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Time Trends in Reported Diagnoses of Childhood Neuropsychiatric Disorders

A Danish Cohort Study

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Objectives: To examine trends in autism (autism spectrum disorder and childhood autism) in the context of 3 additional childhood neuropsychiatric disorders: hyperkinetic disorder, Tourette syndrome, and obsessive-compulsive disorder.

Design: Population-based cohort study.

Setting: Children were identified in the Danish Medical Birth Registry. Relevant outcomes were obtained via linkage with the Danish National Psychiatric Register, which included reported diagnoses through 2004 by psychiatrists using diagnostic criteria from the *International Statistical Classification of Diseases, 10th Revision*.

Participants: All children born in Denmark from 1990 through 1999, a total of 669 995 children.

Main Outcome Measures: Cumulative incidence proportion by age, stratified by year of birth, for each disorder.

Results: Statistically significant increases were found in cumulative incidence across specific birth years for autism spectrum disorder, childhood autism, hyperkinetic disorder, and Tourette syndrome. No significant change in cumulative incidence was observed for obsessive-compulsive disorder.

Conclusions: Recent increases in reported autism diagnoses might not be unique among childhood neuropsychiatric disorders and might be part of a more widespread epidemiologic phenomenon. The reasons for the observed common pattern of change in reported cumulative incidence could not be determined in this study, but the data underscore the growing awareness of and demand for services for children with neurodevelopmental disorders in general.

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AUTISM SPECTRUM DISORDER (ASD), often referred to as autism, comprises a group of conditions characterized by qualitative abnormalities in reciprocal social interactions and in patterns of communication, and by a restricted, stereotyped, repetitive repertoire of interests and activities.[1] A public health debate surrounding the prevalence of autism has become a prominent feature in both the public[2,3] and professional[4-8] autism literature in the United States and abroad. The debate is fueled by numerous studies reporting marked increases in recent years in the prevalence of autism[9] or its proxy measure, the prevalence of individuals receiving autism services.[10-17] This study attempts to add a new perspective to the debate by examining trends in autism in the context of trends in 3 additional childhood neuropsychiatric disorders: (1) hyperkinetic disorder (HKD), characterized by lack of persistence in activities that require cognitive involvement and a tendency to move from one activity to another without completing any one, together with disorganized, ill-regulated, and excessive activity[1]; (2) Tourette syndrome (TS), a form of tic disorder with multiple motor tics and 1 or more vocal tics[1]; and (3) obsessive-compulsive disorder (OCD), characterized by recurrent obsessional thoughts or compulsive acts.[1]

These 4 disorders are among the most common neuropsychiatric disorders, and they have a number of factors in common: (1) age at onset is in childhood, (2) the disorders have specific diagnostic criteria and are reported by a common source type (child psychiatrists), and (3) the disorders are diagnostically closely aligned and may be comorbid.[18,19]

The time trend in autism has been evaluated in reviews comparing prevalence and incidence reports across different studies[5-8] and in studies estimating autism incidence or prevalence at different time points in the same population.[9-17] In contrast, no studies, to our knowledge, have been conducted on trends over time of OCD, TS, or HKD, although some stud-

Table 1. Characteristics of Cohorts of Selected Childhood Neuropsychiatric Disorders Among Children Born in Denmark, 1990-1999, and Followed Up From 1995 Through 2004

Disorder	*ICD-10* Code	Birth Year	No. of Cases/ No. of Births
Hyperkinetic disorder	F90	1992-1993	703/135 095
		1994-1995	662/139 438
		1996-1997	465/135 286
		1998-1999	203/132 394
Obsessive-compulsive disorder	F42	1990-1991	252/127 782
		1992-1993	169/135 095
		1994-1995	64/139 438
Tourette syndrome	F95.2	1990-1991	95/127 782
		1992-1993	87/135 095
		1994-1995	77/139 438
Autism spectrum disorder	F84.0, F84.1, F84.5, F84.8, F84.9	1994-1995	805/139 438
		1996-1997	632/135 286
		1998-1999	423/132 394
Childhood autism	F84.0	1994-1995	248/139 438
		1996-1997	232/135 286
		1998-1999	234/132 394

Abbreviation: *ICD-10*, *International Statistical Classification of Diseases, 10th Revision*.

ies have reported a recent increase in prevalence of attention-deficit/hyperactivity disorder (ADHD).[20-22] The HKD code in *International Statistical Classification of Diseases, 10th Revision* (*ICD-10*) replaces the ADHD code in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*).[23] There is a significant overlap in the HKD diagnosis (*ICD-10*) and the ADHD diagnosis (*DSM-IV*), although ADHD includes a broader group of children than does HKD. The main difference in diagnosis is that ADHD, unlike HKD, permits symptoms of inattention in the absence of hyperactivity.[24]

For the present study, we adopted a population-based birth cohort approach to estimate and compare time trends in these childhood neuropsychiatric disorders in Denmark. The strengths of the study include the following: (1) the cohort is large, (2) all diagnostic data were obtained from a nationwide register based on standardized diagnostic reporting procedures, and (3) a common diagnostic coding system (*ICD-10*) was used. These strengths address some of the methodologic limitations of previous work and also enhance sample sizes and comparability of results across the 4 diagnostic conditions.

METHODS

STUDY DESIGN

The study cohort included all children born in Denmark from January 1, 1990, through December 31, 1999, identified in the Danish Medical Birth Registry, totaling 669 995 children. The Danish Medical Birth Registry comprises data on all live births and stillbirths by women with permanent residence in Denmark. All live-born children in Denmark are assigned a central population registry number, a unique, 10-digit number used for all official personal registrations in Denmark since 1968.[25]

Data on the 4 childhood neuropsychiatric outcomes were obtained from the Danish National Psychiatric Registry (DNPR). As of 1969, the DNPR includes all inpatient admissions to psychiatric hospitals and psychiatric wards in Denmark; since January 1, 1995, information from all psychiatric outpatient clinic contacts also has been included. In Denmark, children are referred to specialists in child psychiatry by general practitioners, schools, and psychologists if behavioral abnormalities are suspected. Because Denmark provides universal health care coverage that is free of charge and there are no private psychiatric hospitals, the inpatient and outpatient contacts recorded in the DNPR are believed to capture the majority of individuals diagnosed as having the study outcomes. The DNPR includes data on clinical diagnoses, dates of admission and discharge, and terms of admission.[26] All diagnoses reported to the DNPR are made by psychiatrists, and *ICD-10* diagnostic criteria have been used since 1994. The specific *ICD-10* diagnostic codes used for this study are provided in **Table 1**. Diagnoses such as mental retardation and specific developmental disorders of speech and language were not included in this study. Children with these disorders are generally examined and evaluated either in special competence centers or by their general practitioners, and the diagnoses from these are not reported to the DNPR. Study cohort data from the Danish Medical Birth Registry and DNPR were linked via the central population registry number.

For this study, follow-up for a reported diagnosis was restricted to the period after inclusion of both inpatient and outpatient registration and adoption of *ICD-10* in the DNPR (January 1, 1995, through December 31, 2004). The youngest age at reported diagnosis varied among the 4 conditions: HKD, 3 years; ASD, 1 year; and OCD and TS, 5 years. To ensure that no children included in the analyses for a particular disorder had received a diagnosis before January 1, 1995, different birth cohorts within the larger study cohort were used for the analysis of each disorder. Table 1 displays the different analytic birth cohorts for each disorder.

This study was approved by the National Board of Health and the Danish Data Protection Agency.

ANALYTIC APPROACH

Survival analysis methods were used in the statistical analyses of each birth cohort for each disorder. Within each analytic birth cohort, follow-up time began for all children at time of birth and continued until the first date of the relevant reported diagnosis, death, or the end of follow-up on December 31, 2004. Survival analysis methods adjust for the difference in follow-up time: the difference in follow-up time for children born in different years and the difference in follow-up time for children born in January compared with children born in December within the same year. No attempts were made to adjust for emigration because Denmark is believed to be characterized by a very homogeneous and stable population with a low migration rate.[15]

Each disorder was analyzed separately; for ASD, analyses were performed for ASD overall as well as for childhood autism specifically. Some children had multiple diagnoses; in those cases, the child was included as an outcome in the analysis for each separate condition. Because of this approach, the analysis of each condition could include children with either a single diagnosis or multiple diagnoses of the condition of interest plus 1 or more of the other study conditions. Conceivably, the time trend could differ between these 2 groups of children. It was not feasible to estimate separately the time trend for children with multiple conditions, eg, TS and ASD, because of the limited overlap in analytic birth cohorts and correspondingly small numbers of eligible cases. However, we did perform a sensitivity analysis by excluding children with multiple diagnoses and reestimating the time trend for each condition based only on children with a single diagnosis.

Table 2. Cumulative Incidence Estimates (95% Confidence Intervals) per 10 000 Children for Each 2-Year Analytic Birth Cohort for Each Disorder at Select Ages*

Birth Cohort	Age, y					
	3	5	7	9	11	13
Hyperkinetic Disorder (Test for Trend: $P<.001$)						
1992-1993	0.5 (0-1.1)	2.3 (1.4-3.2)	10.4 (8.7-12.2)	24.7 (22.0-27.3)	42.2 (38.8-45.7)	
1994-1995	0.6 (0.2-1.1)	2.9 (2.0-3.8)	13.0 (11.1-14.9)	35.2 (32.0-38.3)		
1996-1997	0.4 (0.1-0.7)	4.7 (3.6-5.9)	20.2 (17.8-22.5)			
1998-1999	0.4 (0.1-0.7)	7.0 (5.6-8.4)				
Tourette Syndrome (Test for Trend: $P=.001$)						
1990-1991		0.1 (0-0.2)	0.6 (0.2-1.1)	2.3 (1.4-3.1)	4.5 (3.4-5.7)	6.6 (5.2-8.0)
1992-1993		0.1 (0-0.2)	0.6 (0.2-1.0)	2.4 (1.5-3.2)	4.8 (3.6-6.0)	
1994-1995		0.4 (0-0.7)	1.5 (0.9-2.2)	3.9 (2.9-4.9)		
Obsessive-Compulsive Disorder (Test for Trend: $P=.82$)						
1990-1991		0.1 (0-0.2)	0.5 (0.1-0.8)	2.5 (1.6-3.4)	8.0 (6.4-9.5)	16.5 (14.3-18.7)
1992-1993		0.1 (0-0.2)	1.0 (0.5-1.6)	3.3 (2.4-4.3)	8.3 (6.8-9.8)	
1994-1995		0.1 (0-0.3)	0.5 (0.1-0.9)	2.7 (1.9-3.6)		
Autism Spectrum Disorder (Test for Trend: $P=.008$)						
1994-1995	2.7 (1.9-3.6)	16.1 (14.0-18.2)	35.9 (32.7-39.0)	50.8 (47.0-54.5)		
1996-1997	4.1 (3.0-5.2)	20.7 (18.3-23.2)	40.0 (36.6-43.4)			
1998-1999	4.7 (3.5-5.8)	23.0 (20.4-25.6)				
Childhood Autism (Test for Trend: $P<.001$)						
1994-1995	1.7 (1.0-2.4)	8.9 (7.3-10.4)	14.8 (12.8-16.9)	17.1 (15.0-19.3)		
1996-1997	2.8 (1.9-3.7)	11.4 (9.6-13.3)	16.1 (14.0-18.3)			
1998-1999	2.7 (1.8-3.5)	14.4 (12.4-16.5)				

*Empty cells indicate that it was not possible to estimate incidence.

To maintain sufficient statistical power, the analytic birth cohorts for each condition were stratified by year of birth into 2-year intervals (Table 1). The cumulative incidence proportion for each 2-year birth cohort was estimated by using the Kaplan-Meier curve. Presenting data in this way demonstrates how both age and year of birth affect the cumulative incidence of reported diagnoses.

Primarily, a test for trend was performed for each disorder; consequently, significance tests for equal cumulative incidence among different 2-year birth cohorts of each disorder were performed to establish which birth cohorts particularly displayed a significant change in cumulative incidence. All *P* values were derived by means of a Wilcoxon (Breslow-Gehan) version of a log-rank test. This version of a log-rank test does not require the proportionality of the hazards.

The analyses were performed with Stata version 8.0 (StataCorp, College Station, Tex).

RESULTS

A total of 4376 children were given a total of 4637 diagnoses. The cumulative incidence (per 10 000) estimates, stratified by year of birth for each condition, are provided in **Table 2**. For each disorder, results from tests for trend are displayed in Table 2. The **Figure** illustrates the cumulative incidence proportion curves for HKD, TS, ASD overall, and childhood autism.

The diagnoses HKD, TS, ASD, and childhood autism displayed a statistically significant test for trend. For HKD, an increase in cumulative incidence was observed across all cohorts such that each successive birth cohort had a significantly higher cumulative incidence than the previous cohort ($P<.001$). For example, at 5 years of age the cumulative incidences of HKD for the 1994-1995 cohort, 1996-1997 cohort, and 1998-1999 cohort were 26%, 100%, and 200% higher, respectively, than the cumulative incidence for the 1992-1993 cohort. For TS, the 1994-1995 cohort had a significantly higher cumulative incidence than both the 1990-1991 cohort ($P=.005$) and the 1992-1993 cohort ($P=.006$); for example, at 9 years of age, the cumulative incidence for the 1994-1995 cohort was 70% higher than the cumulative incidence for both the 1990-1991 and 1992-1993 cohorts. There was no significant change in the cumulative incidence between the 1990-1991 birth cohort and the 1992-1993 birth cohort of TS. For ASD overall, the 1998-1999 birth cohort had significantly higher cumulative incidence proportions than the 1994-1995 birth cohort ($P=.004$); for example, at 5 years of age, the cumulative incidence of the 1998-1999 cohort was 43% higher than the cumulative incidence for the 1994-1995 cohort. No significant increase in cumulative incidence was observed between other birth cohorts of ASD. For childhood autism (38% of all children with ASD), the cumulative incidence proportion was significantly higher for children born in 1998-1999 than for both the 1994-1995 ($P<.001$) and 1996-1997 ($P=.02$) birth cohorts; for example, at 5 years of age, the cumulative incidence for the 1998-1999 cohort was 62% and 28% higher, respectively, than the cumulative incidences for the 1994-1995 and 1996-1997 cohorts. There was no change in the cumulative incidence between the 1994-1995 birth cohort and the 1996-1997 birth cohort of childhood autism.

There were no significant differences in the cumulative incidence proportions across birth cohorts for OCD

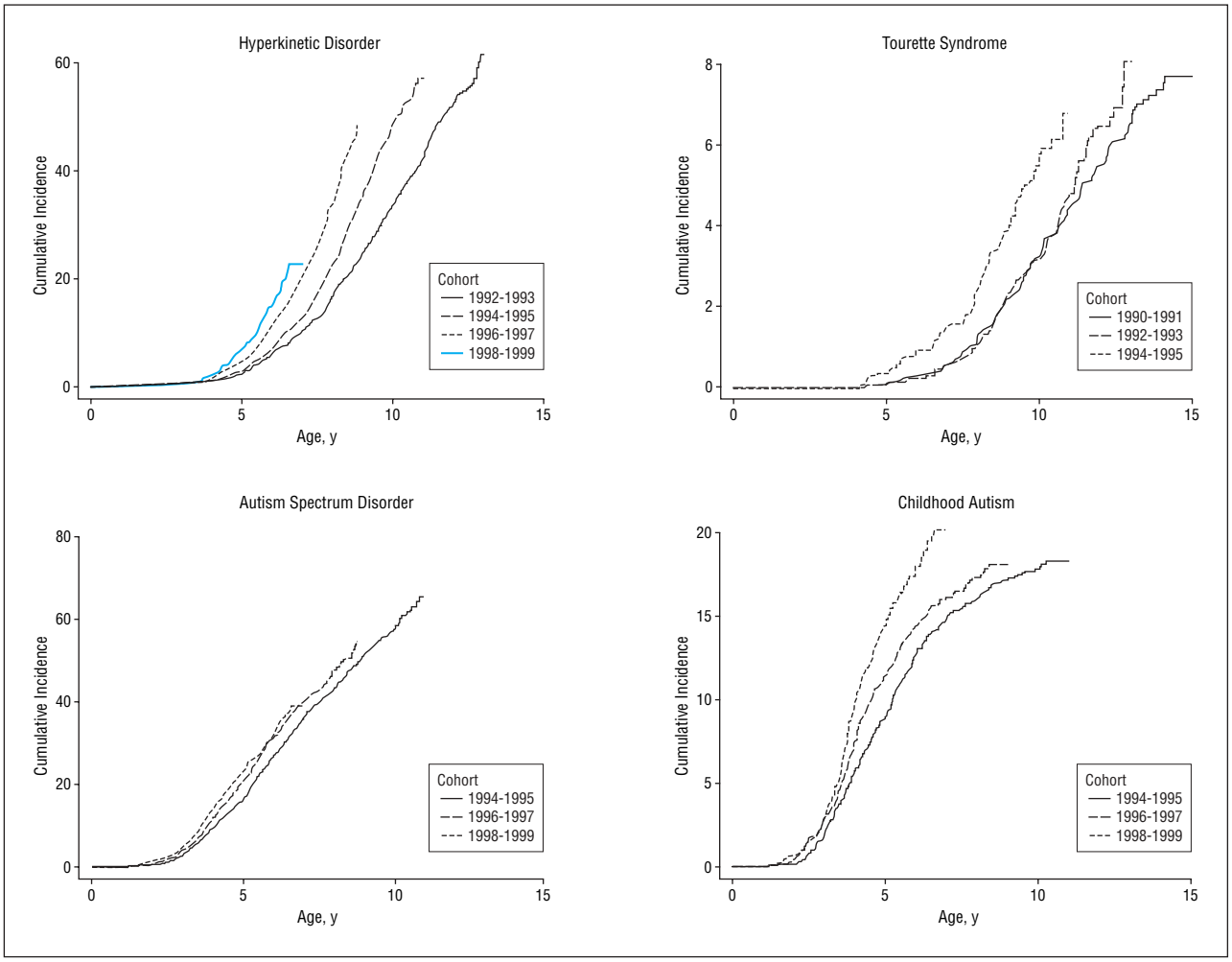

Figure. Time trend of childhood neuropsychiatric disorders among children born in Denmark, 1990 to 1999, and reported 1995 to 2004: cumulative incidence proportion (per 10 000) for each 2-year analytic birth cohort for each disorder.

(a nonsignificant test for trend). Also, the cumulative incidence estimates and results of the Wilcoxon log-rank tests based on the sensitivity analyses for each disorder that only included children with a single diagnosis did not differ substantially from the preceding results.

COMMENT

OVERVIEW

The present study is the first, to our knowledge, to compare time trends in cumulative incidence of reported diagnoses for 4 common childhood neuropsychiatric disorders: HKD, OCD, TS, and ASD. This population-based study reports time trends in OCD, TS, and HKD and adds to the small number of studies examining trends in incidence of reported diagnosis of ASD. We have described a common pattern of increased cumulative incidence estimates over time in the same population in reported *ICD-10* diagnoses for HKD, TS, ASD overall, and childhood autism.

The general pattern of increase in cumulative incidence was similar for HKD, TS, ASD overall, and childhood autism, but the extent of change was specific to each disorder. For HKD, the cumulative incidence of reported diagnoses was significantly increased between every birth cohort. For ASD, childhood autism, and TS, the difference in cumulative incidence between birth cohorts was generally limited to 1 cohort being significantly different from the other 2 cohorts.

No significant change in cumulative incidence was reported for OCD. It is difficult to explain why OCD was the only disorder displaying another pattern; the reason may be etiologic, due to nonetiologic diagnostic differences, or due to the relatively short follow-up.

COMPLETENESS OF REPORTED DIAGNOSES

Most of the previous articles on secular trend have estimated prevalence. Therefore, to evaluate the completeness of the data, we compared the cumulative incidence of the oldest cohort of each disorder reported in the present study with the prevalence estimates reported in previous studies. In the present study, the follow-up period ended before the children were past the risk of receiving the diagnoses being studied; therefore, we expect the estimates of the cumulative incidence to be slightly lower than the prevalence estimates.

The prevalence rates of ASD and childhood autism previously reported in recent studies based on either epidemiologic studies of existing data or population screening methods fall within a fairly consistent range. The prevalence of ASD has generally been reported to range from 45 to 67 per 10 000.[9,12,13,27] Childhood autism is most commonly reported to have a prevalence of approximately 20 per 10 000.[9,14,15,17,28] The cumulative incidence estimates observed in this study in the oldest cohort (Table 2, 1994-1995 cohort, aged 9 years: 50.8 per 10 000 for ASD and 17.1 per 10 000 for childhood autism) are comparable to results from previous studies.

The prevalence of OCD has been reported in a number of studies, primarily for adolescents and based on screening, diagnostic interviews, or both, in community or clinical populations.[29,30] Published rates range from 6 per 10 000[31] to 400 per 10 000[32] and are highly dependent on the age of the child (increasing with age) and whether the source of behavioral information is the parent (lowest rates) or the child (highest rates), supporting the belief that children with OCD typically conceal their behavior from adult caregivers,[30] which leads to underreporting.[29] The cumulative incidence of 16.5 per 10 000 reported in 13-year-olds (Table 2, 1990-1991 cohort) observed in our study falls within the published rate range.

The published age-specific prevalence of TS has also varied widely, from 15 to 380 per 10 000, in mainstream school populations, as reported in a recent review.[33] Notably, the rates cited in the review were all based on intense case-finding methods such as direct observation, interview, or clinical examination. A Swedish study comparing registry-based vs screening-based case-finding methods for TS in the same population noted higher rates based on screening and that most cases identified by their screening methods had not been previously diagnosed.[34] The cumulative incidence of 6.6 per 10 000 reported in 13-year-olds (Table 2, 1990-1991 cohort) observed in our study is lower than these published estimates, likely related to our use of registry data rather than population screening.

The prevalence of HKD, which is more narrowly defined than ADHD, is believed to range from 40[35] to 140 per 10 000,[36] based on population surveys. The presence of HKD is believed to be underdiagnosed in the general population because not all children with HKD are referred for assessment and treatment in child psychiatry.[37] The cumulative incidence of 42.2 per 10 000 reported in 11-year-olds (Table 2, 1992-1993 cohort) observed in this study is at the lower end of the reported range and probably reflects the expected lower prevalence for HKD based on discharge diagnoses rather than population surveys.

In summary, the completeness of the DNPR data on reported cases of the 4 study conditions appears to be good, albeit not as complete as reported from systematic community surveys. The estimates of OCD, TS, and perhaps ASD observed in this study could also be influenced by the relatively short follow-up. The age at diagnosis of TS, OCD, and certain subgroups of ASD (eg, Asperger syndrome) is often in late childhood or the early teens and, therefore, additional follow-up time would have resulted in later diagnoses for these disorders, ie, a different cumulative incidence trajectory could be found for ages beyond those studied herein.

VALIDATION OF REPORTED DIAGNOSES

The diagnoses reported in the DNPR are generally not validated. The validity of reported diagnoses of childhood autism in the DNPR was assessed in a small pilot sample of 40 children with infantile autism, and 37 (92%) met the criteria for a correct diagnosis based on a coding scheme developed by the Centers for Disease Control and Prevention.[38] An unofficial confirmation of 171 children diagnosed as having HKD in the DNPR was performed in 2004; the agreement percentage on a full diagnosis of ADHD according to *DSM-IV* was 89%, while the remaining 11% lacked only 1 symptom to fulfill the ADHD diagnosis.[39] No validations have been performed for the other diagnoses. While not comprehensive or definitive, these efforts support the belief that, in general, validity of the reported diagnoses to the DNPR is good.

CONCLUSIONS

This study used nationwide data to compare the time trends of multiple childhood psychiatric conditions, and the results suggest that the previously reported increase in the incidence of autism might not be a solitary event among child neuropsychiatric disorders. If true, the debate surrounding explanations for the increase in autism incidence should also consider the evidence of a more widespread epidemiologic phenomenon across different diagnostic conditions.[17] Although these data cannot resolve the debate, future work might want to build on the following opposing explanatory models:

- **Independent Factors Model:** A common pattern of increase among different childhood psychiatric conditions reported in the same population during the same period is coincidental and is attributable to separate and independent factors promoting the increase in each condition. These separate factors could be etiologic, nonetiologic, or some unique combination of the two, depending on the condition. The only common feature across the different conditions is that the factors are promoting the increases in the same population at the same time.
- **Shared Factors Model:** A common pattern of increase among different childhood psychiatric conditions reported in the same population during the same period is not coincidental and is attributable to 1 or more shared factors. The shared factors model could consist of (1) shared nonetiologic factors, ie, the way in which children with neuropsychiatric disorders have been identified and diagnosed in Denmark since the mid-1990s; (2) shared etiologic factors, ie, factors from genetics or the environment; or (3) some combination of etiologic and nonetiologic factors.

Although the reasons for the observed common pattern of change in reported cumulative incidence in TS, HKD, and ASD cannot be addressed with these data, it is clear that the number of children with neuropsychiatric disorders and their families in need of support and

services has been growing in recent years. Furthermore, while the search for causes should proceed unabated, the ultimate value of these data are their contribution to the growing awareness of child neurodevelopment problems in general and understanding of the resources needed to ensure optimal development for all children.

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