

Rapid Systematic Review of the Safety of MMRV Vaccine

A. Background

The measles-mumps-rubella-varicella (MMRV) vaccine (ProQuad, Merck) was licensed in the United States in 2005 for use in children 12 months through 12 years of age. While not licensed for use in the United States, Priorix-Tetra, a MMRV vaccine manufactured by GlaxoSmithKline, first received licensing in some European countries in 2006, and in Canada in 2007. Both ProQuad and Priorix-Tetra are tetravalent vaccines with similar measles, mumps, rubella and varicella viral strain composition.[1] Henceforth, any reference to MMRV in this report refers to ProQuad, unless otherwise specified.

In 2006, the Advisory Committee on Immunization Practices (ACIP) noted that use of combination vaccines, like MMRV, was preferred over separate injections of equivalent component vaccines (e.g., MMR vaccine and varicella vaccine [MMR+V]).[2] Post-licensure safety surveillance data indicated an increased risk for febrile seizures following the administration of the first dose of MMRV among children aged 12-23 months compared to those receiving separate MMR and varicella vaccines.[3] Based on this data, ACIP and the Centers for Disease Control and Prevention updated its guidance to note that the first dose of MMR and varicella vaccines are preferred to be given separately in this age group, but MMRV may be used as a first dose in children aged 12-47 months based on parent or caregiver preference.[4] Given the importance of maintaining a thorough awareness and assessment of MMRV vaccine safety publications, we propose a review of the literature assessing MMRV vaccine safety to inform the public and healthcare providers, and aid in public health policy discussions.

B. Methods

B.1. Key Question Development

The below question is formulated according to the PI/ECO(ST) strategy, and for this review, those elements include and *are not limited to* those identified in Table 1.

1. For children aged 12 months to 12 years, what is the safety of MMRV vaccine?

Table 1

PI/ECO(ST) Criteria for Key Question

PI/ECO(ST) Element	Criteria
Population	Pediatric population that includes: <ul style="list-style-type: none">○ Infants and toddlers aged 12 months – 23 months○ Young children and children aged 12 months – 12 years
Intervention or Exposure	MMRV vaccination. Including ProQuad, Priorix-Tetra, and brand unspecified.
Comparator (if applicable)	Any or none
Outcome(s)	Adverse events

PI/ECO(ST) Element	Criteria
	Adverse outcomes Safety outcomes Side effects
Setting	Any
Time Frame	Any publication years

B.2. Literature Search

A CDC informationist (J.T.) developed search strategies from the Key Question and PI/ECO criteria, and performed the search in MEDLINE, EMBASE, CINAHL, and Cochrane Library from the start of each database to August 1, 2025. Search strategies and results are provided in Table 3 in the Appendix.

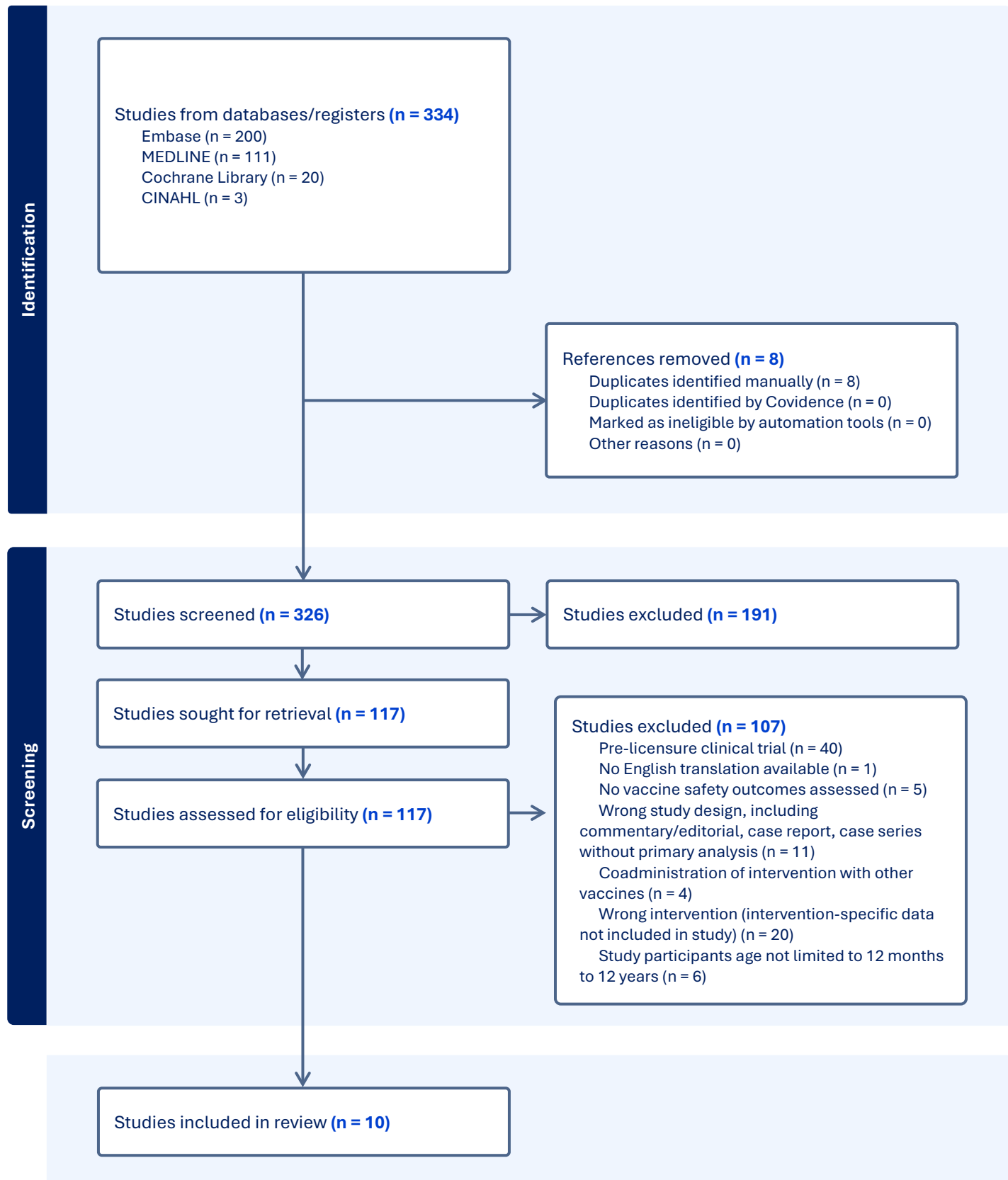
B.3. Study Selection

Results of the literature searches were uploaded into EndNote 21 (Clarivate Analytics®, Thomson Reuters, New York, NY, USA), duplicate records were removed, and unique titles and abstracts were uploaded to Covidence (Veritas Health Innovation Ltd., Melbourne, VIC, Australia) where a second round of deduplication was conducted. Three reviewers (JR, EQ, JS) independently screened all titles and abstracts and removed irrelevant references; disagreements were resolved by consensus. Relevant full texts were screened independently by three reviewers (JR, EQ, JS); disagreements were resolved by consensus. All studies were screened according to the pre-identified exclusion criteria below, and results of the study selection process are provided in *Figure 1*.

Criteria for excluding studies from the literature review include:

1. No full text available;
2. Not available in English;
3. Pre-licensure clinical trials;
4. Not relevant to key question;
5. No primary data or analysis, or secondary data not systematically collected;
6. Insufficient methodologic reporting (i.e., meeting abstract or poster);
7. Study population includes participants <12 months or >12 years of age; or
8. Indeterminate age range of study population receiving vaccine.

Figure 1. Results of the Study Selection Process



B.4. Data Extraction and Outcome Summarization

Data from studies meeting inclusion criteria were independently extracted by four reviewers using a standardized Microsoft Excel (2021) form, and differences were reconciled by discussion. Outcome data were extracted as presented in the studies. For the purposes of this review, statistical significance was defined as $p \leq 0.05$. The evidence was summarized and synthesized for each outcome domain.

C. Summary of Evidence

C.1. Summaries of Evidence

A review of literature was conducted addressing safety of MMRV vaccine (ProQuad or Priorix-Tetra). This review focused on the vaccine safety for children aged 12 months to 12 years of age. Priorix-Tetra is not licensed for use in the United States, but was included in the review due to a similar viral strain composition as the ProQuad formulation and a desire to report on comprehensive MMRV safety data. Additionally, this review focused on safety data related to post-licensure studies, and did not include studies that did not present data on MMRV administration without other vaccines coadministered on the same day. Refer to Section B3 for full exclusion criteria for this review. The 10 studies reviewed are listed in Table 2. In the narrative text below, studies performed in the United States are presented first, and have a brief summary introduction for each outcome discussed; studies performed outside of the United States are briefly summarized under the international headings.

Table 2*Characteristics of studies meeting inclusion criteria*

Lead author last name, year of publication	Study design	MMRV trade name (ProQuad or Priorix-Tetra)	Data collection period	Sample size, N	Surveillance system (if applicable)	Country
Cocchio, 2016 [5]	Prospective cohort	Priorix-Tetra	August 1, 2013 – July 31, 2014	10395	Not reported	Italy
Deichman, 2015 [6]	Randomized comparative study	ProQuad	January 12, 2007 – February 13, 2008	947	Not reported	Germany and Italy
Haas, 2019 [7]	Randomized comparative study	ProQuad	Pre-2019, otherwise not defined	405	Not reported	France
Hambidge, 2014 [8]	Self-controlled case series	ProQuad	2004 – 2010	5667	Vaccine Safety Datalink	United States
Jacobsen, 2009 [9]	Retrospective cohort	ProQuad	February 2006 – June 2007	62596	Kaiser Permanente Southern California electronic data system	United States
Klein, 2010 [10]	Self-controlled case series	ProQuad	2000 – 2008	459461	Vaccine Safety Datalink	United States
Klein, 2012 [11]	Retrospective cohort	ProQuad	2006-2008 for MMRV 2000 – 2008 for MMR + V	154188	Vaccine Safety Datalink	United States
MacDonald, 2014 [12]	Retrospective cohort	Priorix-Tetra	2006 – 2012	277774	Canadian Institute for Health Information database	Canada
O’Leary, 2011 [13]	Self-controlled case series	ProQuad	2000 – 2009	1.8 million	Vaccine Safety Datalink	United States
Rowhani-Rahbar, 2013 [14]	Retrospective cohort	ProQuad	2001-2011	840348	Vaccine Safety Datalink	United States

Table 3*Selected outcomes reviewed in studies meeting inclusion criteria*

Lead author last name, year of publication	MMRV trade name (ProQuad or Priorix-Tetra)	Country	Outcome(s) summarized
Cocchio, 2016 [5]	Priorix-Tetra	Italy	Febrile seizure, afebrile seizure, fever, irritability, parotid swelling, arthralgia, local reactions (pain, swelling, redness)
Deichman, 2015 [6]	ProQuad	Germany and Italy	Febrile seizure, fever, irritability, local reactions (pain, swelling, redness)
Haas, 2019 [7]	ProQuad	France	Fever, mumps-like illness
Hambidge, 2014 [8]	ProQuad	United States	Seizure (not otherwise specified)
Jacobsen, 2009 [9]	ProQuad	United States	Febrile seizure
Klein, 2010 [10]	ProQuad	United States	Febrile seizure
Klein, 2012 [11]	ProQuad	United States	Febrile seizure, fever
MacDonald, 2014 [12]	Priorix-Tetra	Canada	Seizure (not otherwise specified)
O'Leary, 2011 [13]	ProQuad	United States	Immune thrombocytopenic purpura
Rowhani-Rahbar, 2013 [14]	ProQuad	United States	Seizure (not otherwise specified), fever

Neurological outcomes

Febrile seizure

One retrospective cohort (Jacobsen, 2009) and one self-controlled case series within the Vaccine Safety Datalink (VSD) (Klein, 2010) suggested an increased risk for febrile seizures following MMRV vaccination compared to separately administered MMR and varicella vaccines on the same day in children aged 12-60 months and children aged 12-23 months, respectively. Another retrospective cohort within VSD (Klein, 2012) suggested that MMRV and MMR + V were not associated with increased risk of febrile seizures among children aged 4-6 years old.

- Retrospective cohort (Jacobsen, 2009) of 62596 children aged 12-60 months who either received MMRV vaccination (n=31298) or MMR+V vaccination given separately at the same visit (n=31298). The study identified 84 cases of confirmed febrile convulsion; there were 1.41/1000 (n=44) confirmed febrile convulsion diagnoses in the MMRV cohort, and 1.28/1000 (n=40) confirmed febrile convulsion diagnoses in the MMR+V cohort. The analysis suggested no significant difference between MMRV and MMR+V in confirmed febrile convulsion in the 30

days following vaccination (RR=1.1 [95% CI, 0.72-1.69]). In days 5-12 following vaccination, the study identified 32 cases of confirmed febrile convulsion, with 0.7/1000 (n=22) confirmed febrile convulsion diagnoses in the MMRV cohort, and 0.32/1000 (n=10) confirmed febrile convulsion diagnoses in the MMR+V cohort; there was a suggested increased risk in the MMRV cohort in the 5-12-day post-vaccination window (RR=2.2 [95% CI, 1.04-4.65]).

- Self-controlled case series (Klein, 2010) analyzed 459461 healthy children aged 12-23 months within VSD, comparing MMRV vaccine recipients (n=83107) to recipients of MMR + V vaccines given on the same day (n=376354). The analysis suggested an increased risk for febrile seizures after MMRV compared to separately administered same-day MMR and V vaccines (RR=1.98 [95% CI, 1.43-2.73]); the excess risk per 10,000 doses was 4.6 (95% CI, 2.8-5.9).
- Retrospective cohort study (Klein, 2012) of 154188 children aged 4-6 years within VSD analyzed whether MMRV (n=86750) or same-day MMR+V (n=67438) affects risk for febrile seizure. There was one febrile seizure 7-10 days after MMRV and 0 after MMR+V. Febrile seizure risk was 1 per 86750 MMRV doses (95% CI, 1 per 3426441, 1 per 15570), and 0 per 67438 MMR+V doses (95% CI, 0, 1 per 18282).

Seizure (not otherwise specified)

A self-controlled case series within VSD (Hambidge, 2014) suggested an association of more postvaccination seizures in delayed MMRV vaccination (administered between age 12-15 months) compared to on-time MMRV vaccination (administered between age 16-23 months).

A retrospective cohort within VSD (Rowhani-Rahbar, 2013) found that the incidence of seizures during the 7-10 days following immunization with MMRV was significantly greater than that following immunization with MMR with or without varicella administered separately on the same day. The study suggested a 2-fold increase in the risk of seizures in the 7-10 days following MMRV vaccination compared with MMR administered with or without varicella vaccine in both younger (12 to 15 months of age) and older children (16 to 23 months of age).

- Self-controlled case series within VSD (Hambidge, 2014) analyzed timely versus delayed early childhood vaccination in a cohort of 5667 children with diagnosis of first seizure between 38 and 730 days of life. For on-time MMRV vaccination (administered at age 361 – 488 days), the IRR for seizure in the 7-10 days after vaccination was 4.95 (95% CI, 3.68-6.66). For delayed receipt of MMRV (administered at age 489-730 days), the IRR was 9.8 (95% CI, 4.35-22.06). The vaccine-seizure association was most pronounced if MMRV vaccine was administered between 16 and 18 months of age (IRR 11 [95% CI, 4.26-28.38]).
- Retrospective cohort study within VSD (Rowhani-Rahbar, 2013) examined the effect of age on the risk of fever and seizures following immunization with measles-containing vaccines in children aged 12 to 23 months of age (N =840348). A MMRV vs MMR +/- V cohort analysis in participants aged 12-15 months indicated an increased risk in seizures among MMRV recipients (IRR 2.0 [95% CI, 1.4-2.8]), with an excess risk of 4.2 cases per 10000 doses (95% CI, 1.8-16.3). A MMRV vs MMR +/- V cohort analysis in participants aged 16-23 months indicated an increased risk in seizures among MMRV recipients (IRR 2.1 [95% CI, 1.3-3.3]), with an excess risk of 9 cases per 10000 doses (95% CI, 1.8-16.3). The relative risk of seizure during the 7-10 days following MMRV immunization (MMR with or without varicella administered separately on

the same day as the reference) was not statistically different between children 16 to 23 months of age and those 12 to 15 months of age. The attributable risk of seizures during the 7-10 days following MMRV immunization (MMR with or without varicella administered separately on the same day as the reference) was greater among children 16 to 23 months of age than among children 12 to 15 months of age; however, the difference did not gain statistical significance.

MMRV vaccine safety in international settings – Neurological outcomes

- One **prospective cohort from Italy** (Cocchio, 2016) of 10395 healthy fourteen-month old children eligible for their first vaccination against measles, mumps, rubella, and varicella assessed adverse events relating to two different vaccination strategies: Priorix-Tetra vaccination (n=5265) or separate MMR and varicella vaccination administered on the same day (n=5130). This study **reported no difference in risk of febrile seizure following MMR + V compared to Priorix-Tetra [RR 0.80 (95% CI, 0.30-2.15)] or afebrile seizure following MMR + V compared to Priorix-Tetra [RR 2.05 (95% CI, 0.18-22.6)].**
- One **randomized comparative study** (Deichmann, 2015) of 947 healthy German and Italian children aged ≥ 12 to <24 months randomly assigned the children to one of three vaccination arms in a 2:1:1. Group 1 received one MMRV dose and one hexavalent vaccine concomitantly at separate injection sites, group 2 received MMRV only, and group 3 received the hexavalent vaccine only. In the MMRV-only group (n=234), **no participants were reported to have febrile convulsion within 0-28 days following vaccination.**
- One **retrospective cohort study from Canada** (MacDonald, 2014) compared the risk of seizures after the first dose of Priorix-Tetra with the risk after same-day administration of separate MMR + V in 277774 children aged 12 to 23 months. **The risk of seizures 7-10 days after vaccination was twice as high with Priorix-Tetra as with MMR + V (RR 1.99 [95% CI, 1.3-3.05]). The excess absolute risk of seizures was 3.52 seizures per 10000 doses of Priorix-Tetra relative to MMR_V.** In high-risk children (those with a personal history of febrile seizure; seizure disorder; central nervous system injury, infection or neoplasm; encephalopathy; or a progressive, evolving or unstable neurologic condition), the risk was not differentially higher for Priorix-Tetra (RR 1.3 [95% CI, 0.6-2.79]).

Systemic reaction outcomes

Fever

A retrospective cohort within VSD (Klein, 2012) reported that there was no apparent peak in outpatient fever visits during days 7 to 10 after MMRV, MMR or varicella vaccines, and that outpatient fever visits 7 to 10 days were not significantly higher after MMR + V than after MMR alone, although there was a trend in that direction.

Another retrospective cohort study within VSD (Rowhani-Rahbar, 2013) found that the incidence of fever during the 7-10 days following immunization with MMRV was significantly greater than that following immunization with MMR with or without varicella administered separately on the same day. The study suggested a 1.4-fold increase in the risk of fevers in the 7-10 days

following MMRV vaccination compared with MMR administered with or without varicella vaccine in both younger (12 to 15 months of age) and older children (16 to 23 months of age).

- The Klein (2012) retrospective cohort within VSD reported outpatient fever visits for MMRV recipients occurred at an adjusted rate of 5.2 per 100 person-years (95% CI, 3.9-6.8) in the 7-10-day post-vaccination window, and 5 per 100 person-years (95% CI, 4.5-5.4) in the 0-42-day post-vaccination window. Outpatient fever visits for MMR+V recipients occurred at an adjusted rate of 8.8 per 100 person-years (95% CI, 6.2-12) in the 7-10-day post-vaccination window, and 6.4 per 100 person-years (95% CI, 5.7-7.2) in the 0-42-day post-vaccination window.
- The Rowhani-Rahbar (2013) retrospective cohort within VSD reported that a MMRV vs MMR +/- V cohort analysis in participants aged 12-15 months indicated an increased risk in fever among MMRV recipients (IRR 1.4 [95% CI, 1.3-1.5]), with an excess risk of 8.9 cases per 10000 doses (95% CI, 3.2-15.2); in a cohort of participants aged 16-23 months the IRR was 1.4 (95% CI, 1.1-1.7).

MMRV vaccine safety in international studies – systemic reactions outcomes

- **Randomized comparative study** (Deichmann, 2015) of 947 healthy German and Italian children aged ≥ 12 to < 24 months randomly assigned the children to one of three vaccination arms in a 2:1:1. Group 1 received one MMRV dose and one hexavalent vaccine concomitantly at separate injection sites, group 2 received MMRV only, and group 3 received the hexavalent vaccine only. In the MMRV-only group (n=234), 61.1% (n=143) were reported to have at least one rectal (or equivalent) **temperature ≥ 38 degrees Celsius** within 0-28 days following vaccination (48 of those study participants were reported to have at least one rectal (or equivalent) **temperature ≥ 39.4 degrees Celsius**); 1.3% (n=3) were reported to have **irritability** within 0-28 days following vaccination; no participants were reported to have mumps/mumps-like illness within 0-28 days following vaccination.
- One **prospective cohort from Italy** (Cocchio, 2016) of 10395 healthy fourteen-month old children eligible for their first vaccination against measles, mumps, rubella, and varicella assessed adverse events relating to two different vaccination strategies: Priorix-Tetra vaccination (n=5265) or separate MMR and varicella vaccination administered on the same day (n=5130). The findings suggested a **decreased risk of fever ≤ 39.4 degrees Celsius following MMR + V compared to Priorix-Tetra** [RR 0.58 (95% CI, 0.54-0.63)]. This study reported **no difference in risk of fever ≥ 39.5 degrees Celsius** following MMR + V compared to Priorix-Tetra [RR 0.80 (95% CI, 0.69-1.00)], an **increased risk of irritability following MMR + V compared to MMRV*** [RR 1.35 (95% CI, 1.21-1.51)], **increased risk of parotid swelling following MMR + V compared to Priorix-Tetra** [RR 1.73 (95% CI, 1.02-2.92)], and an **increased risk of arthralgia following MMR + V compared to Priorix-Tetra** [RR 1.82 (95% CI, 1.17-2.82)].
- **Randomized comparative study** (Haas, 2019) of 405 healthy French children aged 12-18 months compared intramuscular (IM) and subcutaneous (SC) administration of two doses of MMRV given one month apart. In the 0-28 days following the first MMRV dose administered by IM route (n=202) or by SC route (n=203), **vaccine-related pyrexia** was reported in 35.6% (n=72) and 39.4% (n=80) of recipients, respectively; and **mumps/mumps-like illness** was reported in the 0.5% (n=1) and 0% (n=0) of participants, respectively. In the 0-28 days following the second

MMRV dose administered by IM route (n=201) or SC route (n=200), **vaccine-related pyrexia** was reported in 16.9% (n=34) and 17% (n=34) of participants, respectively; and **mumps/mumps-like illness** was reported in the 0.5% (n=1) and 0% (n=0) of participants, respectively.

Local reactions outcomes

There were no studies from the United States in this review that assessed local reactions outcomes.

MMRV vaccine safety in international studies – pain outcome

- One **prospective cohort from Italy** (Cocchio, 2016) of 10395 healthy fourteen-month old children eligible for their first vaccination against measles, mumps, rubella, and varicella assessed adverse events relating to two different vaccination strategies: Priorix-Tetra vaccination (n=5265) or separate MMR and varicella vaccination administered on the same day (n=5130). The findings suggested **an increased risk of pain following MMR+V compared to Priorix-Tetra** [RR 3.33 (95% CI, 2.79-3.98)].
- One **randomized comparative study** (Deichmann, 2015) of 947 healthy German and Italian children aged ≥12 to <24 months randomly assigned the children to one of three vaccination arms in a 2:1:1. Group 1 received one MMRV dose and one hexavalent vaccine concomitantly at separate injection sites, group 2 received MMRV only, and group 3 received the hexavalent vaccine only. In the MMRV-only group (n=234), 14.1% (n=33) were reported to have injection-site pain within 0-28 days following vaccination. owing vaccination in groups 1 and 3, respectively.

MMRV vaccine safety in international studies – swelling outcome

- One **prospective cohort from Italy** (Cocchio, 2016) of 10395 healthy fourteen-month old children eligible for their first vaccination against measles, mumps, rubella, and varicella assessed adverse events relating to two different vaccination strategies: Priorix-Tetra vaccination (n=5265) or separate MMR and varicella vaccination administered on the same day (n=5130). The findings suggested an **increased risk of swelling following MMR + V compared to Priorix-Tetra** [RR 3.38 (95% CI, 2.45-4.68)].
- One **randomized comparative study** (Deichmann, 2015) of 947 healthy German and Italian children aged ≥12 to <24 months randomly assigned the children to one of three vaccination arms in a 2:1:1. Group 1 received one MMRV dose and one hexavalent vaccine concomitantly at separate injection sites, group 2 received MMRV only, and group 3 received the hexavalent vaccine only. In the MMRV-only group (n=234), 2.6% (n=6) were reported to have **injection-site swelling** within 0-28 days following vaccination.

MMRV vaccine safety in international studies – redness outcome

- One **prospective cohort from Italy** (Cocchio, 2016) of 10395 healthy fourteen-month old children eligible for their first vaccination against measles, mumps, rubella, and varicella assessed adverse events relating to two different vaccination strategies: Priorix-Tetra vaccination (n=5265) or separate MMR and varicella vaccination administered on the same day

(n=5130). The findings **suggested an increased risk of redness following MMR + V compared to Priorix-Tetra** [RR 4.89 (95% CI, 3.73-6.42)].

- One **randomized comparative study** (Deichmann, 2015) of 947 healthy German and Italian children aged ≥ 12 to < 24 months randomly assigned the children to one of three vaccination arms in a 2:1:1. Group 1 received one MMRV dose and one hexavalent vaccine concomitantly at separate injection sites, group 2 received MMRV only, and group 3 received the hexavalent vaccine only. In the MMRV-only group (n=234), 10.7% (n=25) were reported to have **injection site erythema** within 0-28 days following vaccination.

Hematological outcome

Immune thrombocytopenic purpura (ITP)

- A **self-controlled case series** (O'Leary, 2011) with a cohort of 1.8 million children aged 6 weeks to 17 years within VSD identified a total of 197 chart-confirmed ITP cases. The analysis **indicated no significant elevated risk of ITP in MMRV recipients aged 12-19 months within the 1- to 42-day post-vaccination window** (IRR 2.87 [95% CI, 0.78-10.56]).

Appendix

Table 3

Primary search strategy of MEDLINE (OVID), Embase (OVID), Cochrane Library CINAHL (EBSCOHost),

DATABASE	STRATEGY	RUN DATE	RECORD COUNT
Medline (OVID) 1946-	<ol style="list-style-type: none"> 1. (Measles-Mumps-Rubella-Varicella OR chickenpox measles mumps rubella vaccine OR MMRV OR ProQuad).mp 2. Exp Safety/ OR exp Treatment Outcome/ OR "Drug-Related Side Effects and Adverse Reactions"/ 3. (safety OR (vaccin* ADJ2 safe*) OR treatment outcome* OR adverse* OR harm OR harmful OR harms OR side effect*).ti,ab,kf. OR ae.fs 4. 2 OR 3 5. Exp Clinical Study/ OR exp Product Surveillance, Postmarketing/ 6. (trial* OR observational stud* OR observation stud* OR clinical stud* OR surveillance OR reporting system* OR VAERS OR postmarket* OR post-market*).ti,ab,kf,hw. 7. 5 OR 6 8. 1 AND 4 AND 7 9. Exp animals/ NOT exp humans/ 10. 10 NOT 11 	08/1/2025	111
Embase (OVID) 1947-	<ol style="list-style-type: none"> 1. chickenpox measles mumps rubella vaccine/ 2. (Measles-Mumps-Rubella-Varicella OR chickenpox measles mumps rubella vaccine OR MMRV OR ProQuad).ti,ab,kf. 3. 1 OR 2 4. Exp Safety/ OR exp Treatment Outcome/ OR adverse drug reaction/ 5. (safety OR (vaccin* ADJ2 safe*) OR treatment outcome* OR adverse* OR harm OR harmful OR harms OR side effect*).ti,ab,kf. OR ae.fs 6. 4 OR 5 7. Exp Clinical Study/ OR exp Postmarketing Surveillance/ 8. (trial* OR observational stud* OR observation stud* OR clinical stud* OR surveillance OR reporting system* OR VAERS OR postmarket* OR post-market*).ti,ab,kf,hw. 9. 7 OR 8 10. 3 AND 6 AND 9 11. Exp animal/ NOT exp human/ 12. 10 NOT 11 13. limit 12 to "pubmed/medline" 	08/1/2025	297 - DUPLICATES =200 UNIQUE RECORDS

DATABASE	STRATEGY	RUN DATE	RECORD COUNT
	14. 12 NOT 13 15. limit 14 to conference abstract status 16. 14 NOT 15 17.		
Cochrane Library	#1 (Measles-Mumps-Rubella-Varicella:ti,ab,kw OR "chickenpox measles mumps rubella vaccine":ti,ab,kw OR MMRV:ti,ab,kw OR ProQuad:ti,ab,kw) #2 [mh Safety] OR [mh "Treatment Outcome"] #3 (safety:ti,ab,kw OR (vaccin*:ti,ab,kw NEAR/2 safe*:ti,ab,kw) OR ("treatment" NEXT outcome*):ti,ab,kw OR adverse*:ti,ab,kw OR harm:ti,ab,kw OR harmful:ti,ab,kw OR harms:ti,ab,kw OR ("side" NEXT effect*):ti,ab,kw) #4 #2 OR #3 #5 [mh ^"Clinical Study"] OR [mh ^"Product Surveillance, Postmarketing"] #6 (trial*:ti,ab,kw OR ("observational" NEXT stud*):ti,ab,kw OR ("observation" NEXT stud*):ti,ab,kw OR ("clinical" NEXT stud*):ti,ab,kw OR surveillance:ti,ab,kw OR ("reporting" NEXT system*):ti,ab,kw OR VAERS:ti,ab,kw OR postmarket*:ti,ab,kw OR post-market*:ti,ab,kw) #7 #5 OR #6 #8 #1 AND #4 AND #7	08/1/2025	54 - DUPLICATES =20 UNIQUE RECORDS
CINAHL (EBSCOHost)	S1 (Measles-Mumps-Rubella-Varicella OR "chickenpox measles mumps rubella vaccine" OR MMRV OR ProQuad) S2 (MH Safety+) OR (MH "Treatment Outcomes+") OR (MH "Adverse Drug Event+") S3 ((TI safety OR AB safety OR SU safety) OR ((TI vaccin* OR AB vaccin* OR SU vaccin*) N2 (TI safe* OR AB safe* OR SU safe*)) OR (TI "treatment outcome*" OR AB "treatment outcome*" OR SU "treatment outcome*") OR (TI adverse* OR AB adverse* OR SU adverse*) OR (TI harm OR AB harm OR SU harm) OR (TI harmful OR AB harmful OR SU harmful) OR (TI harms OR AB harms OR SU harms) OR (TI "side effect*" OR AB "side effect*" OR SU "side effect*")) S4 S2 OR S3 S5 (MH "Clinical Study+") OR (MH "Product Surveillance, Postmarketing+")	08/1/2025	5 - DUPLICATES =3 UNIQUE RECORDS

DATABASE	STRATEGY	RUN DATE	RECORD COUNT
	<p>S6 ((TI trial* OR AB trial* OR SU trial*) OR (TI "observational stud*" OR AB "observational stud*" OR SU "observational stud*") OR (TI "observation stud*" OR AB "observation stud*" OR SU "observation stud*") OR (TI "clinical stud*" OR AB "clinical stud*" OR SU "clinical stud*") OR (TI surveillance OR AB surveillance OR SU surveillance) OR (TI "reporting system*" OR AB "reporting system*" OR SU "reporting system*") OR (TI VAERS OR AB VAERS OR SU VAERS) OR (TI postmarket* OR AB postmarket* OR SU postmarket*) OR (TI post-market* OR AB post-market* OR SU post-market*))</p> <p>S7 S5 OR S6</p> <p>S8 S1 AND S4 AND S7</p> <p>S9 Limiters - Exclude MEDLINE records</p>		

References

1. Tillieux, S.L., et al., *Comparative analysis of the complete nucleotide sequences of measles, mumps, and rubella strain genomes contained in Priorix-Tetra and ProQuad live attenuated combined vaccines*. Vaccine, 2009. **27**(16): p. 2265-73.
2. CDC, *Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP)*. MMWR, 2007. **56**: p. No. RR-4.
3. CDC, *Update: recommendations from the Advisory Committee on Immunization Practices (ACIP) regarding administration of combination MMRV vaccine*. MMWR, 2008. **57**: p. 258--60.
4. Marin, M., et al., *Use of combination measles, mumps, rubella, and varicella vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP)*. MMWR Recomm Rep, 2010. **59**(Rr-3): p. 1-12.
5. Cocchio, S., et al., *A postmarket safety comparison of 2 vaccination strategies for measles, mumps, rubella and varicella in Italy*. Hum Vaccin Immunother, 2016. **12**(3): p. 651-4.
6. Deichmann, K.A., et al., *Immunogenicity and safety of a combined measles, mumps, rubella and varicella live vaccine (ProQuad ®) administered concomitantly with a booster dose of a hexavalent vaccine in 12-23-month-old infants*. Vaccine, 2015. **33**(20): p. 2379-86.
7. Haas, H., et al., *Immunogenicity and safety of intramuscular versus subcutaneous administration of a combined measles, mumps, rubella, and varicella vaccine to children 12 to 18 months of age*. Hum Vaccin Immunother, 2019. **15**(4): p. 778-785.
8. Hambidge, S.J., et al., *Timely versus delayed early childhood vaccination and seizures*. Pediatrics, 2014. **133**(6): p. e1492-9.
9. Jacobsen, S.J., et al., *Observational safety study of febrile convulsion following first dose MMRV vaccination in a managed care setting*. Vaccine, 2009. **27**(34): p. 4656-61.
10. Klein, N.P., et al., *Measles-mumps-rubella-varicella combination vaccine and the risk of febrile seizures*. Pediatrics, 2010. **126**(1): p. e1-8.
11. Klein, N.P., et al., *Measles-containing vaccines and febrile seizures in children age 4 to 6 years*. Pediatrics, 2012. **129**(5): p. 809-14.
12. MacDonald, S.E., et al., *Risk of febrile seizures after first dose of measles-mumps-rubella-varicella vaccine: a population-based cohort study*. Cmaj, 2014. **186**(11): p. 824-9.
13. O'Leary, S.T., et al., *The risk of immune thrombocytopenic purpura after vaccination in children and adolescents*. Pediatrics, 2012. **129**(2): p. 248-55.
14. Rowhani-Rahbar, A., et al., *Effect of age on the risk of Fever and seizures following immunization with measles-containing vaccines in children*. JAMA Pediatr, 2013. **167**(12): p. 1111-7.