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A POPULATION-BASED STUDY OF MEASLES, MUMPS, AND RUBELLA VACCINATION AND AUTISM

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ABSTRACT

Background It has been suggested that vaccination against measles, mumps, and rubella (MMR) is a cause of autism.

Methods We conducted a retrospective cohort study of all children born in Denmark from January 1991 through December 1998. The cohort was selected on the basis of data from the Danish Civil Registration System, which assigns a unique identification number to every live-born infant and new resident in Denmark. MMR-vaccination status was obtained from the Danish National Board of Health. Information on the children's autism status was obtained from the Danish Psychiatric Central Register, which contains information on all diagnoses received by patients in psychiatric hospitals and outpatient clinics in Denmark. We obtained information on potential confounders from the Danish Medical Birth Registry, the National Hospital Registry, and Statistics Denmark.

Results Of the 537,303 children in the cohort (representing 2,129,864 person-years), 440,655 (82.0 percent) had received the MMR vaccine. We identified 316 children with a diagnosis of autistic disorder and 422 with a diagnosis of other autistic-spectrum disorders. After adjustment for potential confounders, the relative risk of autistic disorder in the group of vaccinated children, as compared with the unvaccinated group, was 0.92 (95 percent confidence interval, 0.68 to 1.24), and the relative risk of another autistic-spectrum disorder was 0.83 (95 percent confidence interval, 0.65 to 1.07). There was no association between the age at the time of vaccination, the time since vaccination, or the date of vaccination and the development of autistic disorder.

Conclusions This study provides strong evidence against the hypothesis that MMR vaccination causes autism. (N Engl J Med 2002;347:1477-82.)

IT has been suggested that the measles, mumps, and rubella (MMR) vaccine causes autism.[1-4] The widespread use of the MMR vaccine has reportedly coincided with an increase in the incidence of autism in California,[5] and there are case reports of children in whom signs of both developmental regression and gastrointestinal symptoms developed shortly after MMR vaccination.[1] Measles virus has been found in the terminal ileum in children with developmental disorders and gastrointestinal symptoms but not in developmentally normal children with gastrointestinal symptoms.[6] The measles virus used in the MMR vaccine is a live attenuated virus that normally causes no symptoms or only very mild ones. However, wild-type measles can infect the central nervous system and even cause postinfectious encephalomyelitis, probably as a result of an immune-mediated response to myelin proteins.[7-9]

Studies designed to evaluate the suggested link between MMR vaccination and autism do not support an association, but the evidence is weak and based on case-series, cross-sectional, and ecologic studies. No studies have had sufficient statistical power to detect an association, and none had a population-based cohort design.[10-16] The World Health Organization and other organizations have requested further investigation of the hypothetical association between the MMR vaccine and autism.[2,17-20] We evaluated the hypothesis in a cohort study that included all children born in Denmark in 1991 through 1998.

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METHODS

Study Design

We designed a retrospective follow-up study of all children born in Denmark during the period from January 1, 1991, to December 31, 1998. The cohort was established on the basis of data obtained from the Danish Civil Registration System and five other national registries.

All live-born children and new residents in Denmark are assigned a unique personal identification number (a civil-registry number), which is stored in the Danish Civil Registration System together with information on vital status, emigration, disappearance, address, and family members (mother, father, and siblings).[21] The registry is updated once a week, and all changes in the stored information are reported to the registry according to established legal procedures. The civil-registry number is used as the link to information at the individual level in all other national registries. This system provides completely accurate linkage of information between registries at the individual level.

We determined MMR-vaccination status on the basis of vaccination data reported to the National Board of Health by general practitioners, who administer all MMR vaccinations in Denmark. The general practitioners are reimbursed by the state on the basis of these reports. We retrieved information on vaccinations from 1991 through 1999. The MMR vaccine was introduced in Denmark in 1987, and the single-antigen measles vaccine has not been used. The MMR vaccine used in Denmark during the study period was identical to that used in the United States and contained the following vaccine strains: Moraten (measles), Jeryl Lynn (mumps), and Wistar RA 27/3 (rubella).

The national vaccination program recommends that children be vaccinated at 15 months of age and again at 12 years. No change was made in the program during the study period. We obtained information on MMR vaccination at 15 months of age, since only this exposure is relevant to the end point under study. Since the vaccination data are transferred to the National Board of Health once a week, we chose Wednesday as the day of vaccination. When the vaccination information was recorded with the child's own civil-registry number, the information was directly linked with other registries. Before 1996, in most cases the vaccination information and the age of the child were recorded with the civil-registry number of the accompanying adult; we used information from the Danish Civil Registration System to identify the link from the accompanying adult to the child. Thus, 98.5 percent of the children were identified with the use of the child's civil-registry number or the civil-registry number of the mother or father and the age of the child at vaccination. The remaining 1.5 percent of children were identified on the basis of additional information from the Danish Civil Registration System on other relatives and information on the address at the time of vaccination.

Information about diagnoses of autism was obtained from the Danish Psychiatric Central Register, which contains information on all diagnoses received by patients in psychiatric hospitals, psychiatric departments, and outpatient clinics in Denmark.[22] In our cohort, 93.1 percent of the children were treated only as outpatients, and 6.9 percent were at some point treated as inpatients in a psychiatric department. All diagnoses were based on the *International Classification of Diseases, 10th Revision* (ICD-10), which is similar to the 4th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) with regard to autism.[23-26] In Denmark, children are referred to specialists in child psychiatry by general practitioners, schools, and psychologists if autism is suspected. Only specialists in child psychiatry diagnose autism and assign a diagnostic code, and all diagnoses are recorded in the Danish Psychiatric Central Register. We identified all children given a diagnosis of autistic disorder (ICD-10 code F84.0 and DSM-IV code 299.00) or another autistic-spectrum disorder (ICD-10 codes F84.1 through F84.9 and DSM-IV codes 299.10 and 299.80). When a child was given diagnoses of both autistic disorder and one or more other autistic-spectrum disorders, we classified the diagnosis as autistic disorder. Autism is associated with the inherited genetic conditions tuberous sclerosis, Angelman's syndrome, and the fragile X syndrome and with congenital rubella. To maximize the homogeneity of the study population, data for children with these conditions were censored when the diagnosis was made. We obtained information on these conditions from the National Hospital Registry.

We performed an extensive record review for 40 children with autistic disorder (13 percent of all the children with autistic disorder) to validate the diagnosis of autism. A consultant in child psychiatry with expertise in autism examined the medical records. Thirty-seven of the children (92 percent) met the operational criteria for autistic disorder according to a systematic coding scheme developed by the Centers for Disease Control and Prevention for surveillance of autism and used in a prevalence study in Brick Township, New Jersey.[27] The three children who did not meet the criteria for autistic disorder were all classified as having other autistic-spectrum disorders. For two of the children, the diagnosis of autistic disorder was questionable because of profound intellectual impairment. For the third child, we did not have information about the onset of symptoms before the age of three years, which is a prerequisite for the diagnosis of autistic disorder.

We obtained information on birth weight and gestational age from the Danish Medical Birth Registry and the National Hospital Registry.[28,29] Information on potential confounders, including socioeconomic status (as indicated by the employment status of the head of the household) and mother's education was obtained from Statistics Denmark from the time when the child was 15 months of age.

Statistical Analysis

Follow-up for the diagnosis of autistic disorder or another autistic-spectrum disorder began for all children on the day they reached one year of age and continued until the diagnosis of autism or an associated condition (the fragile X syndrome, Angelman's syndrome, tuberous sclerosis, or congenital rubella), emigration, death, or the end of follow-up, on December 31, 1999, whichever occurred first. The incidence-rate ratios for autistic disorder and other autistic-spectrum disorders in the group of vaccinated children, as compared with the unvaccinated group, were examined in a log-linear Poisson regression model with the use of PROC GENMOD (SAS, version 6.12).[30] We treated vaccination as a time-dependent covariate. The children were assigned to the nonvaccinated group until they received the MMR vaccine. From that date, they were followed in the vaccinated group. In additional analyses, the MMR-vaccinated children were grouped according to their age at the time of vaccination, the interval since vaccination, and the calendar period when vaccination was performed.

In reporting the results, we refer to the incidence-rate ratios as relative risks. For all risk estimates, we considered possible confounding by age (1, 2, 3, 4, 5, 6, 7, or 8 to 9 years), sex, calendar period (1992 to 1993, 1994, 1995, 1996, 1997, 1998, or 1999; for other autistic-spectrum disorders, the years 1992, 1993, and 1994 were grouped together), socioeconomic status (six groups), mother's education (five groups), gestational age ($\leq$36, 37 to 41, or $\geq$42 weeks), and birth weight ($\leq$2499, 2500 to 2999, 3000 to 3499, 3500 to 3999, or $\geq$4000 g).

RESULTS

A total of 537,303 children were included in the cohort and followed for a total of 2,129,864 person-years. Follow-up of 5811 children was stopped before December 31, 1999, because of a diagnosis of autistic disorder (in 316 children), other autistic-spectrum disorders (in 422), tuberous sclerosis (in 35), congenital

rubella (in 2), or the fragile X or Angelman's syndrome (in 8), and because of death or emigration in the cases of 5028 children, whose data were censored. For children who received MMR vaccine, there were 1,647,504 person-years of follow-up, and for children who did not receive the vaccine, there were 482,360 person-years of follow-up.

Table 1 shows the distribution of the MMR cohort according to vaccination status, sex, birth weight, gestational age, socioeconomic status, mother's education, and age when autism was diagnosed. The mean age at diagnosis was four years and three months for autistic disorder and five years and three months for other autistic-spectrum disorders. The mean age at the time of the MMR vaccination was 17 months, and 98.5 percent of the vaccinated children were vaccinated before 3 years of age. The proportion of children who were vaccinated was the same among boys and girls (82.0 percent).

Table 2 shows the association between variables related to MMR vaccination and the risk of autism. We calculated the relative risk with adjustment for age, calendar period, sex, birth weight, gestational age, mother's education, and socioeconomic status. Overall, there was no increase in the risk of autistic disorder or other autistic-spectrum disorders among vaccinated

TABLE 1. CHARACTERISTICS OF THE 537,303 CHILDREN IN THE DANISH COHORT.

CHARACTERISTIC	VACCINATED CHILDREN (N=440,655)	UNVACCINATED CHILDREN (N=96,648)	P VALUE*
	number (percent)		
Sex			0.55
Male	226,042 (51.3)	49,680 (51.4)	
Female	214,613 (48.7)	46,968 (48.6)	
Birth weight			<0.001
≤2499 g	21,633 (4.9)	5,164 (5.3)	
2500–2999 g	53,874 (12.2)	12,062 (12.5)	
3000–3499 g	135,630 (30.8)	29,262 (30.3)	
3500–3999 g	135,255 (30.7)	29,143 (30.2)	
≥4000 g	66,358 (15.1)	14,563 (15.1)	
Data missing	27,905 (6.3)	6,454 (6.7)	
Gestational age			<0.001
≤36 wk	19,029 (4.3)	3,129 (3.2)	
37–41 wk	272,345 (61.8)	40,609 (42.0)	
≥42 wk	27,349 (6.2)	3,986 (4.1)	
Data missing†	121,932 (27.7)	48,924 (50.6)	
Socioeconomic status‡			<0.001
Manager (very high)	41,367 (9.4)	9,940 (10.3)	
Wage earner (high)	85,772 (19.5)	16,187 (16.7)	
Wage earner (medium)	70,906 (16.1)	13,753 (14.2)	
Wage earner (low)	116,503 (26.4)	26,699 (27.6)	
Wage earner (minimal)	57,408 (13.0)	10,996 (11.4)	
Unemployed	67,841 (15.4)	18,519 (19.2)	
Data missing	858 (0.2)	554 (0.6)	
Mother's education			<0.001
Postgraduate education	26,118 (5.9)	5,856 (6.1)	
College	67,776 (15.4)	14,599 (15.1)	
Vocational training	178,553 (40.5)	34,006 (35.2)	
Secondary school	42,667 (9.7)	10,164 (10.5)	
Primary school	114,768 (26.0)	28,680 (29.7)	
Data missing	10,773 (2.4)	3,343 (3.5)	
Age at diagnosis of autistic disorder			0.87
≤2 yr	48 (0.01)	9 (0.01)	
3–5 yr	187 (0.04)	31 (0.03)	
≥6 yr	34 (0.01)	7 (0.01)	
Age at diagnosis of another autistic-spectrum disorder			0.19
≤2 yr	32 (0.01)	3 (0.003)	
3–5 yr	202 (0.05)	37 (0.04)	
≥6 yr	118 (0.03)	30 (0.03)	

*P values are based on the chi-square test of statistical independence.

†Data were available from the Danish Medical Birth Registry only until December 31, 1996.

‡The employment status of the head of the household was used to indicate socioeconomic status.

TABLE 2. ADJUSTED RELATIVE RISK OF AUTISTIC DISORDER AND OF OTHER AUTISTIC-SPECTRUM DISORDERS IN VACCINATED AND UNVACCINATED CHILDREN.*

VACCINATION	PERSON-YEARS†	AUTISTIC DISORDER		OTHER AUTISTIC-SPECTRUM DISORDERS	
		NO. OF CASES	ADJUSTED RELATIVE RISK (95% CI)	NO. OF CASES	ADJUSTED RELATIVE RISK (95% CI)
Total	2,129,864	316		422	
Vaccination					
No	482,360	53	1.00	77	1.00
Yes	1,647,504	263	0.92 (0.68–1.24)	345	0.83 (0.65–1.07)
Age at vaccination					
Not vaccinated	482,360	53	1.00	77	1.00
≤14 mo	200,003	38	1.18 (0.78–1.80)	43	0.88 (0.60–1.28)
15–19 mo	1,320,753	195	0.86 (0.63–1.17)	270	0.83 (0.64–1.08)
20–24 mo	69,242	17	1.19 (0.69–2.07)	12	0.62 (0.33–1.13)
25–35 mo	40,935	11	1.20 (0.63–2.31)	15	1.09 (0.63–1.91)
≥36 mo	16,572	2	0.56 (0.14–2.30)	5	0.64 (0.26–1.59)
Interval since vaccination					
Not vaccinated	482,360	53	1.00	77	1.00
<6 mo	212,805	3	0.39 (0.11–1.32)	8	1.18 (0.51–2.75)
6–11 mo	197,931	21	1.38 (0.76–2.51)	4	0.31 (0.10–0.91)
12–17 mo	183,460	22	1.07 (0.59–1.95)	16	0.92 (0.47–1.80)
18–23 mo	168,045	31	0.86 (0.52–1.41)	16	0.47 (0.26–0.86)
24–29 mo	154,290	42	0.99 (0.61–1.58)	32	0.77 (0.46–1.27)
30–35 mo	139,258	33	0.86 (0.54–1.38)	27	0.69 (0.43–1.11)
36–59 mo	406,320	90	0.99 (0.66–1.50)	158	1.05 (0.77–1.45)
≥60 mo	185,396	21	0.67 (0.34–1.33)	84	0.75 (0.51–1.09)
Date of vaccination					
Not vaccinated	482,360	53	1.00	77	1.00
1991–1992	248,646	31	1.00 (0.59–1.70)	61	0.75 (0.51–1.09)
1993–1994	659,152	81	0.73 (0.50–1.06)	146	0.74 (0.56–0.99)
1995–1996	475,990	96	0.91 (0.63–1.30)	116	1.13 (0.81–1.56)
1997–1999	263,716	55	1.35 (0.84–2.17)	22	0.71 (0.40–1.24)

*The relative risk was adjusted for age, calendar period, sex, birth weight, gestational age, mother's education, and socioeconomic status of the family. The reference group was the group of children who were not vaccinated. The distribution of cases of autistic disorder or other autistic-spectrum disorders according to vaccination status differs from that in Table 1 because, in this analysis, children who were vaccinated after the disorder had been diagnosed were classified according to their vaccination status at the time of the diagnosis (i.e., as unvaccinated). CI denotes confidence interval.

†Because of rounding, the numbers of person-years do not necessarily sum to the total shown.

children as compared with unvaccinated children (adjusted relative risk of autistic disorder, 0.92; 95 percent confidence interval, 0.68 to 1.24; adjusted relative risk of other autistic-spectrum disorders, 0.83; 95 percent confidence interval, 0.65 to 1.07). Furthermore, we found no association between the development of autistic disorder and the age at vaccination ($P=0.23$), the interval since vaccination ($P=0.42$), or the calendar period at the time of vaccination ($P=0.06$).

Adjustment for potential confounders with the exception of age resulted in similar estimates of risk. Changing the start of follow-up for autistic disorder and other autistic-spectrum disorders to the date of birth or 16 months of age had little effect on the estimates (data not shown). Furthermore, including children with the fragile X syndrome, tuberous sclerosis, congenital rubella, or Angelman's syndrome in the analysis did not change the estimates (data not shown).

DISCUSSION

This study provides three strong arguments against a causal relation between MMR vaccination and autism. First, the risk of autism was similar in vaccinated and unvaccinated children, in both age-adjusted and fully adjusted analyses. Second, there was no temporal clustering of cases of autism at any time after immunization. Third, neither autistic disorder nor other autistic-spectrum disorders were associated with MMR vaccination. Furthermore, the results were derived from a nationwide cohort study with nearly complete follow-up data.

All previous studies of an association between autism and MMR vaccination have been case series,[1,14,15] ecologic studies,[11,12] or cross-sectional studies,[10,13] and the majority have not used optimal data for risk assessment. In a well-conducted, cross-sectional prevalence study, Taylor and colleagues[10] found that there was no sharp increase in the prevalence of autism after the in-

troduction of the MMR vaccine. However, it could be argued that a more gradual increase would be expected, since autism is characterized by an insidious onset and a delay in diagnosis. A case-series study by Peltola et al.[15] also provides evidence against a causal connection.

One of the main reasons for public concern has been that the widespread use of the MMR vaccine in some regions appeared to coincide with an increase in the incidence of autism. However, this is not a uniform finding. In Denmark, the prevalence of autism (according to the criteria of the *International Classification of Diseases, 8th Revision*) was less than 2.0 cases per 10,000 children between the ages of five and nine years in the 1980s and the beginning of the 1990s. Since then, the rates have increased in all age groups except for children younger than two years of age, and in 2000, the prevalence of autism (according to the ICD-10 criteria) was higher than 10.0 cases per 10,000 children five to nine years of age (unpublished data). Thus, the increase in autism both in California[5] and in Denmark occurred well after the introduction of the MMR vaccine.

Our study was based on individual reports of vaccination and diagnoses of autism in a well-defined geographic area. The exposure data were collected prospectively, independently of parental recall and before the diagnosis of autism. Furthermore, the diagnosis was recorded independently of the recording of MMR vaccination. Thus, there was little possibility of differential misclassification of exposure or outcome measures. Furthermore, our analysis was based on complete follow-up data.

We assume that the data on MMR vaccination are almost complete, since general practitioners in Denmark are reimbursed only after reporting immunization data to the National Board of Health. We had an unvaccinated reference group with almost 500,000 person-years of follow-up, even though the study was numerically imbalanced in favor of the vaccinated group. The power of the study is reflected in the narrow 95 percent confidence intervals.

We had no information on the presence or absence of a family history of autism, which could explain our negative findings only if families with a history of autism avoided MMR vaccination. If so, we would expect to have found high relative risks at the beginning of the study period, before the hypothetical link between vaccination and autism was publicized. This was not the case. We had no information on whether the children with autism had regression, and thus we could not perform a subgroup analysis. However, the fact that the overall relative risk of autism or an autistic-spectrum disorder was less than 1.0 does not support the possibility of a subgroup of vulnerable children.

The Danish vaccination program recommends that children receive the MMR vaccine at 15 months of age and provides the vaccination free of charge. Among the children in our cohort who were born in 1995, the rate of MMR vaccination was lower than the rate of vaccination with the first *Haemophilus influenzae* type B vaccine (86.9 percent vs. 97.0 percent). However, the rate of MMR vaccination in our study was similar to that in the United States (87.6 percent in 1995) and Belgium (83.0 percent in 1997).[31,32] Nevertheless, the main concern is the comparability of vaccinated and nonvaccinated children in relation to the end point under study. In all analyses, when risk estimates were calculated, we controlled for possible confounders (age, sex, calendar period, socioeconomic status, mother's education, gestational age, and birth weight). Except for age, none of these possible confounders changed the estimates. The confounding by age was a function of the time available for follow-up, since much of the follow-up for the unvaccinated group involved young children, in whom autism is often undiagnosed.

We assessed the validity of the diagnosis of autistic disorder in a subgroup of children and found it to be high. This was to be expected, since only specialists in child and adolescent psychiatry are authorized to code the diagnosis of autism in the Danish Psychiatric Central Register. All schools have access to health care personnel as well as psychologists. Because of the comprehensive health care surveillance for children in Denmark, all severe cases of autism are likely to be diagnosed and reported to the registry at some point. Reporting of the other autistic-spectrum disorders is less complete than that for autistic disorder, and some diagnoses are almost certainly missed. However, it is unlikely that this misclassification would be associated with vaccination status. It is very difficult to determine the onset of autism, and many cases are probably due to prenatal factors. Our records did not contain information on when the first autistic symptoms were noted, and we could not adjust for a differential delay in the diagnosis. Again, it is highly unlikely that a delayed diagnosis was associated with MMR vaccination in this study.

There are few published data on the incidence of autism, but the prevalence rates reported in the literature vary widely, from 1.2 cases per 10,000 (according to the criteria of the third edition of the *Diagnostic and Statistical Manual of Mental Disorders*) to 30.8 per 10,000 (according to the ICD-10 criteria).[33,34] The prevalence rates among eight-year-old children in our cohort were 7.7 per 10,000 for autistic disorder and 22.2 per 10,000 for other autistic-spectrum disorders. These rates are similar to the prevalence rates of 5.4 per 10,000 for autistic disorder and 16.3 per 10,000 for other autistic-spectrum disorders in a cohort of 325,347 French children (ICD-10 criteria), reported

by Fombonne et al.,[35] and the rate of 11 per 10,000 for autistic disorder in a cohort of U.S. children (DSM-IV criteria), reported by Croen and colleagues.[36] The DSM-IV classification system used in the United States and the ICD-10 classification system used in many European countries are almost identical with regard to the classification of autistic disorder.[23-26] In our validity substudy, we found that 93 percent of cases diagnosed according to the ICD-10 criteria met the DSM-IV operational criteria for the diagnosis of autistic disorder.

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REFERENCES

1. Wakefield AJ, Murch SH, Anthony A, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. Lancet 1998;351:637-41.
2. Stratton K, Gable A, Shetty P, McCormick M, eds. Immunization safety review: measles-mumps-rubella vaccine and autism. Washington, D.C.: National Academy Press, 2001.
3. Wakefield AJ, Montgomery SM. Measles, mumps, rubella vaccine: through a glass, darkly. Adverse Drug React Toxicol Rev 2000;19:265-83.
4. Autism: present challenges, future needs — why the increased rates? Hearing before the Committee of Government Reform, U.S. House of Representatives, 106th Congress, second session, April 6, 2000. Washington, D.C.: Government Printing Office, 2000.
5. Department of Developmental Services. Changes in the population of persons with autism and pervasive developmental disorders in California's Developmental Services System: 1987 through 1998: a report to the Legislature. Sacramento: California Health and Human Services Agency, March 1999.
6. Uhlmann V, Martin CM, Sheils O, et al. Potential viral pathogenic mechanism for new variant inflammatory bowel disease. Mol Pathol 2002; 55:84-90.
7. Griffin DE, Ward BJ, Jauregui E, Johnson RT, Vaisberg A. Immune activation in measles. N Engl J Med 1989;320:1667-72.
8. Singh VK, Lin SX, Newell E, Nelson C. Abnormal measles-mumps-rubella antibodies and CNS autoimmunity in children with autism. J Biomed Sci 2002;9:359-64.
9. Johnson RT, Griffin DE, Hirsch RL, et al. Measles encephalomyelitis — clinical and immunologic studies. N Engl J Med 1984;310:137-41.
10. Taylor B, Miller E, Farrington CP, et al. Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association. Lancet 1999;353:2026-9.
11. Kaye JA, del Mar Melero-Montes M, Jick H. Mumps, measles, and rubella vaccine and the incidence of autism recorded by general practitioners: a time trend analysis. BMJ 2001;322:460-3.
12. Dales L, Hammer SJ, Smith NJ. Time trends in autism and in MMR immunization coverage in California. JAMA 2001;285:1183-5.
13. Fombonne E, Chakrabarti S. No evidence for a new variant of measles-mumps-rubella–induced autism. Pediatrics 2001;108:991. abstract.
14. Patja A, Davidkin I, Kurki T, Kallio MJ, Valle M, Peltola H. Serious adverse events after measles-mumps-rubella vaccination during a fourteen-year prospective follow-up. Pediatr Infect Dis J 2000;19:1127-34.
15. Peltola H, Patja A, Leinikki P, Valle M, Davidkin I, Paunio M. No evidence for measles, mumps, and rubella vaccine-associated inflammatory bowel disease or autism in a 14-year prospective study. Lancet 1998;351: 1327-8.
16. Taylor B, Miller E, Lingram L, Andrews N, Simmons A, Stowe J. Measles, mumps, and rubella vaccination and bowel problems or developmental regression in children with autism: population study. BMJ 2002;324:393-6.
17. Causality assessment of adverse events following immunization. Wkly Epidemiol Rec 2001;76:85-9.
18. Smeeth L, Hall AJ, Rodrigues LC, Huang X, Smith PG, Fombonne E. Measles, mumps, and rubella (MMR) vaccine and autism: ecological studies cannot answer main question. BMJ 2001;323:163.
19. Edwardes M, Baltzan M. MMR immunization and autism. JAMA 2001;285:2852-3.
20. Measles, MMR, and autism: the confusion continues. Lancet 2000; 355:1379.
21. Malig C. The civil registration system in Denmark. IIVRS technical paper no. 66. Bethesda, Md.: International Institute for Vital Registration and Statistics, 1996.
22. Munk-Jorgensen P, Mortensen PB. The Danish Psychiatric Central Register. Dan Med Bull 1997;44:82-4.
23. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization, 1993.
24. Filipek PA, Accardo PJ, Baranek GT, et al. The screening and diagnosis of autistic spectrum disorders. J Autism Dev Disord 1999;29:439-84. [Erratum, J Autism Dev Disord 2000;30:81.]
25. Volkmar FR, Klin A, Siegel B, et al. Field trial for autistic disorder in DSM-IV. Am J Psychiatry 1994;151:1361-7.
26. Hill A, Bolte S, Petrova G, Beltcheva D, Tacheva S, Poustka F. Stability and interpersonal agreement of the interview-based diagnosis of autism. Psychopathology 2001;34:187-91.
27. Bertrand J, Mars A, Boyle C, Bove F, Yeargin-Allsopp M, Decoufle P. Prevalence of autism in a United States population: the Brick Township, New Jersey, investigation. Pediatrics 2001;108:1155-61.
28. Knudsen LB, Olsen J. The Danish Medical Birth Registry. Dan Med Bull 1998;45:320-3.
29. Andersen TF, Madsen M, Jorgensen J, Mellemkjoer L, Olsen JH. The Danish National Hospital Register: a valuable source of data for modern health sciences. Dan Med Bull 1999;46(3):263-8.
30. Clayton D, Hills M. Statistical models in epidemiology. Oxford, England: Oxford University Press, 1993.
31. Vellinga A, Depoorter AM, Van Damme P. Vaccination coverage estimates by EPI cluster sampling survey of children (18-24 months) in Flanders, Belgium. Acta Paediatr 2002;91:599-603.
32. Epidemiology and prevention of vaccine-preventable diseases. 7th ed. Atlanta: Centers for Disease Control and Prevention, 2002.
33. Burd L, Fisher W, Kerbeshian J. A prevalence study of pervasive developmental disorders in North Dakota. J Am Acad Child Adolesc Psychiatry 1987;26:700-3.
34. Baird G, Charman T, Baron-Cohen S, et al. A screening instrument for autism at 18 months of age: a 6-year follow-up study. J Am Acad Child Adolesc Psychiatry 2000;39:694-702.
35. Fombonne E, Du Mazaubrun C, Cans C, Grandjean H. Autism and associated medical disorders in a French epidemiological survey. J Am Acad Child Adolesc Psychiatry 1997;36:1561-9.
36. Croen LA, Grether JK, Hoogstrate J, Selvin S. The changing prevalence of autism in California. J Autism Dev Disord 2002;32:207-15.