

Effectiveness of M-M-R® II in Outbreaks: A Systematic Literature Review of Real-World Observational Studies

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Background

- Measles, mumps, and rubella are highly contagious diseases that can lead to potentially fatal illnesses, disabilities, and death¹
- M-M-R® II was approved for the prevention of measles, mumps, and rubella in 1978 in the US and has been used globally for over 40 years
- Widespread use of M-M-R® II has resulted in dramatic declines in incidence, morbidity, and mortality of measles, mumps, and rubella in the US and other countries²⁻⁴
- Vaccine immunogenicity and efficacy were established in multiple placebo-controlled trials of each vaccine component
- A systematic literature review (SLR) was conducted to summarize the vaccine effectiveness (VE) of M-M-R® II from real-world observational studies

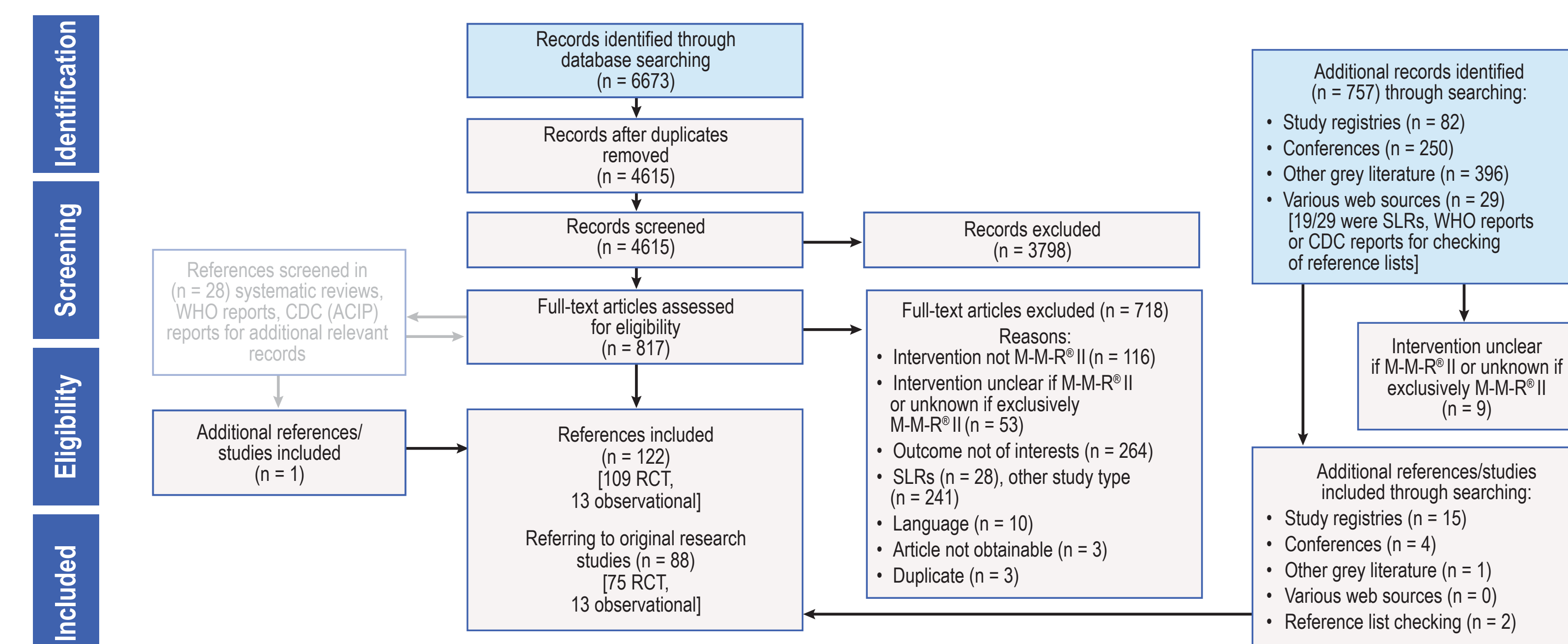
Methods

- The literature search was conducted in MEDLINE, Embase, and Cochrane CENTRAL through May 2019 and complemented by a search for grey literature including trial registries, conferences, grey literature databases, and various other web sources without time or geographic restriction but limited to English language
- The search included any observational studies related to VE of M-M-R® II/M-M-RVAXPRO®. M-M-R® II is referred to as M-M-RVAXPRO in the EU. If vaccine brand was not specified in the publication, it was assumed to be M-M-R® II, if the study was conducted in the US after 1978. (M-M-R® II is the only vaccine used in the US.)
- Findings were screened against predefined eligibility criteria. Critical appraisal of included studies was carried out using CASP (Critical Appraisal Skills Programme) Cohort Studies checklist
- All publications and findings were screened by two independent reviewers. The study characteristics and VE results were extracted into an Excel®-based grid for each study

Results

- A total of 13 observational studies were identified from the search (Figure 1). Three of the studies were further excluded since they did not report VE, but only the attack rates of disease after vaccination

Figure 1. Systematic Literature Review Flow Chart Including Both Randomized Control Trials (RCT, Reported Separately) and Observational Studies



Note: 13 observational studies were identified from the search, including 10 studies that reported VE and are the focus of this poster

- The 10 full-text publications related to VE of M-M-R® II were all identified from outbreak investigations. Eight were conducted in US, one in Canada, and one in the Netherlands
- For measles outbreaks (n = 4), VE ranged from 71% to 96% in different age groups⁵⁻⁸ (Table 1)
 - Among a study of high school students, VE of ≥1-dose of M-M-R® II was 94%-96%⁶
 - Among a study of young adolescents, VE of ≥2-dose vs 1-dose of M-M-R® II was 94.1%⁷
 - Among a study in children 6 months to 19 years old, when a single dose of M-M-R® II was used as post-exposure prophylaxis within 72 hours of exposure during an outbreak, the VE was 83.4%⁵
 - In another study among infants 6 to 14 months old, VE of a single dose of M-M-R® II was 71% against laboratory-confirmed measles⁸

Table 1. M-M-R® II Effectiveness Results From Measles Outbreaks (n = 4)

Author, Year	Country	Study Period	Study Size	Age Range	Comparison Groups (Vaccine Effectiveness)	Notes
Arciuolo, 2017 ⁵	US	2013	318	6 mo -19 yrs	1D vs 0D (83.4%)	Post exposure prophylaxis effectiveness during an outbreak
De Serres, Lynn, 2004 ⁷	Canada	2011	1,306	15 yrs (median), high school students	1D vs 0D (95.9%) ≥2D vs 0D (95.5% for classical cases, 94.2% for classical + attenuated cases)	Generally, M-M-R® II was used, but mixed with small numbers of Connaught Canada, monovalent measles vaccine
Woudenberg, 2017 ⁸	Netherlands	2013-2014	1,230	6-14 months	1D vs 0D (71% for clinical cases, 43% for self-reported cases)	Effectiveness of M-M-R® II during a measles epidemic

0D, unvaccinated; 1D, 1 dose; 2D, 2 doses.

Table 2. M-M-R® II Effectiveness Results From Mumps Outbreaks (n = 6)

Author, Year	Country	Study Period	Study Size	Age Range	Comparison Groups (Vaccine Effectiveness)	Notes
Cardemil, 2017 ⁹	US	2015-2016	20,496	18-24 yrs	3D vs 2D (range from 60.0% -78.1%) 2D vs 0D (89.4%, vaccinated <13 yrs before outbreak) 2D vs 0D (31.8%, vaccinated ≥13 yrs before outbreak)	
Hersh, 1991 ¹⁰	US	1988-1989	1,713	Junior high school students	1D or 2D vs 0D (83%)	Only 8 unvaccinated; Vaccines may include both monovalent mumps vaccine and M-M-R® II
Livingston, 2014 ¹¹	US	2010	2,176	≥5 yrs	1D vs 0D (82.9%) 2D vs 0D (86.3%) ≥1D vs 0D (85.8%)	
Marin, 2008 ¹²	US	2006	2,363	≥7 yrs, college students	1D vs 0D (84%) 2D vs 0D (80%)	
Nelson, 2013 ¹³	US	2009-2010	3,239	9-14 yrs	3D vs ≤2D (60%)*	
Ogbuanu, 2012 ¹⁴	US	2009-2010	2,265	11-17 yrs	3D vs ≤2D (88.0%)	

*VE was not provided in the original publication, and estimated by one minus the reported relative risk. 0D, unvaccinated; 1D, 1 dose; 2D, 2 doses; 3D, 3 doses.

- Among mumps outbreaks (n = 6), the VE of 1-dose and 2-dose M-M-R® II compared to unvaccinated individuals was 83%-84% and 80%-89%, respectively⁹⁻¹² (Table 2)
 - Three studies evaluating the effectiveness of a third dose of M-M-R® II showed a mumps VE of 60%-88% for 3-dose vs ≤2-dose^{9,13,14}
 - One study found that individuals who had received a second dose of M-M-R® II <13 years before the outbreak had a lower risk for contracting mumps than those receiving a second dose ≥13 years before the outbreak⁹
- No study reported use of M-M-R® II in a rubella outbreak

Limitations

- The studies were conducted in different settings and age groups, and the study designs and comparisons groups varied

Conclusions

- We identified vaccine effectiveness (VE) studies conducted only in outbreak settings. There were no studies reporting use of M-M-R® II in rubella outbreaks
- This systematic literature review of the effectiveness of M-M-R® II vaccine in real-world observational studies showed that M-M-R® II was effective against measles and mumps during outbreaks
- More effectiveness studies are warranted to further address questions about the relationship of VE and time since vaccination as well as the effectiveness of a third dose of M-M-R® II for measles or mumps outbreak control

Acknowledgments

The study was supported by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Disclosures

ES, MN, LK, and MA are employees of Certara, which received funding from Merck & Co., Inc. MP, LPS, ER, SL, and BK are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA and stockholders of Merck & Co., Inc., Kenilworth, NJ, USA, which provided funding for this study.

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