Causation

Measles, mumps, and rubella vaccine was not associated with autism in children


QUESTION: Is the measles, mumps, and rubella (MMR) vaccine associated with autism in children?

Design
Population based cohort study with data obtained by database linkage.

Setting
Denmark.

Participants
537 303 children (51% boys).

Assessment of risk factors
MMR vaccination status was obtained from the Danish National Board of Health (compiled by general practitioner reports). Data on birth weight, sex, gestational age, family socioeconomic status, and mother’s education were also collected.

Main outcome measures
Children’s autism status was obtained from the Danish Psychiatric Central Register; diagnoses of autistic disorder or another autistic spectrum disorder were assigned by specialists in child psychiatry. If a child was diagnosed with both autistic disorder and ≥1 other autistic spectrum disorder, the diagnosis was classified as autistic disorder.

Main results
The 537 303 children had follow up for a total of 2 129 864 person years. 440 655 children (82%) received the MMR vaccine; mean age at time of vaccination (p<0.06). Analysis adjusted for age, calendar period, sex, birth weight, gestational age, mother’s education, and socioeconomic status showed that children who received the MMR vaccine did not have an increased risk of autistic disorder or other autistic spectrum disorders compared with children who did not receive the vaccine (table).

Risk of autistic disorder was not associated with age at time of vaccination (p=0.25), time interval since vaccination (p=0.42), or calendar period at time of vaccination (p=0.06).

Conclusion
The measles, mumps, and rubella vaccine was not associated with autism in children.

COMMENTARY

Vaccination represents one of the great victories of preventive health care and is a major factor that separates the child health statistics of the developed world from those of the developing world. Because vaccines are given to large numbers of healthy children, ensuring that risk does not exceed benefit is important and becomes more of an issue as the risk of disease becomes very small. Parents in the developed world are not familiar with the possible consequences of many of the diseases against which children are routinely vaccinated. This may explain why even questionable evidence about vaccine safety generates such publicity, discussion, and disquiet.

The study by Madsen et al is further evidence that refutes a link between MMR vaccination and development of autism. The study of a large Danish sample is important because it has the statistical power to provide stronger evidence than previous studies. The study was carefully documented and followed up a large cohort of children, of whom 316 developed autism. The unbiased sampling strategy, completeness of follow up, and sample size are major strengths, contrasting sharply with the report that generated many of the questions about the relation between MMR and autism (a case series of 12 children with autism).

Vaccination risks do exist, and parents must be informed of them. Relative risk is a complex concept; parents may not be reassured unless a healthcare provider can assert that no risk exists, which is not possible. However, parents can easily understand the concept of unrelated co-occurrence, which likely explains suspicions about MMR; ie, autism symptoms often occur at the same age as MMR vaccination. Healthcare providers have a responsibility to counter unsubstantiated accusations about vaccine safety in order to assure the safety of children in our community and the world.

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Relative risk of autistic disorder or other autistic spectrum disorder in children who received the measles, mumps, and rubella vaccine v children who were unvaccinated

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Adjusted relative risk (95% CI)*</th>
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<tbody>
<tr>
<td>Autistic disorder</td>
<td>0.92 (0.68 to 1.24)</td>
</tr>
<tr>
<td>Other autistic spectrum disorder</td>
<td>0.83 (0.65 to 1.07)</td>
</tr>
</tbody>
</table>

*Adjusted for age, calendar period, sex, birth weight, gestational age, mother’s education, and socioeconomic status.
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