There is little evidence that combined vaccination against measles, mumps, and rubella is associated with autism

Madsen K, Hviid A, Vestergaard M *et al.* A population-based study of measles, mumps, and rubella vaccination and autism. *N Engl J Med* 2002 Nov; **347**:1477–82.

QUESTION: Is the combined measles, mumps and rubella (MMR) vaccination associated with autism?

Design and setting

Retrospective population study of all children born in Denmark between January 1991 and December 1998.

Participants

537,303 children were born during the study period; 49% girls. 82% received the MMR vaccine.

Assessment of risk factors

The Danish Civil Registration System assigns a unique identification number to every live birth and new resident in Denmark. MMR vaccination status was obtained from the Danish National Board of Health. Information about potential confounders was obtained from the Danish Medical Birth Registry, the National Hospital Registry and Statistics Denmark.

Main outcome measures

Autism status was obtained from the Danish Psychiatric Central Register, containing all diagnoses from psychiatric hospitals and outpatient clinics in Denmark.

Main results

Children receiving the MMR vaccination were no more likely to develop autism than non-vaccinated children (table). There was no clustering of autism diagnoses according to time after vaccination, age of the child at vaccination or date of vaccination.

Conclusions

The authors found no evidence that the combined measles, mumps and rubella vaccination is associated with the development of autism.

COMMENTARY

This is the most direct evaluation of whether MMR causes autism published to date. Though all epidemiological studies conducted in recent years have found no association between the MMR vaccine and onset of autism, design limitations have left some doubt about this issue.^{1–5} This historical cohort included all Danish children born between 1991 and 1998 when prevalence rates for autism and autistic spectrum disorders were increasing. Because of the thoroughness of the Danish system of registration, ascertainment of vaccination status and health problems was remarkably accurate and complete. Since the cohort was composed of the entire population, both vaccinated and unvaccinated children had the same risk of autism prior to exposure to the vaccine. Nearly all children were accounted for at the end of the study period. Specialists using the same diagnostic classification system made the diagnosis of autism in a uniform manner.

This study suggests that there was no difference in the risk of autism in the vaccinated versus unvaccinated groups and that there was no clustering of cases at any time after immunization. The registry data did not include information about children with developmental regression. The issue of whether there is a subgroup of children vulnerable to the vaccination cannot be entirely laid to rest from this study. One would think that if such a group existed, relative risk would be greater than 1.0 for the vaccinated children. The opposite was true, though not to a significant degree.

Based on the size of this cohort and the lack of evidence of differential risk for autism, this study suggests that parents should continue vaccinating their children to avoid future outbreaks of measles and the risk of serious neurological sequelae.

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Relationship between MMR vaccination and risk of autism

	MMR vaccinated children (n=440655)	No MMR vaccination (n=96648)	Adjusted relative risk from MMR (95% CI)
Number who developed autism	263	53	0.92 (0.68 to 1.24)
Number who developed autism-spectrum disorder	345	77	0.83 (0.65 to 1.07)

Note: Relative risk is adjusted for age and other confounders.