Admissions to hospital for any type of infection and childhood vaccinations

An observational study in Denmark finds that admissions to hospital for any infection after receiving the combined vaccine for measles, mumps and rubella are lower than after receiving the combined vaccine for diphtheria, tetanus, pertussis, polio, and *Haemophilus influenzae* type b.

**Overview:** The combined vaccine for measles, mumps and rubella (MMR) is a live vaccine made of attenuated viable organisms. Other types of vaccine, such as the vaccines against pertussis and polio, are made from inactivated (killed) organisms or from products secreted by the organism, recombinant components or constituents of its cell walls.

Since its introduction into the UK in 1998, MMR has achieved an uptake of 90%, reducing the incidence of these once common childhood diseases ([Public Health England 2013](https://www.gov.uk/government/publications/measles-in-uk)). For example, recorded deaths from measles dropped from a maximum of 1145 in 1941 to about 1 per year from 2000 until 2013 ([Public Health England 2014](https://www.gov.uk/government/publications/measles-in-uk)).

Observational studies and randomised trials from low-income countries show that vaccines may have non-specific effects that affect morbidity and mortality from non-targeted diseases. The World Health Organization commissioned a working group to undertake a review of the evidence of non-specific effects of selected vaccines, including for measles (single vaccine and MMR), to inform policy recommendations. Their report concluded that current evidence ‘neither excludes nor confirms the possibility of beneficial or deleterious non-specific immunological effects of vaccines on all cause-mortality’.

**Current advice:** NICE has public health guidance on [reducing differences in the uptake of immunisations](https://www.nice.org.uk/guidance/TA263), but does not produce guidance on specific vaccination programmes. Public Health England maintains ‘the Green Book’, which covers vaccination programmes in the UK. The MMR vaccine is administered twice: first within a month of the child’s first birthday, and second at the age of 3 years and 4 months. The combined diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* type b (DTaP-IPV-Hib) vaccine should be given in 3 doses at 2, 3 and 4 months, with further doses before school entry and at around 14 years old. The Green Book does not cover potential health benefits of vaccination other than the protection from the specific diseases. The NICE Pathway on [immunisation for children and young people](https://www.nice.org.uk/guidance/TA263) brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

**New evidence:** Sørup et al. (2014) studied hospital admissions for infections in Denmark for children in the second year of life, comparing outcomes for children whose most recent vaccination was the live vaccine MMR with outcomes for children whose most recent vaccination was the inactivated vaccine DTaP-IPV-Hib. Hospital admission and diagnosis data were obtained from the Danish National Patient Register and matched to vaccination records using a unique personal identification number.

Children were assigned to a cohort depending on their vaccination schedule. The first cohort (recommended schedule; n=456,043) had 3 doses of DTaP-IPV-Hib and MMR administered at a later point. The second cohort (reversed schedule; n=19,219) had 2 doses of DTaP-IPV-Hib and then...
MMR – the third dose of DTaP-IPV-Hib may have been administered later. Most children were followed from vaccination to age 2 years (n=436,258, 91.8%) or to administration of another vaccine (n=38,533, 8.1%). Overall, 56,889 admissions attributable to any type of infection were recorded. Analyses were adjusted to account for differences between cohorts in birth, health and demographic variables.

In the recommended schedule cohort, fewer children whose most recent vaccination was MMR were admitted to hospital with infection than children whose most recent vaccination was DTaP-IPV-Hib (8.9 admissions per 100 person-years versus 12.4 9 admissions per 100 person-years rs, incidence rate ratio [IRR]=0.86, 95% CI 0.84 to 0.88, p<0.001). In the reversed schedule cohort, the rate of hospital admission for infection was higher in children whose most recent vaccination was DTaP-IPV-Hib than in those whose most recent vaccination was MMR (12.8 9 admissions per 100 person-years versus 9.9 admissions per 100 person-years, IRR=1.62, 95% CI 1.28 to 2.05, p<0.001). When type of infection was considered, the strongest association between vaccination schedule and admission to hospital was for lower respiratory tract infections in the recommended schedule cohort (IRR=0.80, 95% CI 0.76 to 0.84). The rate of hospital admissions did not differ between groups in the first 15 days after vaccination.

The authors concluded that recent receipt of the live MMR vaccine was associated with a lower rate of hospital admission for infection than recent receipt of the inactivated DTaP-IPV-Hib vaccine. They noted that selection bias could be a possibility if children who received MMR first were healthier than those who received DTaP-IPV-Hib first. However, they discounted this possibility for several reasons, including that an effect caused by general health should have been seen in the first 2 weeks after vaccination, and that hospital admissions were consistently lower after MMR compared with DTaP-IPV-Hib even when the vaccines were delivered in difference sequences.

Commentary: “MMR coverage in the UK is at the highest level since the vaccine was introduced in 1998. However, coverage at a national level remains below the WHO target of at least 95%, and there are important regional differences, with coverage in London remaining below 90%. There is therefore still work to be done to improve MMR uptake.

“Although a link between MMR and autism has been firmly discredited, another concern has been that MMR might overload the immune system. To counter this, the Green Book cites a small UK study (436 cases) that showed a lower hospital admission rate for serious bacterial infection in the 90 days post-MMR (Miller et al. 2003).

“This much larger Danish study provides far stronger evidence that MMR prevents rather than causes hospital admissions for any infection, and shows that the benefit extends beyond 90 days. The authors estimated that the number needed to vaccinate to avoid one hospital admission was 93 to 201, suggesting that every 1% improvement in MMR coverage in the UK would avoid between 40 and 86 hospital admissions. The Sørup study should further reassure parents about the safety of MMR, and should provide a spur to healthcare professionals to promote the timely administration of MMR.” – Dr Jim Gray, Consultant Microbiologist, Birmingham Children’s Hospital NHS Foundation Trust

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