

# Parental Risk Factors for Fever in their Children 7–10 Days after the First Dose of Measles-containing Vaccines

Ousseny Zerbo, PhD<sup>1</sup>, Sharareh Modaresi, MD, MPH<sup>1</sup>, Kristin Goddard, MPH<sup>1</sup>, Ned Lewis, MPH<sup>1</sup>, Karin Bok, PhD<sup>2</sup>, Hayley Gans, MD<sup>3</sup>, and Nicola Klein, MD, PhD<sup>1</sup>

<sup>1</sup>Vaccine Study Center, Northern California Kaiser Permanente; <sup>2</sup>National Vaccine Program Office, US. Health and Human Services; <sup>3</sup>Stanford University



## Background

- About 5-15% of 1-2 year old children develop fever 7-10 days after a first dose of measles containing vaccines (MCV; MMR or MMRV)
- Fever 7-10 days after a first dose of a MCV clusters among siblings in families, suggesting a genetic basis
- Biological and clinical features affecting risk of fever following MCV are not well understood

## Objective

To investigate whether parental clinical conditions are associated with the child having fever after a first dose of MCV

## Methods

**Study Population:** Children who were born between 2009 – 2016 at Kaiser Permanente Northern California (KPNC) and who received a MCV between ages 1 – 2 years. Each child was linked with his/her mother and father (where possible)

**Study design:** Retrospective cohort study

**Main Outcome:** MCV- associated fever in the child, defined as receipt of a fever code in the outpatient or emergency department 7 – 10 days after the first dose of a MCV

**Exposure and exposure definition:** Clinical conditions present in the parents anytime before or after the child's birth. We defined clinical conditions as Internal Classification of Disease codes 9<sup>th</sup> or 10<sup>th</sup> revision present in the parent's electronic medical record.

### Analyses:

**1. Fever rates:** We calculated rates of fever 7 – 10 days among children who received a first dose of MCV between ages 1 – 2 years

**2. Assessing for association between clinical conditions and MCV-associated fever:** We assessed proportion of clinical conditions present in parents and children, comparing the proportion between children who had MCV-associated fever and children who did not have MCV-associated fever. We used chi square test for categorical variables and a t test for continuous variables. We identified clinical conditions that were statistically significant at p<0.05 in the bivariate analyses. We included these conditions, in addition to socio-demographic factors and healthcare seeking behavior (defined by the number of visits by the child before receiving a MCV) in multivariate logistic regression models. The adjusted models estimated parental and child clinical conditions associated with MCV-associated fever in the child

## Results

- The study included 244,128 children, 192,253 mothers (100% of children were linked to their mother) and 118,046 fathers (59% of children were linked to their father)
- Among the children, 17,763 (7.3%) were born preterm and 124,494 (51%) were males
- 3,750 (1.54%) of the children had MCV-associated fever
- Children who had MCV-associated fever had ≥4 clinic visits before MCV than children who did not have MCV-associated fever
- In crude analyses, 29 maternal, 8 paternal and 10 child clinical conditions were statistically significantly (p < 0.05) associated with child fever after MCV (Table 1)

**Table 1: Maternal, paternal and child clinical factors significantly associated with child MCV-associated Fever**

Maternal clinical conditions			Paternal clinical conditions	Child clinical conditions
Any fever	Sleep disorder	Herpes	Any fever	Febrile seizure
Maternal fever after MCV	Syncope	Abnormal Lipid	Fever after respiratory infection	Asthma
Fever after respiratory infection	Essential thrombocytopenia	Liver disease	Respiratory infection	Epilepsy
Respiratory infections	Vitamin deficiency	Migraine	Thyroid condition	Respiratory infection
Hypertension	Gastro intestinal disease/GERD	Obesity	Gastro intestinal disease/GERD	Allergy
Asthma	Adison disease	Pain	vitiligo	Anemia
Allergy	Alopecia	Polycystic ovarian syndrome	Alopecia	Herpes
Anemia	Abnormal white blood cell count		Vitamin deficiency	Respiratory failure
Dizziness	Gestational diabetes			Sleep disorder
Type 2 diabetes	Dysuria			Gastro intestinal disease/GERD
Arrhythmia	Endometritis			

- Adjusting simultaneously for parental, child socio-demographic factors and health seeking behavior, maternal and paternal fever, autoimmune diseases (alopecia, vitiligo), maternal migraines, arrhythmia, syncope and essential thrombocytopenia were associated with child fever after MCV (Table 2)
- Child febrile seizure and respiratory infection were associated with fever after MCV (**Table 2**)

## Strengths and Limitations

- **Strengths:** Large study including more than 244,000 children and ability to simultaneously adjust for parental and child confounding factors
- **Limitations:** Exploratory study and results may still be affected by other confounding factors

**Table 2: Association Between Parental and child Clinical Conditions and MCV-Associated Fever in the Child**

Health conditions	Infant fever (7-10 days) after MCV N = 3721 n(%)	No Infant fever (7-10 days) after MCV N = 238588 n(%)	Adjusted OR <sup>1</sup> (95% CI)
<b>Maternal health conditions</b>			
Any fever	444 (11.93)	20836 (8.73)	1.19 (1.06 – 1.33)
Maternal fever after MCV	2 (0.05)	18 (0.01)	5.90 (1.34 – 25.78)
Fever after respiratory infection	253 (6.80)	12612 (5.29)	1.20 (1.09 - 1.31)
Addison's disease	724 (19.46)	43791 (18.35)	2.90 (0.90 - 9.33)
Migraine	903 (24.27)	45744 (19.17)	1.14 (1.05 - 1.24)
Arrhythmia	122 (3.28)	5646 (2.37)	1.21 (1.00 - 1.45)
Syncope	354 (9.51)	17606 (7.38)	1.14 (1.01 - 1.27)
Essential thrombocytopenia	15 (0.40)	442 (0.19)	1.93 (1.15 - 3.25)
<b>Paternal health conditions</b>			
Any fever	192 (8.85)	8876 (6.29)	1.14 (0.97 - 1.35)
Fever associated with respiratory infection	166 (7.65)	6299 (4.46)	1.47 (1.23 - 1.75)
Respiratory infection	1531 (70.59)	91828 (65.07)	1.14 (1.03 - 1.26)
Vitiligo	21 (0.97)	759 (0.54)	1.61 (1.04 - 2.50)
<b>Child health conditions</b>			
Febrile seizure	77 (2.05)	1285 (0.53)	2.99 (2.36 - 3.78)
Respiratory infection	2648 (70.61)	141162 (58.73)	1.25 (1.15 - 1.35)
Respiratory failure	9 (0.24)	138 (0.06)	2.76 (1.40 - 5.46)
Sleep disorder	47 (1.25)	1552 (0.65)	1.52 (1.13 - 2.04)
Gastrointestinal disorders/GERD	768 (20.48)	34759 (14.46)	1.22 (1.13 - 1.33)

<sup>1</sup> Adjusted for parental age, race/ethnicity, child age and sex, health condition included in Table1 and healthcare seeking behavior

## Conclusions

Specific parental clinical conditions were associated with fever in their child 7-10 days after a MCV. These results suggest that in addition to genetic factors, children's risk for MCV-associated fever may be generally related to familial immune responses

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