

Papers

MMR vaccine and Crohn's disease: ecological study of hospital admissions in England, 1991 to 2002

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It has been hypothesised that the measles, mumps, and rubella vaccine (MMR vaccine) increases the risk of autism and Crohn's disease. Although a possible link with autism has been extensively studied and refuted,¹ a link with Crohn's disease has not. I tested this hypothesis by analysing trends in age specific admission rates for Crohn's disease in children and adolescents to determine if the introduction of MMR vaccine in 1988 increased rates in those populations that were offered the vaccine as infants.

Methods and results

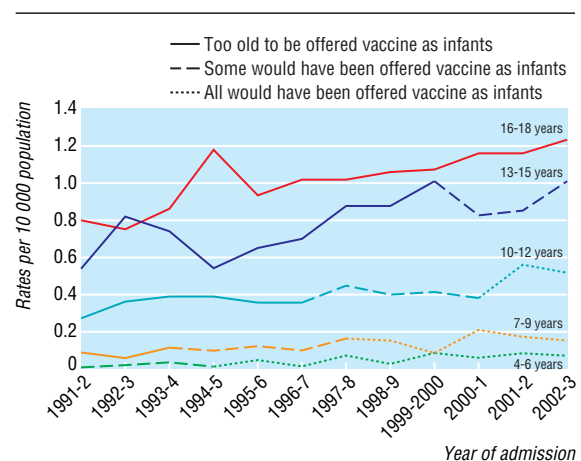
Counts of admissions, taken as the first consultant episode in a hospital stay, in patients aged ≤ 18 years with a main diagnosis of Crohn's disease in England (population 50 million) were available for the 12 years from April 1991 to March 2003.^{w1} I restricted the analysis to emergency admissions as these were probably less susceptible to changes in thresholds for admission and clinical practice than elective admissions. In the first two years of the MMR vaccination programme, the percentages of children completing a primary course of MMR vaccine in their second year of life were 7% and 68%; thereafter the percentage was at least 84%.^{w2}

Initially, temporal trends in age specific rates were plotted, differentiating between the rates for those born before and after the introduction of the vaccine. (Rates for patients aged 16 to 18 years—too old to have been offered the vaccine as infants—provided information on underlying trends unaffected by MMR vaccination in infancy.) Data for those born in 1987-8, of whom only 68% were vaccinated as infants, were excluded from the analysis. The MMR vaccination programme was then modelled as a variable with two levels (vaccination rate of $\geq 84\%$ and of $\leq 7\%$) using Poisson regression, with adjustment for year of admission and age in single years (as categorical variables).

There were 4463 admissions for Crohn's disease, 923 of which occurred in populations with a vaccination rate of $\geq 84\%$ (those born in 1988-9 or later). Although the age specific rates increased over the study period, no obvious changes occurred that coincided with the introduction of MMR vaccine (figure). The estimated rate ratio for the MMR vaccination programme (rates in populations with a vaccination rate of $\geq 84\%$ compared with those with a rate of $\leq 7\%$) was 0.95 (95% confidence interval 0.84 to 1.08).

Comment

The introduction of MMR vaccine, replacing the single measles vaccine, was not associated with an increase in Crohn's disease. Given the precision of the rate ratio, all but a small risk would



Age specific rates per 10 000 population per year for emergency hospital admissions for Crohn's disease in England, 1991 to 2002. Rates in children aged <4 years were relatively low and so were excluded from the figure. Three-year groups, rather than the more conventional five-year groups, were used in order to discriminate between rates in children born before and after the introduction of MMR

have been detected. This was an ecological study, and findings from such studies generally need to be treated cautiously because of potential for confounding. Could the negative finding from this analysis be due to confounding? If so, some factor(s) would have to be negatively associated with Crohn's disease, be introduced over the same three year period, and be targeted at the same population of infants as MMR vaccine to mask a true association. This seems highly unlikely.

A smaller ecological study² and two case-control studies^{3 w3} also found no increased risk of Crohn's disease associated with MMR vaccine.

Initially, measles vaccine was reported to be associated with higher rates of Crohn's disease,⁴ but this was not confirmed by subsequent studies.^{3 5} Natural infections with measles and mumps within one year were also associated with an increased risk of Crohn's disease.^{w4} Although that finding has yet to be confirmed, it raised the possibility that infections with multiple viruses in MMR vaccine might increase the risk of Crohn's disease. My study provides strong evidence against that hypothesis and adds to the evidence that MMR vaccine is no less safe in this respect than the single measles vaccine.

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Additional references (w1-w4) are on bmj.com

What is already known on this topic
It has been hypothesised that the measles, mumps, and rubella vaccine (MMR vaccine) increases the risk of Crohn's disease, though the evidence base for this hypothesis is sparse
What this study adds
An ecological analysis of national data on hospital admissions found no increase in Crohn's disease associated with the introduction of the MMR vaccination programme, providing strong evidence against the hypothesis that MMR vaccine increases the risk of Crohn's disease

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2 Pebody RG, Paunio M, Ruutu P. Measles, measles vaccination, and Crohn's disease. Crohn's disease has not increased in Finland. *BMJ* 1998;316:1745-6.

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