	8,335	497	7.4% (6.8–8.0)	36	0.50% (0.36–0.69)	230	3.5% (3.0–3.9)	1,912	29% (28–31)	832	13% (12–14)				
Other <sup>b</sup>	41,669	757	2.2% (2.1–2.4)	20	0.06% (0.04–0.09)	449	1.3% (1.2–1.5)	6,903	21% (20–21)	3,297	10% (10–10)				
3–9 years	16,691	118	0.9% (0.7–1.0)	*	-	78	0.6% (0.5–0.7)	2,441	18% (17–19)	1,101	8% (8–9)				
10–13 years	12,456	186	1.9% (1.6–2.2)	*	-	123	1.2% (1.0–1.5)	1,838	18% (18–19)	966	10% (9–11)				
14–17 years	12,522	453	4.4% (4.0–4.8)	19	0.18% (0.11–0.27)	248	2.5% (2.2–2.8)	2,624	26% (25–27)	1,230	12% (12–13)				
None recorded	144,487	1,861	1.5% (1.5–1.6)	65	0.05% (0.04–0.07)	1,621	1.3% (1.2–1.4)	22,986	19% (19–19)	10,702	9% (9–9)				
3–9 years	47,305	103	0.3% (0.2–0.3)	*	-	149	0.4% (0.3–0.4)	6,388	16% (16–16)	3,017	8% (7–8)				
10–13 years	41,103	478	1.4% (1.3–1.5)	11	0.03% (0.02–0.06)	433	1.2% (1.1–1.3)	5,992	17% (17–18)	3,107	9% (9–10)				
14–17 years	56,079	1,280	2.7% (2.6–2.9)	54	0.12% (0.09–0.15)	1,039	2.2% (2.0–2.3)	10,606	23% (22–23)	4,578	10% (10–10)				
Comparison cohort, no psychiatric comorbidity <sup>c</sup>															
3–9 years	592,981	356	0.1% (0.1–0.1)	*	-	363	0.1% (0.1–0.1)	60,993	12% (12–12)	27,764	6% (6–6)				
10–13 years	510,451	1,309	0.3% (0.3–0.3)	21	0.01% (0.00–0.01)	1,008	0.2% (0.2–0.2)	51,710	12% (12–12)	28,496	7% (6–7)				
14–17 years	702,250	3,626	0.6% (0.6–0.6)	141	0.02% (0.02–0.03)	2,376	0.4% (0.4–0.4)	92,556	15% (14–15)	43,656	7% (7–7)				

\* Not displayed due to low event count

<sup>a</sup> Baseline psychiatric diagnoses on the date of the new anxiety diagnosis or in the prior year

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Excludes children with a baseline diagnosis of depression, bipolar disorder, personality disorder, schizophrenia, and autistic disorder  
N=1,805,682 (removed 174,400 with baseline psychiatric diagnosis)