



Mumps vaccine effectiveness in primary schools and households, the Netherlands, 2008

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ABSTRACT

To estimate the mumps vaccine effectiveness (VE) during a large genotype D mumps outbreak, we conducted a cross-sectional study in eight primary schools and associated households in the Netherlands. Questionnaires were used to collect information on the occurrence of mumps. Multivariate analyses were used to estimate VE. Among schoolchildren we estimated the VE against mumps. Among household contacts where the schoolchild was the index case we estimated the VE against mumps and against mumps infectiousness. In total 1175 children and 2281 household contacts participated in the study. The mumps attack rate among schoolchildren was 17%. The mumps VE in schoolchildren was 92% [95% confidence interval (CI) 83–96%] and 93% [85–97%] for one and two doses of the measles, mumps, rubella (MMR) vaccine, respectively. The adjusted mumps VE among household contacts was 67% [65–95%] and 11% [–4 to 88%] against mumps and mumps infectiousness, respectively. Our study indicates that the mumps component of the MMR vaccine offered adequate protection against mumps among schoolchildren. The relatively low VE among household contacts is of concern.

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1. Introduction

Before introduction of routine childhood vaccination, mumps was a common childhood infection. It is caused by the mumps virus, and is characterized by swelling of the parotid gland. Complications include meningitis, (epididymo-)orchitis, oophoritis, pancreatitis, deafness and encephalitis [1,2].

Mumps vaccination was introduced in the Netherlands in 1987, using the measles, mumps rubella (MMR) combination vaccine, which contains the Jeryl Lynn mumps vaccine strain [3]. From 2006 onwards, also the RIT4385 vaccine strain, which is derived from the Jeryl Lynn strain, was incidentally used due to supply shortages [4]. The uptake of the first MMR vaccination (MMR-I) is high in the Netherlands (>95% from birth cohort 1993 onwards) while the uptake of the second MMR-II vaccination is slightly lower (93%) than the World Health Organization (WHO) target, i.e. 95% [5,6].

Mumps has been a notifiable disease from 1976 to 1998, and from December 1st, 2008 onwards [4].

Following introduction of MMR vaccination in 1987, the incidence of mumps notifications and hospitalizations declined dramatically [7]. In 2004, a genotype G mumps outbreak occurred in the Netherlands at an international school, with an attack rate of 12% among students vaccinated according to the Dutch schedule [8]. The high rate of vaccine failure raised concerns about the effectiveness of mumps vaccination in the Netherlands.

In August 2007, a genotype D mumps outbreak was detected mainly among residents of low vaccination coverage areas, the so-called Bible Belt. In this area, an important part of the population refrains from vaccination due to Orthodox Protestant, religious concerns [9].

This outbreak allowed us to study mumps vaccine effectiveness (VE). To maximize the information regarding vaccine effects obtained from this study, we combined different methods to estimate VE [10]. By combining a household and school study design, we assessed the VE against mumps in the context of a defined and undefined exposure setting, respectively. Furthermore, we assessed the VE against mumps infectiousness by comparing secondary attack rates in households of vaccinated and unvaccinated cases.

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2. Methods

2.1. Design and study population

The study population consisted of children attending primary schools and their household contacts. Schools were eligible when they had at least one laboratory confirmed mumps case or more than one clinical mumps case. We aimed to include schools with a broad range of vaccine coverages to allow studying the effect of mumps incidence on the VE. Parents of the schoolchildren were asked to fill out a questionnaire asking information on the child's vaccination status, occurrence of mumps, and if so date of onset and whether the child was the first mumps case in the household, complications, and information on household contacts (vaccination status and mumps history since September 2007). A mumps case was defined by an affirmative answer (by parental report) to the question: "Has your child had mumps after September 2007?" Symptoms of mumps were described as 'a sudden, painful swelling of one or both cheeks caused by an infection of salivary glands'. Children who were vaccinated more than twice were excluded. For VE estimations children who reported to have had mumps before September 2007 were excluded. The study was approved by the medical ethics committee of the University Medical Centre Utrecht. Written informed parental consent was requested to allow retrieval of information on participants' vaccination status from the national Dutch vaccination register.

To estimate the VE for mumps vaccination (one or two doses) with a precision of 10% and a power of 80%, we aimed to include 2700 children in 13 primary schools. Hereby we assumed the vaccine coverage to be 50%, the VE to be at least 70% [11,12], the response rate to be 75% and the attack rate in vaccinated to be 10%. The latter was based on observations made during a mumps outbreak at an international school [8].

To define the vaccination status we used individual information registered in the national Dutch vaccination register ('Praeventis'). For 69 pupils (6%) we could not obtain information on vaccination status from this register (66 no informed consent, 3 unknown vaccination status in register). For these children we used the self-reported vaccination status (vaccinated/not vaccinated), whereby assuming for vaccinated children that one dose was received when the child was aged <8.75 years, and two doses when the age was ≥ 8.75 years).

In schoolchildren, we assessed the VE against mumps. In households where a child attending one of the participating schools was the first mumps case in the household, we assessed the VE against mumps and the VE against mumps infectiousness.

The VE against mumps in schoolchildren for one and two doses of mumps vaccine compared to zero doses was estimated as $VE = 1 - \text{the relative risk (RR)}$, whereby the RR was estimated by fitting a Poisson regression model with mumps as outcome variable and vaccination status as central determinant. The model was fitted by Generalized Estimating Equations (GEE), where school was included as cluster variable. Possible confounders were age, attack rate, and mumps cases (yes/no) in the household of the participant occurring prior to the onset of mumps in the participant. A 10% difference between crude and adjusted logRR was considered as suggestive for confounding. We also considered interactions of these possible confounders with vaccination status. We performed a backward model selection (using the Wald test), where non-significant ($p = 0.05$) and non-confounding variables were dropped from the model.

The VE against mumps in households where the schoolchild was the first mumps case was estimated as $VE = 1 - (\text{SAR}_{\text{vaccinated contacts}} / \text{SAR}_{\text{unvaccinated contacts}})$, whereby the SAR (secondary attack rate) included all mumps cases in household contacts where mumps occurred after mumps in the index case.

Table 1

Mumps vaccine effectiveness (VE) estimates for mumps among schoolchildren and their household contacts.

	N	Mumps cases		VE	aVE ^a	95% CI ^b
		n	%			
Schoolchildren						
Unvaccinated	351	183	52%	Ref	Ref	
One dose of MMR	484	13	2.7%	95% ^c	92% ^c	83–96%
Two doses of MMR	301	7	2.3%	96% ^c	93% ^c	85–97%
Household contacts						
Unvaccinated	87	44	51%	Ref	Ref	
Vaccinated	19	3	16%	69% ^c	67% ^c	65–95%
Index cases						
Unvaccinated index case	90	44	49%	Ref	Ref	
Vaccinated index case	16	3	19%	62% ^d	11% ^d	–4 to 88%

^a aVE = adjusted vaccine effectiveness. The VE in schoolchildren the VE was adjusted for possible confounders: age, attack rate, and mumps cases (yes/no) in the household of the participant occurring prior to the onset of mumps in the participant. The estimated VE in household contacts was adjusted for both age and the vaccination status of the index case. The estimated VE against infectiousness in household was adjusted for age and the vaccination status of household contacts.

^b 95% CI = 95% confidence interval of aVE.

^c VE against mumps

^d VE against infectiousness

Household contacts born before 1978 were excluded, as they are likely to be immune through exposure to wild-type mumps virus in the past. This VE was estimated twice: adjusted for age, and adjusted for age of the household contacts and the vaccination status of the index case.

The VE against infectiousness in household was estimated as $VE = 1 - (\text{SAR}_{\text{vaccinated index case}} / \text{SAR}_{\text{unvaccinated index case}})$. This VE was also estimated twice: adjusted for age and adjusted for age and the vaccination status of the household contact.

3. Results

We included eight primary schools with vaccination coverages ranging from 34% to 93% in our study. These schools included 1741 children, of whom 1175 participated (response rate 68%, range by school 36–91%). One child who was vaccinated three times was excluded. For estimations of the VE, three additional children who reported to have had mumps before September 2007 were excluded.

Half of the included participants were male ($n = 593$ (50.5%)). The median age of the included participants was eight years (range 3–13 years). Among these were 203 mumps cases (attack rate (AR) 17%). The AR ranged from 1.5% to 51.3% by school. Of the mumps cases, 7% ($n = 14$) visited a GP because of mumps symptoms and 1% ($n = 2$) were admitted to hospital for mumps related complications. Reported complications were meningitis ($n = 1$), pancreatitis ($n = 1$), orchitis ($n = 1$), persisting fever ($n = 1$), swollen throat and severe headache ($n = 1$), otalgia ($n = 2$) and otitis ($n = 1$). The AR for mumps was highest in the oldest (10–13 years) schoolchildren, but the difference with the youngest (3–5 years) was not significant (20.5% versus 14.9%; $p = 0.07$).

In total, 67.9% ($n = 795$) of the participants were vaccinated with MMR, of whom 61.8% once and 38.2% twice. Most frequently reported reasons for non-vaccination among 372 non-vaccinated participants were religious belief ($n = 328$; 88.2%), choice for alternative medicine ($n = 14$; 3.8%), concerns about adverse events ($n = 51$; 13.7%) and/or other reasons ($n = 31$; 8.3%).

The mumps AR among unvaccinated children was 52.1% versus 2.7% and 2.3% for children vaccinated with 1 and 2 doses of MMR, respectively. The estimated VE in schoolchildren for one and two dose(s) of MMR was 92% (95% confidence interval (CI) 83–96%, Table 1) and 93% (95% CI 85–97%, Table 1), respectively. Age was not

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