

Autism Spectrum Disorder, ADHD, Epilepsy, and Cerebral Palsy in Norwegian Children



WHAT'S KNOWN ON THIS SUBJECT: Prevalence estimates for neurologic and neurodevelopmental disorders in children vary widely, and there is uncertainty as to what extent the individual disorders overlap. Most previous prevalence studies have been based on survey data and not on specialist-confirmed diagnoses.



WHAT THIS STUDY ADDS: This study used nationwide register data to determine the proportions of Norwegian children diagnosed with autism spectrum disorder, attention-deficit/hyperactivity disorder, epilepsy, and cerebral palsy and to study how the disorders overlap. All diagnoses were specialist-confirmed.

abstract

BACKGROUND: Numerous studies have investigated the prevalence of neurologic and neurodevelopmental disorders individually, but few have examined them collectively, and there is uncertainty as to what extent they overlap.

METHODS: The study has determined the proportions of children aged 0 to 11 years with diagnoses of autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), epilepsy, and cerebral palsy (CP) in Norway. The data were obtained from the Norwegian Patient Register, which is nationwide and contains diagnoses assigned by Norwegian specialist health services (hospitals and outpatient clinics). The Norwegian Patient Register started collecting individual-level data in 2008, and the follow-up period for the study is years 2008 through 2010.

RESULTS: For ASD, ADHD, and epilepsy, the proportions were highest in the oldest children. At age 11 years, the incidence was 0.7% for ASD, 2.9% for ADHD, and 0.9% for epilepsy. The cumulative incidence is likely to be higher because some cases diagnosed before 2008 were probably missed. For CP, the proportions were ~0.3% for age ≥ 5 years. There was considerable overlap between diagnoses. For all disorders, boys had a significantly increased risk. In school-age children (aged 6–11 years) the male/female ratio was 4.3 for ASD, 2.9 for ADHD, 1.2 for epilepsy, and 1.3 for CP.

CONCLUSIONS: The findings demonstrate the significant burden of disease associated with neurologic and neurodevelopmental disorders in children and that this burden is disproportionately skewed toward boys. *Pediatrics* 2012;130:e152–e158

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KEY WORDS

developmental disabilities, neurologic disorders, cumulative incidence, population register, autism spectrum disorder, attention-deficit/hyperactivity disorder, epilepsy, cerebral palsy

ABBREVIATIONS

ADHD—attention-deficit/hyperactivity disorder
ASD—autism spectrum disorder
CI—confidence interval
CP—cerebral palsy
DSM-IV—*Diagnostic and Statistical Manual, Fourth Edition*
ICD-10—*International Classification of Diseases, 10th Revision*
NPR—Norwegian Patient Register

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Neurologic and neurodevelopmental disorders account for a large proportion of long-term disabilities in children. Numerous studies have investigated the prevalence of such disorders individually, but only a few have examined them collectively and attempted to estimate the overall disease burden in the general population.^{1–4} Prevalence estimates also vary widely, which may partly be explained by the fact that most prevalence studies derive diagnoses from self-report surveys or chart abstraction, not from in-person specialist assessments.

For autism spectrum disorder (ASD), most recent prevalence estimates are ~0.7%,⁵ but large studies from the United Kingdom⁶ and the United States⁷ have reported proportions as high as 1.2% and 0.9%, respectively. Attention-deficit/hyperactivity disorder (ADHD) prevalence estimates cover a wide range, but the most comprehensive review of available studies worldwide found a mean prevalence of 5.3%.⁸ In general, the use of the *Diagnostic and Statistical Manual, Fourth Edition* (DSM-IV) criteria tends to generate higher prevalence rates of ADHD than the use of *International Classification of Diseases, 10th Revision* (ICD-10) criteria,^{8,9} mainly because DSM-IV, unlike ICD-10, permits the diagnosis of ADHD on the basis of inattention alone, in the absence of hyperactivity.⁸ For epilepsy, the population prevalence in children is usually estimated to be between 0.5% and 1.0%.¹⁰ Recent studies from developed countries have found a decreasing prevalence, which is thought to result from better prevention of causes of epilepsy through improved perinatal care, improved immunization schedules, and reduced incidence of head trauma.¹⁰ Prevalence estimates for cerebral palsy (CP) range from 0.15% to 0.35% in most studies.¹¹

More research is required to determine the extent of overlap between

the individual neurologic and neurodevelopmental disorders. For example, it is well known that comorbid epilepsy is common in children with ASD, but the estimates vary from 5% to 46%.¹² The overlap between ASD and ADHD is also debated.¹³ DSM-IV and ICD-10 preclude comorbid diagnoses of these disorders, but numerous studies have found extensive clinical overlap, with 20% to 50% of children with ADHD meeting criteria for ASD and 30% to 80% of ASD children meeting criteria for ADHD.¹³

The aim of this study was to determine the proportion of children diagnosed with ASD, ADHD, epilepsy, and CP in Norway and to investigate how the disorders overlap. The data were obtained from the Norwegian Patient Register (NPR), which collects data from all specialist health services in Norway.

METHODS

Study Data

The NPR is an administrative database containing activity data from all Norwegian government-owned hospitals and outpatient clinics. Reporting of data to the NPR is mandatory and linked to the governmental reimbursement system for funding of health services. Diagnoses are reported as ICD-10 codes. The NPR was established in 1997, but the 11-digit personal identification number unique to every Norwegian citizen has only been reported since 2008, after a change in the health register act passed by the Norwegian Parliament on March 1, 2007. Consequently, individual-level research data are available from 2008 onward. The personal identification numbers are stored in encrypted form in the NPR.

Health care is free of charge for children up to age 16 years in Norway. All hospitals for children and most child outpatient clinics are government-owned. In addition, there are currently

58 pediatricians and child psychiatrists with private practices, of which 52 receive their funding through government reimbursements. Private practices receiving government reimbursements are obliged to report their data to the NPR in the same way as government-owned institutions. However, the reporting of personal identification numbers from private practices is not yet complete, and private practice data were not included in the data file used for this study. Very few cases of ASD, epilepsy, and CP are diagnosed at private clinics, so the lack of private practice data will not affect the cumulative incidence figures for those disorders. ADHD, however, is more commonly diagnosed by private specialists. We do not know the exact number of cases lost, but government figures show that the number of ADHD diagnoses reported for reimbursements by private practices account for 5% to 10% of the total number of ADHD diagnoses.

When a child has received a diagnosis of ASD, ADHD, epilepsy, or CP, follow-up is usually continued by the children's general practitioners and/or municipal educational services working directly with schools, kindergartens, and day-care facilities. Continued specialist follow-up is provided if the child is receiving ongoing medical treatment or has medical conditions that require specialist follow-up. Therefore, we would not expect all diagnosed cases to be captured by the register every year. If children were diagnosed before 2008 and have not consulted specialist health services since then, they will not be found in the NPR. Consequently, the true cumulative incidence of the disorders will be somewhat higher than the figures calculated on the basis of current NPR data.

For this study, the NPR provided data from 2008 through 2010 for children born from 1999 through 2010 (aged 0–11 years at the end of follow-up) with

diagnoses within the following ICD-10 sections:

- F84 Pervasive developmental disorders (corresponding to ASD in DSM-IV)
- F90 Hyperkinetic disorders (corresponding to ADHD in DSM-IV)
- G40 Epilepsy
- G41 Status epilepticus
- G80 Cerebral palsy (CP)

The data file also included the following information: gender, year of birth, calendar year(s) in which the diagnosis was registered, type of clinic and contact (pediatric/child psychiatry; inpatient/outpatient), and number of contacts per calendar year.

In total, 136 079 inpatient and outpatient contacts with at least 1 of the relevant ICD-10 codes were identified. The personal identification number was available for 99.5% of identified cases. In cases for which the personal identification number was missing, the patient number unique to every patient within each hospital was used as a substitute. The data file did not contain any information that could be traced back to specific subjects. The use of such anonymous research files does not require regulatory ethics approval in Norway.

Statistical Analyses

Proportions for years 2008 through 2010, by gender and year of birth, were calculated by dividing the aggregate NPR numbers by the total number of residents in Norway with years of birth 1999 through 2010 at the end of follow-up on December 31, 2010. Total population numbers, broken down by gender and year of birth, were provided by Statistics Norway. Male-to-female ratios, with 95% confidence intervals (CI), were calculated by using Stata 11 (StataCorp, College Station, TX). To estimate the proportion of diagnosed cases captured by the registry, we divided the diagnoses by calendar year and calculated the proportions captured in

consecutive years. On the basis of these proportions, we used the 2010 proportions to estimate the cumulative incidence of the disorders, assuming that the 2010 data would capture 60% of cases of ASD, ADHD, and epilepsy and 85% of CP cases in the study population. Estimates were made for ages 6 through 11 years combined and for 11-year-olds separately.

Validation of NPR Data

Birth years 1999 through 2010 were chosen for this study because they correspond to the recruitment period for the Norwegian Mother and Child Cohort,¹⁴ which is run by the Norwegian Institute of Public Health and includes 108 593 children and their parents. The cohort has ongoing substudies of ASD and ADHD, and studies of epilepsy and CP are under way. All these substudies are using, or will be using, NPR data for case ascertainment and will undertake independent validation of NPR diagnoses. So far, this has only been done by the ASD substudy, the Autism Birth Cohort study.¹⁵ This study validates NPR diagnoses of ASD by doing in-person clinical assessments. The assessment includes the standard diagnostic instruments for diagnosing ASD: the Autism Diagnostic Interview, Revised¹⁶ and the Autism Diagnostic

Observation Schedule.¹⁷ Diagnoses are based on DSM-IV criteria for ASD. Present validation results are reported here.

RESULTS

The study population included 731 318 children, 374 331 boys and 356 987 girls. The numbers of identified cases, distributed by gender and year of birth, are shown in Table 1. Figures 1 through 4 show the proportions of children with each diagnosis from 2008 through 2010, by year of birth, for boys and girls separately, and for all children combined. Table 2 shows male/female ratios for preschool children (aged 0–5 years) and school-age children (aged 6–11 years). Table 3 shows the overlap between the diagnoses. In Table 4, we have separated the diagnoses by calendar year and calculated the proportion of cases captured in consecutive years. Table 5 contains the proportions for 2010 and the estimates of true cumulative incidence of each disorder.

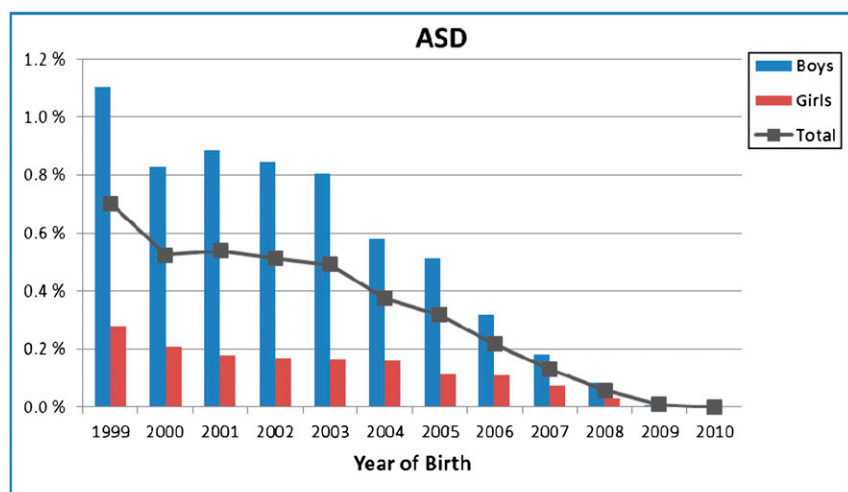
ASD

As shown in Fig 1, the proportions with ASD from 2008 through 2010 reached levels between 0.5% and 0.6% for children aged 7 to 10 and was 0.7% in 11-year-olds. The male/female ratio was

TABLE 1 Study Population and Diagnoses

Birth Year	Population		ASD		ADHD		Epilepsy		CP	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
1999	32 062	30 431	354	85	1336	458	333	253	101	90
2000	31 859	30 355	264	63	1152	365	287	219	116	57
2001	30 506	29 267	270	52	904	302	274	200	104	72
2002	29 777	28 759	252	49	649	202	232	195	94	67
2003	30 447	29 245	245	49	407	129	233	159	87	78
2004	30 703	29 327	178	47	196	74	180	170	105	74
2005	30 520	29 231	157	33	85	29	229	154	103	80
2006	31 333	29 848	100	33	31	12	189	153	93	65
2007	31 119	29 648	57	22	6	4	164	135	74	49
2008	32 055	30 211	27	9	2	2	141	132	68	44
2009	32 376	30 588	3	3	1	3	113	82	40	26
2010	31 574	30 077	0	0	2	1	31	40	2	7
Total	374 331	356 987	1907	445	4771	1581	2406	1892	987	709

Includes diagnoses registered in the Norwegian Patient Register (NPR) from 2008–10. ADHD diagnoses in children born in 2009 and 2010 were assumed to be registration errors and were not included in the other tables and figures.

**FIGURE 1**

Proportion with autism spectrum disorder from 2008 through 2010. Includes ASD diagnoses registered in the NPR from 2008 through 2010 for children born from 1999 through 2010.

TABLE 2 Male to Female Ratios

	Age 0–5 y			Age 6–11 y		
	Boys %	Girls %	M/F Ratio	Boys %	Girls %	M/F Ratio
ASD	0.18	0.06	3.3 (2.6–4.1)	0.84	0.19	4.3 (3.9–4.9)
ADHD	0.07	0.03	2.5 (1.8–3.6)	2.51	0.86	2.9 (2.7–3.1)
Epilepsy	0.46	0.39	1.2 (1.1–1.3)	0.83	0.67	1.2 (1.1–1.3)
CP	0.20	0.15	1.3 (1.1–1.6)	0.33	0.25	1.3 (1.2–1.5)

Includes diagnoses registered in the NPR from 2008 through 2010 for children born 1999 through 2010. Age 0 to 5 y correspond to birth years 2005 through 2010, age 6 to 11 y to birth years 1999 through 2004.

TABLE 3 Overlap Between Diagnoses

	Total	ASD		ADHD		Epilepsy		CP	
		n	%	n	%	n	%	n	%
ASD	2352			408	17.3	263	11.2	18	0.8
ADHD	6345	408	6.4			335	5.3	59	0.9
Epilepsy	4298	263	6.1	335	7.8			552	12.8
CP	1696	18	1.1	59	3.5	552	32.5		

Includes diagnoses registered in the NPR from 2008 through 2010 for children born 1999 through 2010.

TABLE 4 Recapturing of Cases in Consecutive Years

	Registered 2008	Recaptured 2009		Recaptured 2010		Registered 2009	Recaptured 2010		Registered 2010
	n	n	%	n	%	n	n	%	n
ASD	1000	719	72	621	62	1337	985	74	1794
ADHD	2684	2111	79	1580	59	3839	2848	74	4900
Epilepsy	2130	1514	71	1329	62	2623	1780	68	2923
CP	1151	1007	87	989	86	1303	1148	88	1452

Includes diagnoses registered in the NPR from 2008 through 2010 for children born 1999 through 2010.

higher in school-age children than in preschool children, 4.3 for ages 6 to 11 years (95% CI: 3.9–4.9) and 3.3 for ages 1 to 5 years (95% CI: 2.6–4.1). There was

a high level of overlap between ASD and ADHD, with 17.3% of ASD cases also having diagnoses of ADHD. Comorbid epilepsy diagnoses were found in 11.2%

of the ASD cases. The estimated cumulative incidence of ASD was 0.7% for ages 6 to 11 years combined and 0.8% for 11-year-olds.

Validation of ASD Diagnoses

In the ongoing validation of register ASD cases, we have now assessed 32 children invited on the basis of having ASD diagnoses registered in the NPR. Of these, 30 were found to meet the DSM-IV criteria for ASD, generating a positive predictive value of 94% (95% CI: 79%–99%). The participation rate in the validation study was 36% (32 out of 90 invited).

ADHD

ADHD diagnoses were rare in children <4 years of age. In our calculations, we have ignored the ADHD diagnoses recorded in children born in 2009 and 2010, assuming that such diagnoses in children <2 years of age are registration errors. The proportions from 2008 through 2010 were highest in the oldest children, reaching 2.9% at age 11 years (Fig 2). The male/female ratios were relatively similar in preschool and school-age children, 2.5 for ages 2 to 5 years (95% CI: 1.8–3.6) and 2.9 for ages 6 to 11 years (95% CI: 2.7–3.1). Comorbid diagnoses of ASD and epilepsy were common, with 6.4% of ADHD cases also having ASD diagnoses and 5.3% having epilepsy. The estimated cumulative incidence of ADHD was 2.2% for ages 6 to 11 years combined and 3.4% for 11-year-olds.

Epilepsy

As for ASD and ADHD, the proportions with epilepsy from 2008 through 2010 were highest in the oldest children, at 0.9% overall in children aged 11 years (Fig 3). There was a significantly increased risk in boys, with a male/female ratio of 1.2 for the study population as a whole (95% CI: 1.1–1.3). Epilepsy

TABLE 5 Estimated Cumulative Incidence

	Age 6–11 y (n = 362 738)			Age 11 y (n = 62 493)		
	No. Cases 2010	Proportion 2010	Estimated Cumulative Incidence	No. Cases 2010	Proportion 2010	Estimated Cumulative Incidence
ASD	1415	0.4%	0.7%	311	0.5%	0.8%
ADHD	4752	1.3%	2.2%	1257	2.0%	3.4%
Epilepsy	1904	0.5%	0.9%	401	0.6%	1.1%
CP	872	0.2%	0.3%	158	0.3%	0.3%

Age 6 to 11 years corresponds to birth years 1999 to 2004, age 11 years to birth year 1999. Estimates have been calculated by using NPR case numbers from 2010, assuming that within that calendar year, the NPR has captured 60% of all diagnosed cases of ASD, ADHD, and epilepsy and 85% of diagnosed cases of CP.

CP

As shown in Fig 4, the proportions of children with CP diagnoses from 2008 through 2010 were ~0.3% for age ≥5 years. They were higher in boys than girls, with an overall male/female ratio of 1.3 (95% CI: 1.2–1.5). Comorbid epilepsy was found in 32.5% of children with CP. The proportions of CP cases captured in consecutive calendar years were high, and the estimated cumulative incidence (0.3% both for ages 6–11 years combined and for 11-year-olds) was similar to the proportions found for years from 2008 through 2010.

DISCUSSION

ASD

The proportion with ASD from 2008 through 2010 was 0.7% for 11-year-olds, and the estimated cumulative incidence at that age was 0.8%. The increase by age suggests that ASD is often not diagnosed until late childhood or early adolescence in Norway. If future follow-up confirms the estimate of 0.8%, it would be higher than reported in most previous studies but in line with recent findings from the United Kingdom⁶ and the United States.⁷ It is particularly worth noting that our estimate, which is based on specialist-confirmed diagnoses, is close to the latest US estimate of 0.9%,⁷ which was based on review of records. It is also worth noting the high levels of overlap between ASD and ADHD in our study sample, which clearly demonstrates a discrepancy between current diagnostic classification systems and clinical practice in Norway.

Validation of ASD Diagnoses

The results of the validation study indicate a high overall validity of ASD diagnoses assigned by specialist health services and confirm that the technical aspects of the NPR data collection are functioning well. The 2 children out of 32 who did not receive diagnoses of

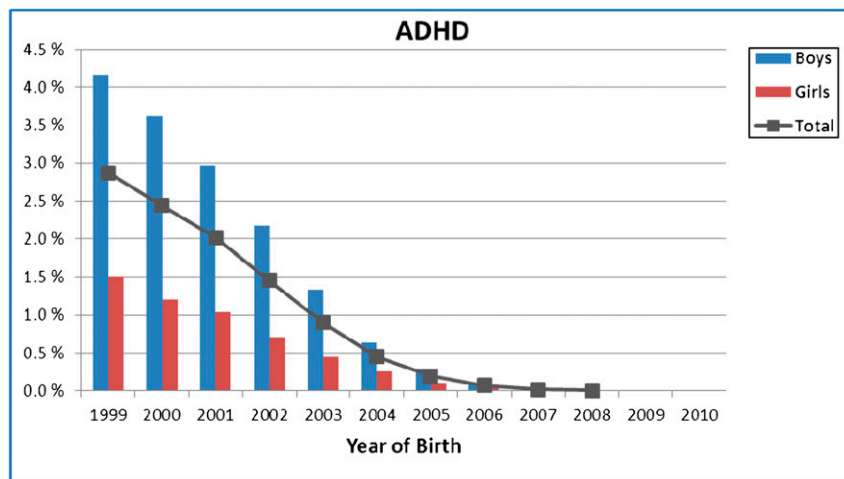


FIGURE 2 Proportion with ADHD from 2008 through 2010. Includes ADHD diagnoses registered in the NPR from 2008 through 2010 for children born from 1999 through 2010.

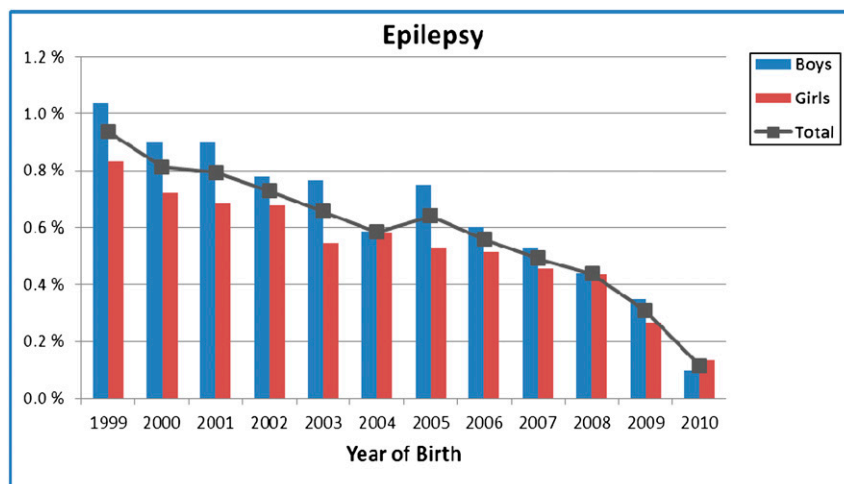


FIGURE 3 Proportion with epilepsy from 2008 through 2010. Includes epilepsy diagnoses registered in the NPR from 2008 through 2010 for children born from 1999 through 2010.

had considerable overlap with the other diagnoses; 6.1% of registered cases had ASD, 7.8% had ADHD, and 12.8% had CP.

The estimated cumulative incidence was 0.9% for ages 6 to 11 years combined and 1.1% for 11-year-olds.

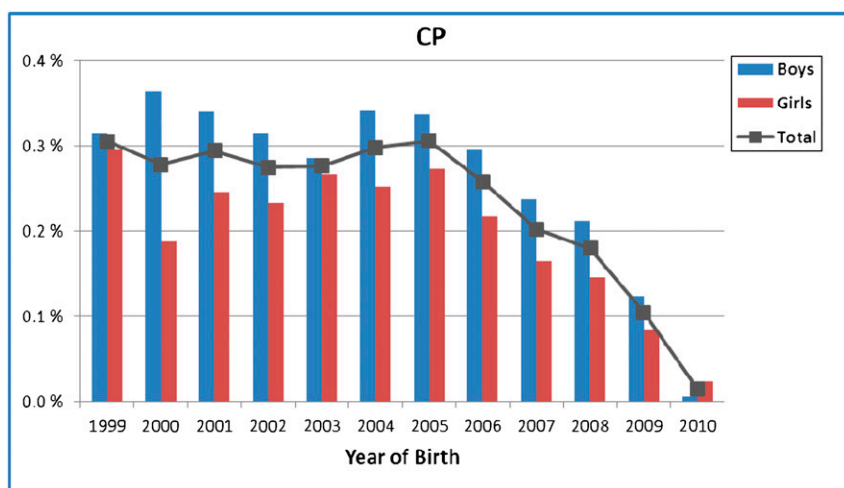


FIGURE 4

Proportion with CP from 2008 through 2010. Includes CP diagnoses registered in the NPR from 2008 through 2010 for children born from 1999 through 2010.

ASD at the independent validation were found to have mental retardation and specific language impairment, respectively. Those diagnoses are both closely aligned with ASD. However, the relatively low participation rate in the validation study (36%) warrants some caution in the interpretation of the findings.

ADHD

The proportion recorded with ADHD from 2008 through 2010 was 2.9% in 11-year-olds, and the estimated cumulative incidence was 3.4% at this age. The lack of data from private specialists caused a loss of some cases but no more than 10% of the total. Data from the Norwegian Prescription Database,¹⁸ which collects information on all drugs dispensed in Norway, show that 2.4% of people aged 10 to 19 years received ADHD medications in 2010. A study from the Norwegian research foundation SINTEF (Stiftelsen for industriell og teknisk forskning ved Norges tekniske høgskole) in 2004¹⁹ (not available in English) found that 70% to 100% of children diagnosed with ADHD in Norway were medicated. However, the fact that the recapture of ADHD cases in consecutive years is as low as 60% to

70% in the NPR suggests that the proportion receiving medications may be lower now than it was 1 decade ago. All in all, the numbers indicate that the proportion of Norwegian children receiving a diagnosis of ADHD at some point during childhood and adolescence is between 3% and 4%, but longer follow-up is required to determine whether the ADHD prevalence in Norway is truly below the authoritative international estimate of 5.3%.⁹ Part of the discrepancy could simply be because the use of ICD-10 criteria, as in the Norwegian health care system, leads to fewer ADHD diagnoses than the use of DSM-IV criteria, as previously mentioned.⁹

Epilepsy

The finding that 0.9% of 11-year-olds had epilepsy diagnoses recorded in the period from 2008 through 2010, and the estimated cumulative incidence of 1.1% at this age are in striking contrast to recent studies in developed countries showing a prevalence closer to 0.5% than 1%.¹⁰ Our findings also differ from other epilepsy studies in that we found a significant increase in boys compared with girls. Additional research is required to find out why Norwegian figures

differ from those of other comparable countries. More follow-up is also warranted to investigate why the recapture of epilepsy cases in consecutive years is as low as 60% to 70%. We had expected it to be higher in this group of patients with a presumably high proportion taking medications.

CP

Most cases of CP appeared to be diagnosed before 5 years of age, and the proportions recorded from 2008 through 2010 were relatively similar from age 5 years onward, at ~0.3% overall. Although somewhat higher than previously reported from Norway,²⁰ our figures are consistent with estimates of population prevalence from other Western countries.¹¹ The high proportion of cases with comorbid epilepsy is also in accordance with previous findings.^{20,21} The proportions of cases recaptured in consecutive years were high, indicating that most children with CP are in contact with specialist health services every year. Consequently, the proportions of CP observed from 2008 through 2010 are likely to be close to the underlying population prevalence of the disorder.

Overall Findings

This is the first study of neurologic and neurodevelopmental disorders in Norway based on nationwide register data. The findings demonstrate the significant burden of disease associated with such disorders in children, and they clearly show how this burden is disproportionately skewed toward boys. For 11-year-olds, 4.3% of the population was registered with ≥ 1 of the 4 diagnoses under study, 5.9% of boys and 2.7% of girls. This is lower than recent figures from the United States,³ but the difference is largely driven by high prevalence rates of ADHD in the United States. We can safely assume that >5% of Norwegian children will have been

diagnosed with ≥ 1 of the 4 disorders by the onset of puberty.

The main limitation of the study is the short duration of follow-up. The NPR has not been operative long enough to enable calculation of the exact cumulative incidence and population prevalence of the disorders under study. Another limitation is the lack of validation data for ADHD, epilepsy, and CP. Validation studies of these diagnoses would

strengthen the research value of NPR data and will be undertaken in the years to come.

The study provides an example of the advantages of the Nordic health registers. The nationwide and mandatory data reporting prevents selection bias and loss to follow-up and provides an excellent framework for surveillance and research. It also makes it easier to study different disorders

simultaneously, which is particularly beneficial for studies of neurologic and neurodevelopmental disorders because they often overlap and may share underlying genetic and environmental causes.

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