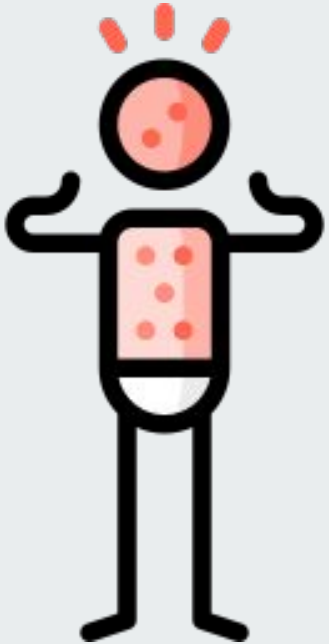
Join MentiMeter ahead of time
Or code **2424 3295** on Menti.com

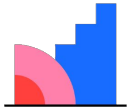
Measles..?



CLINID conference
Hunter Ratliff
03/12/2025

Ages, dates, and other identifying information may have been changed
I have no conflict of interest in relation to this presentation

[1] Are Koplik spots pathognomonic for active measles?



Mentimeter

Setting the scene

It's **Thursday afternoon** on the Khakoo service

- The list has been >10 patients for the past 6 days
- You are finishing seeing the afternoon consults with the team
    - At **3:36pm**, a consult order comes in for "**concern for meningitis**"

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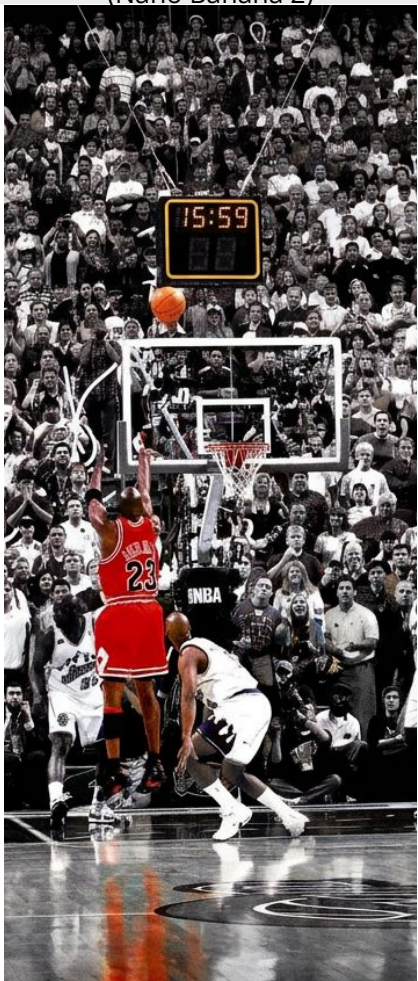
    - At **3:36pm**, a consult order comes in for "concern for meningitis"

At **3:59pm**, a page comes in...

ED/07	
Reason for Consult	**measles ro**
Is the patient being discharged today?	**Yes**
Provider Name & Callback Number	175725

AI generated content
(Nano Banana 2)



Case 1: HPI (per the ED/MyChart)

A **35 y/o F** with no PMH p/w **concern for measles**

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- ❖ Patient's name would imply some connections to **South Asia**
- ❖ Recently **received MMR vaccine** because she was not immune

Case 1: HPI (per the ED/MyChart)

A **35 y/o F** with no PMH p/w **concern f**

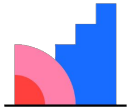
- Tues
- Wed

Measles PEP guidance (NYC.gov)

Age Range	Measles immune status	Type of PEP
Age >12 mo	Non-immune	• Give MMR vaccine
	1 dose MMR	• Give 2nd MMR vaccine
	Unknown status	• Give MMR vaccine

- ❖ Patient's name would imply some connections to **South Asia**
- ❖ Recently **received MMR vaccine** because she was not immune

[2] Is this measles?



Mentimeter

Based off of what the ED told you

Case 1: HPI - Timeline

A **35 y/o F** with no PMH p/w **concern for measles** due to a rash developing 13 days after MMR

- 14 days ago: Received **MMR vaccine**

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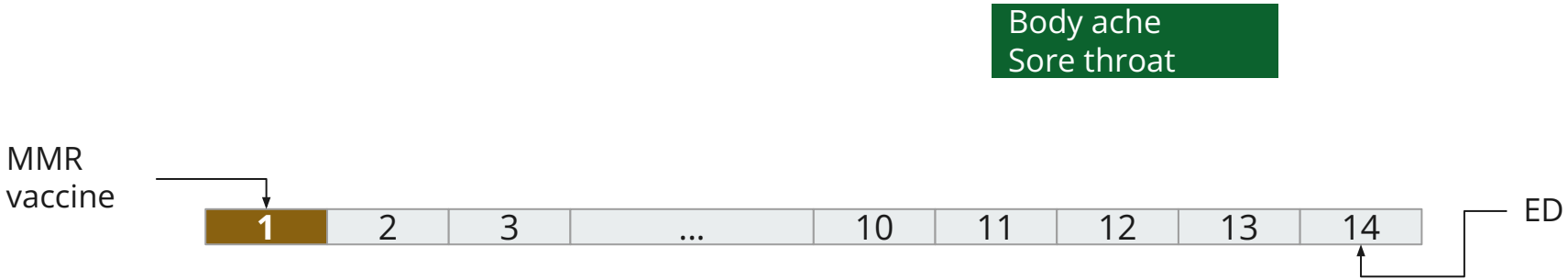

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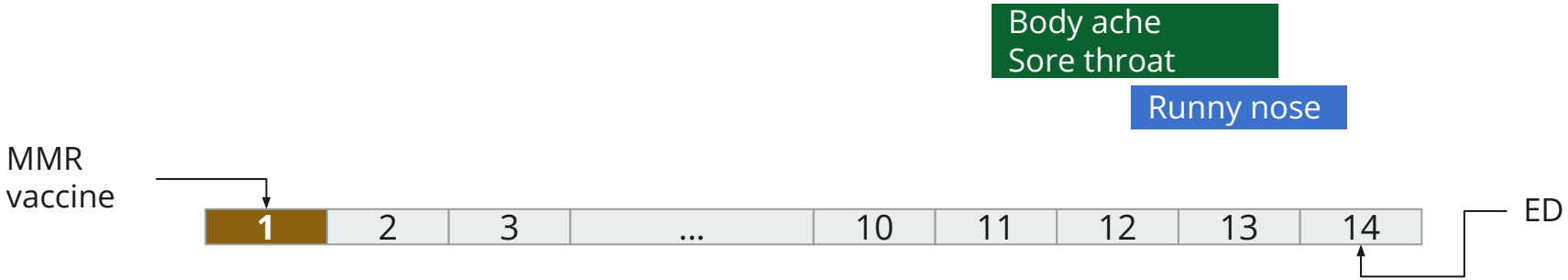

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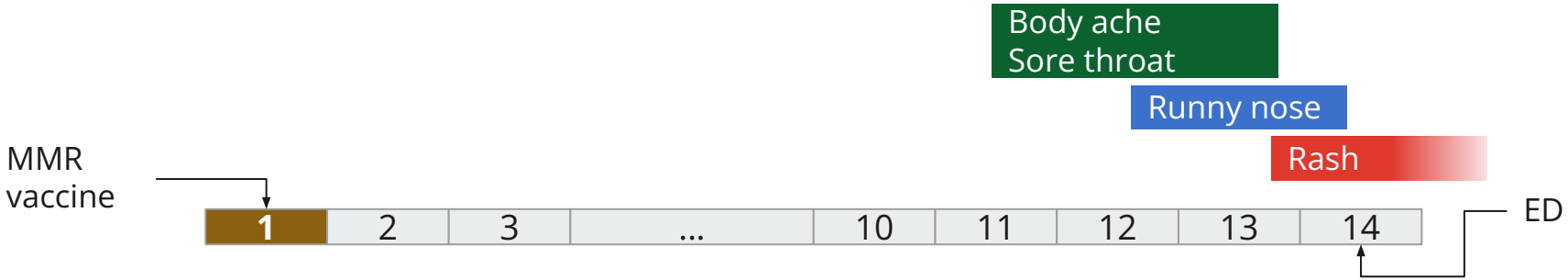
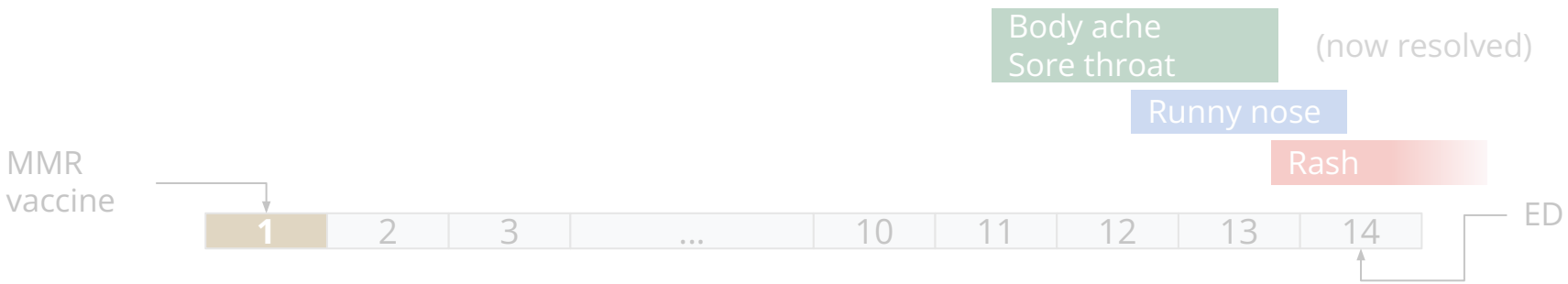


Case 1: HPI

A **35 y/o F** with no PMH p/w **concern for measles** due to a rash developing 13 days after MMR. Rash prodrome was body aches + sore throat, then runny nose, onset just a few days before rash.

Component	2 yr ago
Ref Range & Units (hover)	
RUBELLA IGG QUALITATIVE	Negative !



Case 1: HPI - Timeline

A **35 y/o F** with no PMH p/w **concern for measles** due to a rash developing 13 days after MMR. Rash prodrome was body aches + sore throat, then runny nose, onset just a few days before rash.

- **No fever** (but did have body aches)
- No *noticeable* cough
- Eyes have not been red or watery

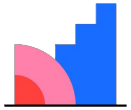
Component	2 yr ago
Ref Range & Units (hover)	
RUBELLA IGG QUALITATIVE	Negative !

Case 1: HPI - The rash

A **35 y/o F** with no PMH p/w **concern for measles** due to a rash developing 13 days after MMR. Rash prodrome was body aches + sore throat, then runny nose, onset just a few days before rash.

- Last night while brushing her teeth, noticed what appeared to be acne appear on face
- During shower, saw similar lesions on her right shoulder
  - Unclear if these appeared before, after, or at the same time as the rash on her face
- This morning, rash on the **face was more numerous**
  - Also now has some rash on her **forearms**

[3] Is this measles?



Mentimeter

Before we see the rash...

Case 1: Physical exam

BP	138/87	**Pulse**	90	**SpO2**	98 %
Temp	98.1 °F	**RR**	18	**BMI**	26 kg/m^2
General	Alert and oriented, NAD, vitals reviewed				
ENT	Buccal mucosa: Normal, no lesions (the flashlight in the room doesn't work)				
Eyes	Anicteric sclerae; No injection				
Skin	Next slide				

Case 1: Physical exam

- Small (<5mm) nonblanching lesions
- Maculopapular (papules/raised > macules)
  - Some do look more acneiform
- Only mild erythema/hyperpigmentation

Distribution:

- Most pronounced on the face but also
  - anterior chest/shoulder > forearms >> back
- Not diffuse, plenty of adjacent skin is uninvolved
  - minimal to no rash on upper arms and neck
  - None on the legs
  - Spares the palms

Unable to take actual pictures due to isolation

Case 1: Labs

CBC	Result
WBC	5.2
Hgb	12.1
Platelets	224
Neut %	49%
Eos %	6%

Chem7	Result
Na	141
K	3.8
HCO3	23
BUN	15
Cr	0.71

Case 1: Summary

A 35 y/o F with no PMH p/w concern for **measles due to a rash** developing 13 days after MMR. Rash prodrome was body aches + sore throat, then runny nose, onset just a few days before rash.

- The rash is certainly worsening
- Seems like it's likely spreading cephalocaudal (head-to-chest)

Component	2 yr ago
Ref Range & Units (hover)	
RUBELLA IGG QUALITATIVE	Negative !

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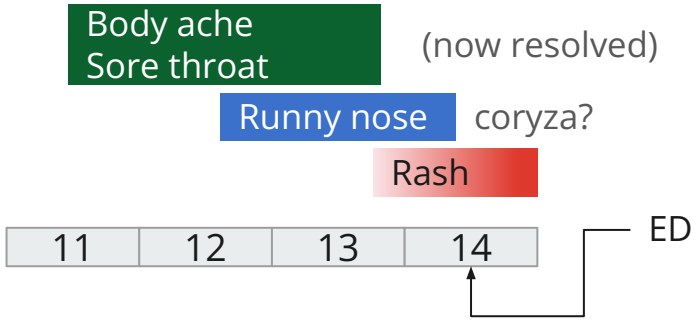


[4] Is this measles?

Mentimeter

We now have all of the info

How should we manage this?

Let’s pretend this is a MARS call

Options:

- Straight to the ED for in person eval
- In person clinic visit
- Video visit
- eConsult

Case 1: Hospital course

Patient was able to access her vaccination records

- Vaccinated for measles (one vaccine) in childhood, but it wasn't the MMR
- No known exposures or risk factors for wild type exposure

Component	2 yr ago
Ref Range & Units (hover)	
RUBELLA IGG QUALITATIVE	Negative !

Case #1.1 (alternate universe)

Disaster case

An unvaccinated patient had a possible measles exposure

They were given the MMR vaccine for **post exposure prophylaxis**

...now they develop a rash

Is the rash from:

1. The vaccine --or--
2. Wild type measles (that was not prevented by PEP)

Discussion

Links to articles discussed here

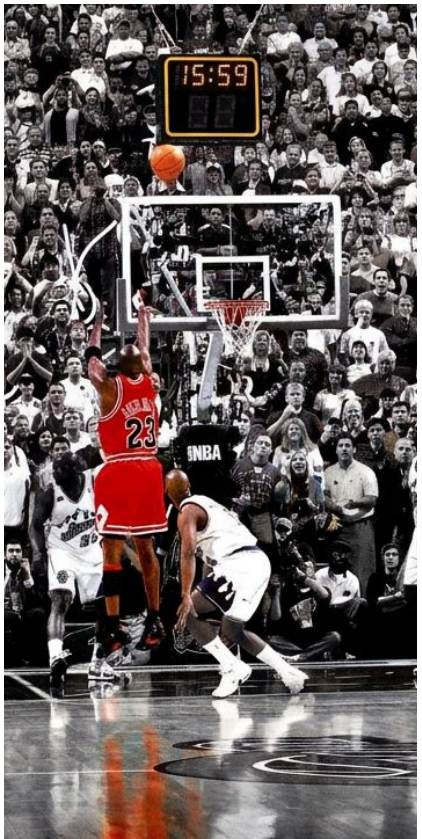
Does MMR “cause” ‘measles’?

My journey through **the weirdest literature search** I’ve done in awhile…

Follow me along my journey

Doesn't the MMR vaccine cause a rash..?

Does ID really need to see them at 4pm?



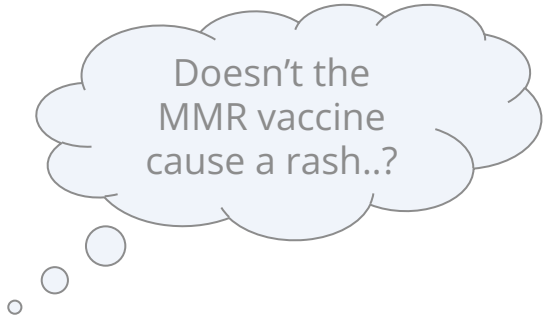
Measles that broke through MMR PEP?

Why are they in the ED? **They might be spreading measles**!

Reactions to MMR(V) vaccine

* I'm using the term "**side effects**" for self limiting reactions, which is distinct from any long lasting sequela, i.e. neurologic changes (see this Cochrane review)

MMR vaccine is well tolerated, but it does have **some predictable side effects** *



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Most common systemic† side effects [2]

- **Fevers** (5 - 15%)
- **Rash** (around 5%)

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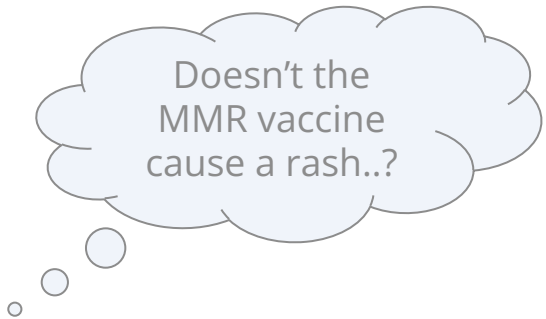

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When do these reactions happen?

- **5 to 12 days** [2,4,6]
  - In the trials, onset occurs during this time frame [4] **in 80% of cases** (where they develop a side effect)

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- **First 3 weeks** [3, CDC 2025]

Note

With recent changes at CDC/ACIP, I've included the year of the publication next to the citation number for all references to federal guidance from the US government (perhaps unnecessary)

Reactions to MMR - Timing of reactions [5]

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When *exactly* do reactions occur?

From an old study in 1986 [5]

- **Robust design**
  - Double blinded, **placebo controlled**
  - Matched **581 pairs of twins**
- Might be **unethical** to do now
  - Ironically, based out of **Helsinki**, Finland
  - Done during their rollout of MMR (1982-83)

Reactions to MMR - Timing of reactions [5]

TABLE I—SYMPTOMS AND SIGNS CAUSED BY MMR VACCINATION AND DAY OF PEAK OCCURRENCE

Symptom or sign	Maximum difference in rate* (%)	$CI_{95\%}$	Peak frequency (days after vaccination)
Local erythema (>2 cm)	0·8	0·1–1·4	2
Other local reaction	0·4	0–1·4	2
Mild fever (⩽38·5°C rectal)	2·7	0–6·1	10
Moderate fever (38·6–39·5°C)	2·9	1·6–4·3	9
High fever (⩾39·5°C)	1·4	0·7–2·1	10
Irritability	4·1	2·1–6·1	10
Drowsiness	2·5	1·4–3·6	11
Willingness to stay in bed	1·4	0·5–2·3	11
Generalised rash	1·6	0–3·0	11
Conjunctivitis	2·1	0·9–3·2	10
Arthropathy	0·8	0·2–1·3	7–9
Peripheral tremor	0·4	0–0·9	9
Cough and/or coryza	−1·5†	−4·6–1·6	9
Nausea and/or vomiting	−0·8†	−1·6–0	7–8
Diarrhoea	0·7	0–1·7	11

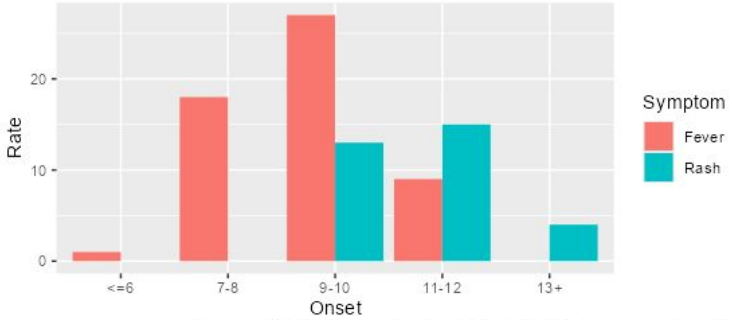
*Between MMR group and placebo group.
†More in placebo-injected children.

When *exactly* do reactions occur?

Placebo vs **MMR** matched study [5]

- **Moderate fever** peaked at **day 9**
  - 38.6 - 39.5 C (101.5 - 103.1 F)
- **Generalized rash** peaked at **day 11**

Reactions to MMR - Timing of reactions [5]



—	Days after injection									
	1–6		7–8		9–10		11–12		13–21	
	No	Rate	No	Rate	No	Rate	No	Rate	No	Rate
Moderate fever (38·6–39·5°C rectal):										
MMR	9	8	34	29	42	36	21	18	7	6
Placebo	9	7	13	11	10	9	10	9	9	8
Difference	0	1	21	18	32	27	11	9	−2	−2
Generalised rash:										
MMR	22	19	28	24	49	43	56	48	27	24
Placebo	23	20	29	25	35	30	39	33	24	20
Difference	−1	−1	−1	−1	14	13	26	15	3	4

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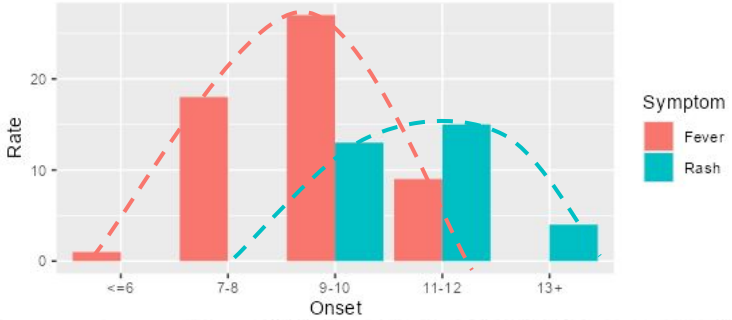

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The distribution of symptom onset *implies* that **fever comes before rash** (similar to wild type measles)

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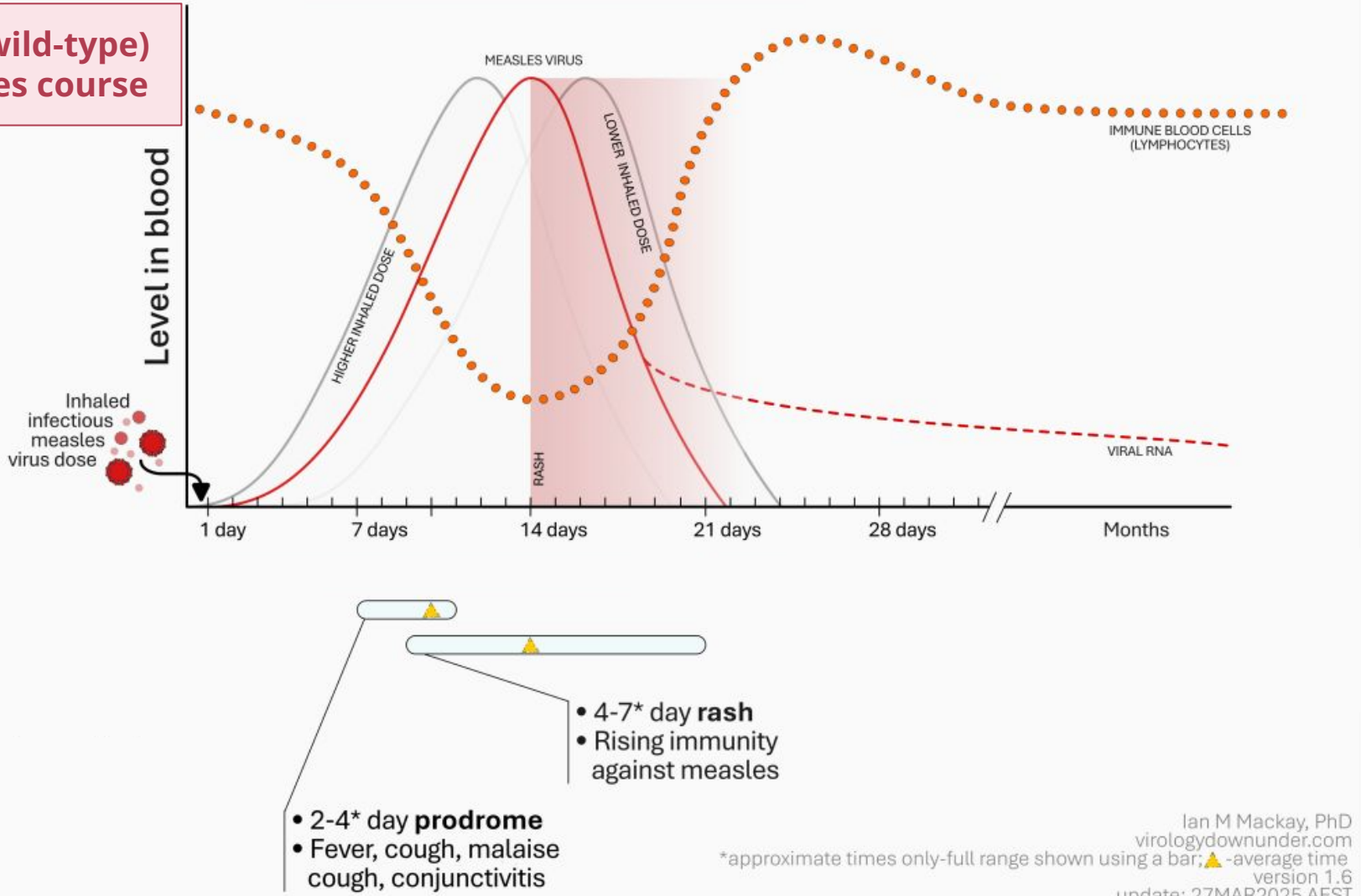
MMR	105	91	156	134	166	143	162	139	153	132
Placebo	100	85	154	132	181	155	177	152	155	134
Difference	5	6	2	2	−15	−12	−15	−13	−2	−2

Interestingly, MMR group had ***lower rates*** **of cough &/or coryza** during this time (compared to placebo)

Real (wild-type) measles course



Ian M Mackay, PhD
virologydownunder.com
*approximate times only-full range shown using a bar; ▲-average time
version 1.6
update: 27MAR2025 AEST

[source]

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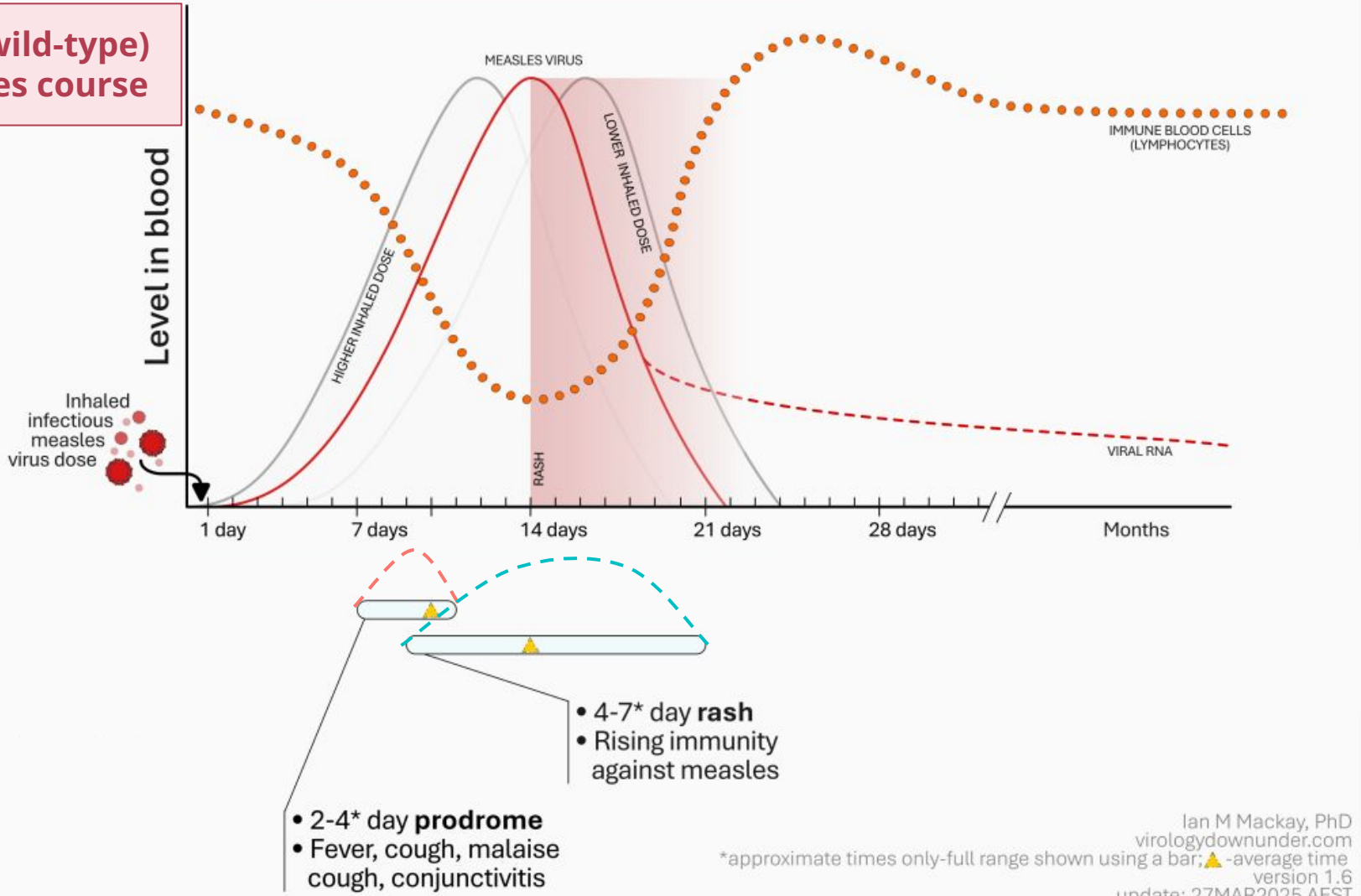

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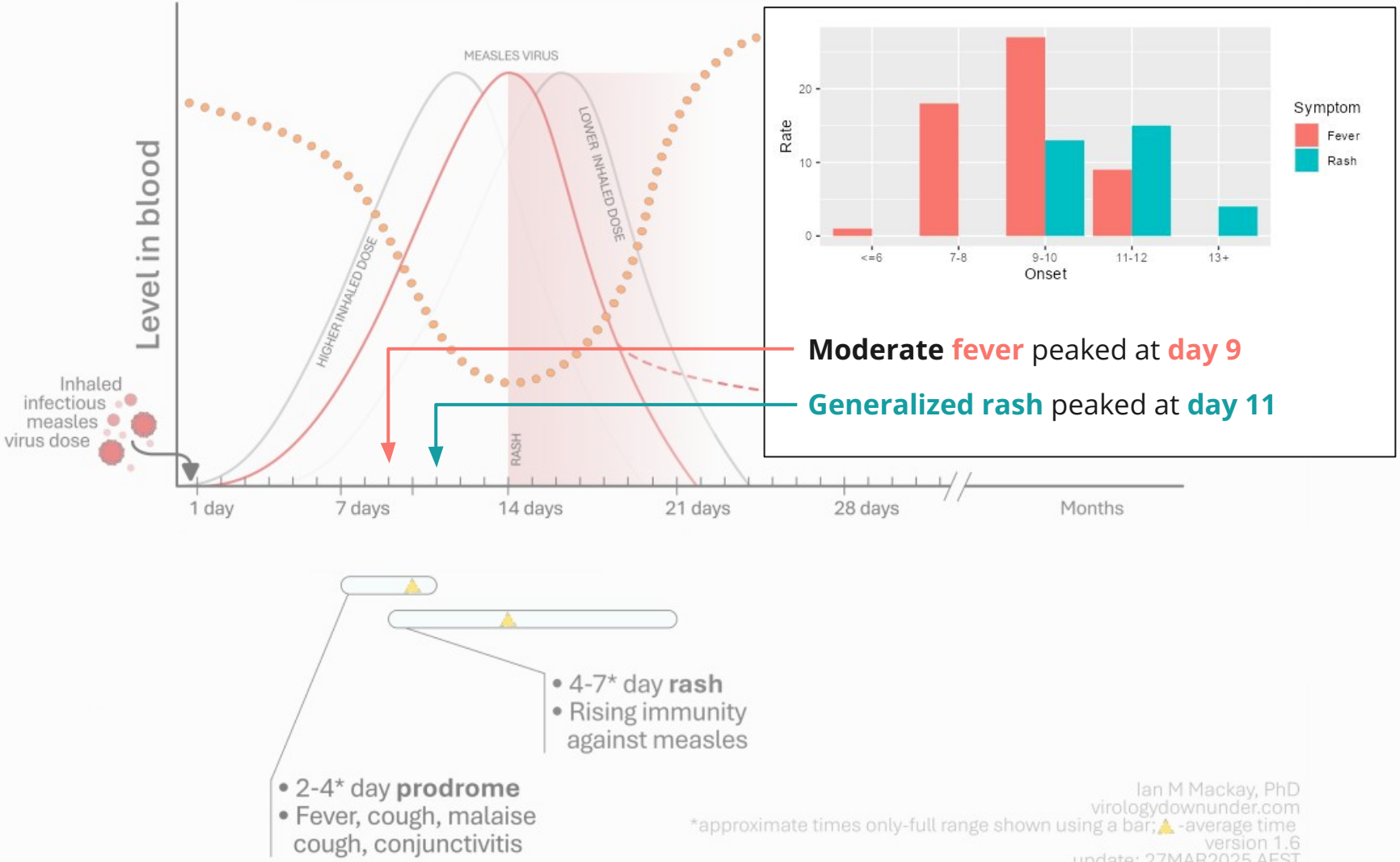

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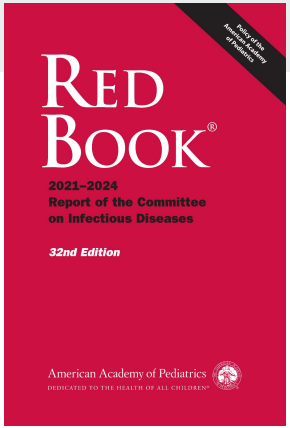
What does the Red Book say? [6]



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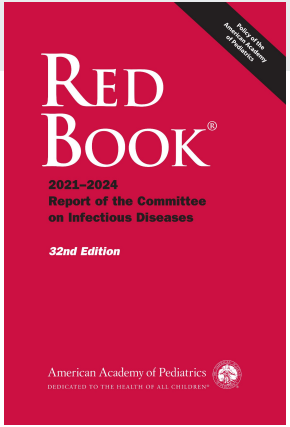

Adverse Events . A body temperature of 39.4°C (103°F) or higher develops in approximately 5% to 15% of vaccine recipients, usually between 5 and 12 days after receipt of MMR vaccine; fever generally lasts 1 to 2 days but may last as long as 5 days. Most people with fever do not have other symptoms.

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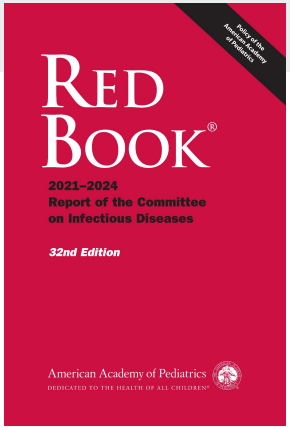

Adverse Events . A body temperature of 39.4°C (103°F) or higher develops in approximately 5% to 15% of vaccine recipients, usually between 5 and 12 days after receipt of MMR vaccine; fever generally lasts 1 to 2 days but may last as long as 5 days. Most people with fever do not have other symptoms. **Transient rashes have been reported in approximately 5% of vaccine recipients**.

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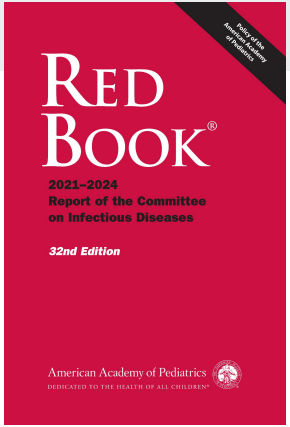

MEASLES 582

Rates of most local and systemic adverse events for children immunized with **MMRV** vaccine are comparable with rates for children immunized with **MMR** and **varicella vaccines** administered concomitantly. However, recipients of a **first dose of MMRV** vaccine have a **greater rate of fever 102°F** (38.9°C) or higher than do recipients of MMR and varicella vaccine administered concomitantly (22% vs 15%, respectively).

The MMRV [1,4]

MMRV is more likely to **cause fevers** compared to **MMR + varicella** (given at separate sites) [6]

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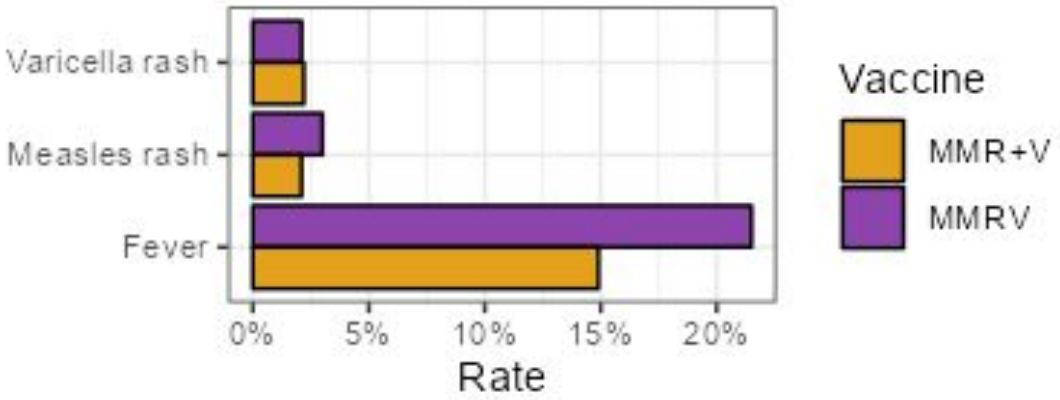

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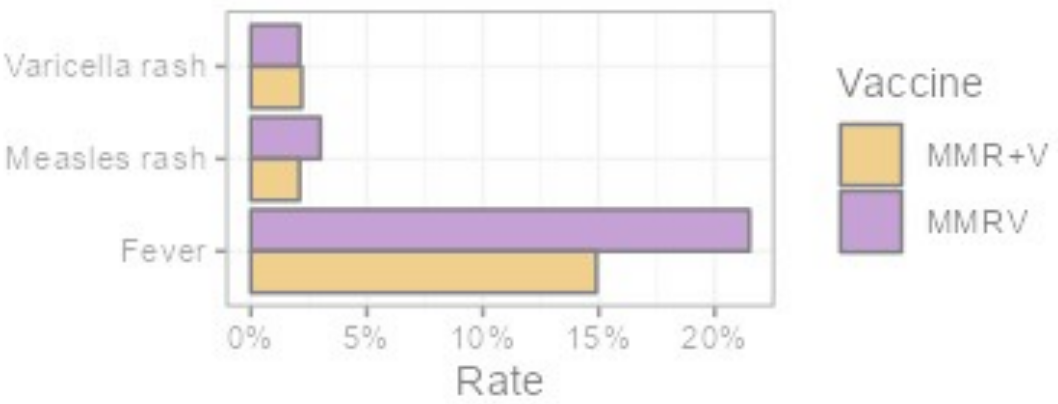

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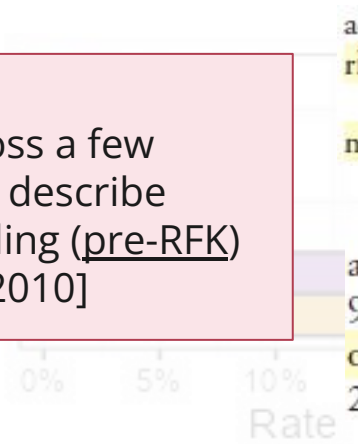
"Measles-like rash"
At this point, I've come across a few places in the literature that describe "**measles-like rash**", including (pre-RFK) **CDC/ACIP documents** [**1**, 2010]

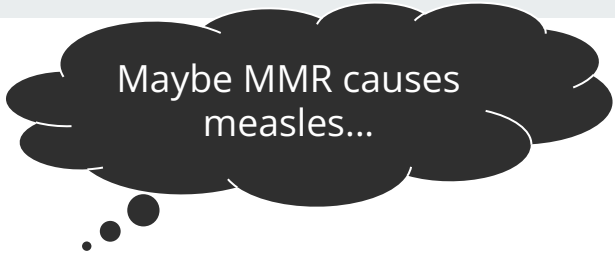
administration of M-M-R®II have not been found to increase the risk of subsequent seizures or neurodevelopmental disabilities.[47]

The logistic regression models for evaluating fever and measles-like rash indicated that no single factor was contributing to



and varicella vaccine recipients (risk difference [RD]: 6.6%; 95% confidence interval [CI] = 4.6–8.5). Measles-like rash was observed in 3.0% of MMRV vaccine recipients compared with 2.1% of those receiving MMR vaccine and varicella vaccine

...am I starting to flirt with anti-vax?



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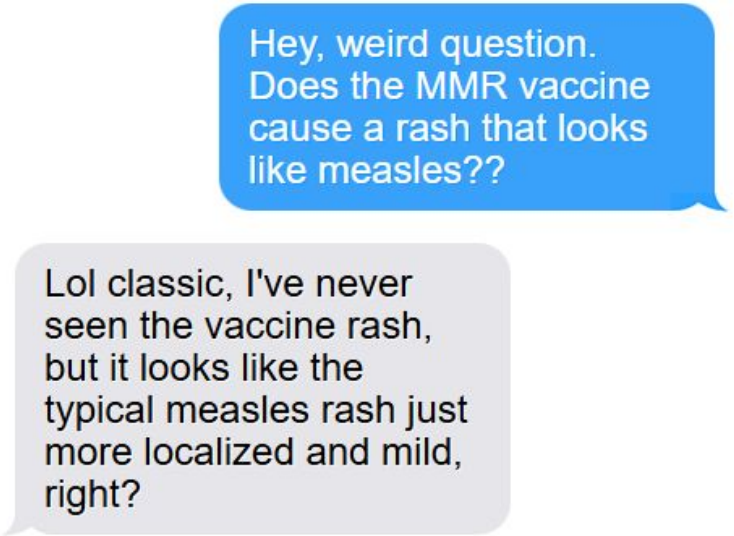

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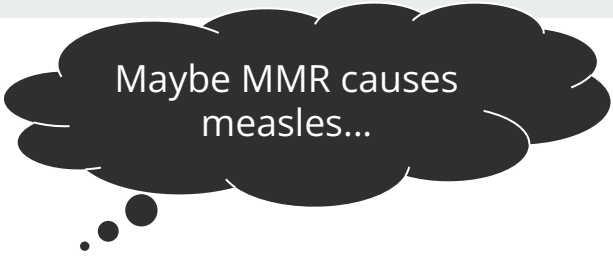

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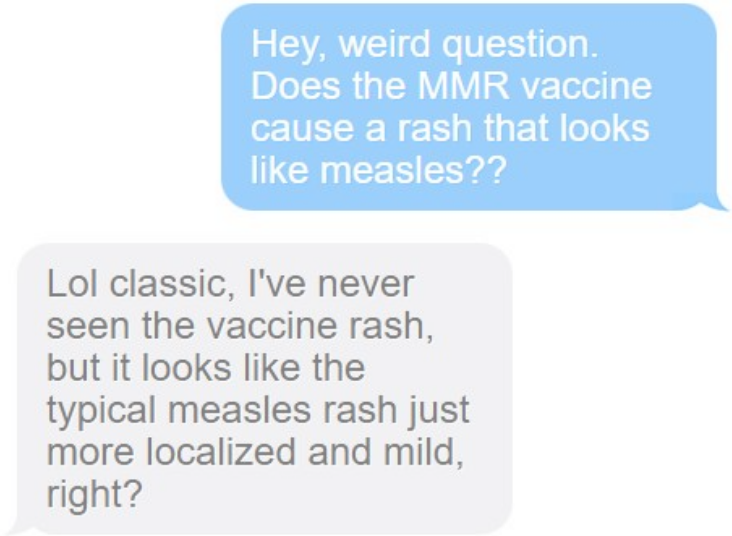
  - **Kids like to get rashes** (pediatrics doesn't get as excited for rashes as we do)



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  - She thinks the rash looks like "**mild measles**" but she's not peds-ID

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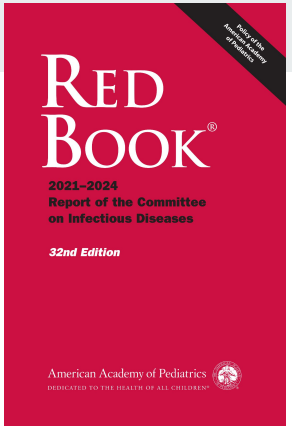
But I was able to find the **"pubmed" terms** describing the rash following the MMR vaccine:

- **MMR vaccine exanthem**
- **Vaccine-associated rash illness** (**VARI**)

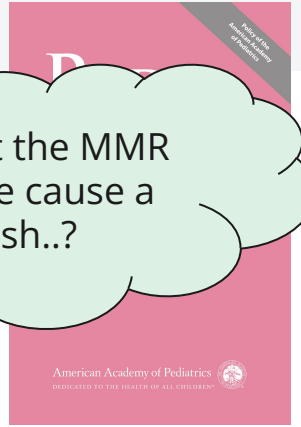
Refined search strategy
No more searching "**does the MMR vaccine cause measles?**"

Back to the Red Book [6]



Adverse Events . ... **Transient rashes** have been reported in approximately **5% of vaccine recipients**.

The more common situation



Doesn't the MMR vaccine cause a rash..?

MEASLES

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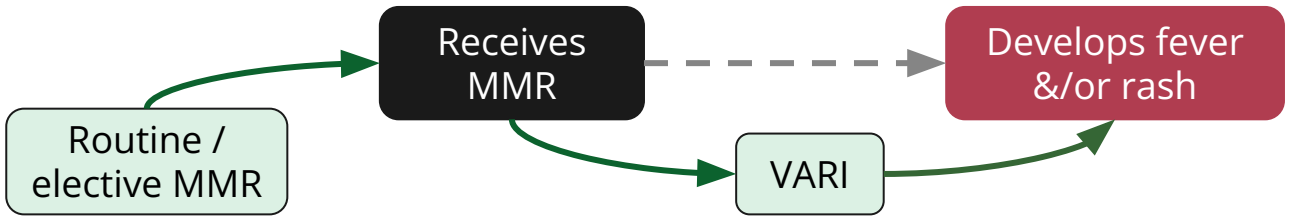

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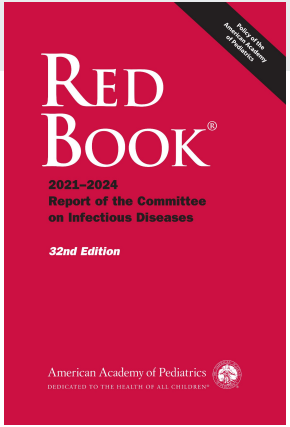

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MEASLES

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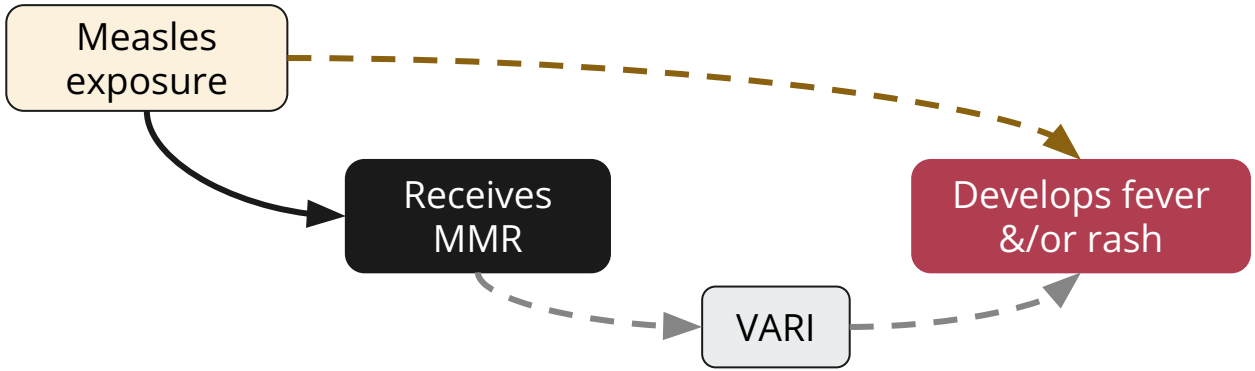

[6] How to distinguish VARI from wild type measles?

Mentimeter

- Distribution of the rash
- Timing of the rash
- Fevers
- The three C's
- Koplik spots
- Sequencing

Distinguishing them clinically

- There is no universally accepted definition for vaccine-associated rash illness (VARI)
  - So meta-analyses are non-existent

Distinguishing them clinically

- There is no universally accepted definition for vaccine-associated rash illness (VARI)
  - So meta-analyses are non-existent
- ...but there is a definition for measles!

CDC's measles case definition * [8]

An acute illness characterized by:

1. Generalized, **maculopapular rash** lasting ≥3 days; **--and--**
2. **Temperature ≥101°F** (38.3 C) **--and--**
3. At least **one of the 3C's**
   - Cough, coryza, or conjunctivitis

* There is some more nuance here

Clinical Infectious Diseases
BRIEF REPORT

Martin et al [7]

During 2017, Minnesota experienced a **major measles outbreak** within the **Somali-Minnesotan community**

- This population had **low MMR vaccination rates** (the **2014 birth cohort** had **42% MMR uptake**)
- As part of the public health response, they **administered over 51k MMR doses** (beyond expected)

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Unintended consequences

They experienced a **surge in VARI**
(while measles was also surging)

Clinical Infectious Diseases
BRIEF REPORT

Martin et al [7]

During 2017, Minnesota ex… **Minnesotan community**

- This popu… **uptak…**
- As part o… d expecte…

They actually **experienced my nightmare**:

- Elevated **risk of measles exposure** (from the outbreak)
- And lots of people getting MMR vaccines

…ces
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Clinical Infectious Diseases
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When they compared **wild-type measles cases** to **VARI** cases:

	Measles n=71	**VARI** n=34
…	…	…

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- Both cases had **high rates of fevers**
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Fever	100%	94%
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Conjunctivitis	**66%**	24%

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But wait... How do I tell the difference?

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All three C's	58%	**6%**

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All **VARI cases still needed isolation** for 4 days from rash onset (or until wild-type infection was ruled out)

- But this was in the context of an outbreak (unlike our patient)

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What about testing?

- **Serologies** are **not very helpful** [**8**, CDC 2025], since it doesn't distinguish between vaccine-induced immunity and natural infection
  - IgM may not be detectable until 8-14 days after vaccination
  - IgG may not be detectable for up to three weeks after vaccination
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- **Measles RT-PCR** does not distinguish between the vaccine RNA -vs- wild-type RNA [**8**, CDC 2025

What about testing?

- **Serologies** and **measles RT-PCR** are **not very helpful** [**8**, CDC 2025]
- **Genotyping** is able to distinguish the two
  - All **measles vaccines** are derived from **genotype A**, which has gone extinct [**10**]
  - But this is **slow and expensive** (but useful in outbreaks)

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  - All **measles vaccines** are derived from **genotype A**, which has gone extinct [**10**]
  - But this is **slow and expensive** (but useful in outbreaks)
- The **Measles Vaccine (MeVA) Assay** comes to save the day! [**8**]
  - RT-PCR for the **measles vaccine strains** --and-- the **standard rRT-PCR assay** (that detects all measles strains)
  - Available at **CDC** and **Association of Public Health Laboratories** reference centers

What about testing?

My inference [citation needed]

MeVA was not available to the folks in Minnesota **during their outbreak**

This must have been a true nightmare

- They had to contact trace and isolate *all these VARIs* while waiting on sequencing
- This probably should have been more than a brief report in *CID*

Clinical Infectious Diseases

BRIEF REPORT

From Martin et al [7]

At the **time of the outbreak**, the measles vaccine-specific RT-PCR test **[MeVA] was not available** at the [MN health dept]

...rapid laboratory confirmation of VARI is the **only way to avoid unnecessary control** measures that can **drain public health and healthcare resources** during measles outbreaks...and **preserve public health resources for true measles case responses**.

Who else has experienced this problem before?

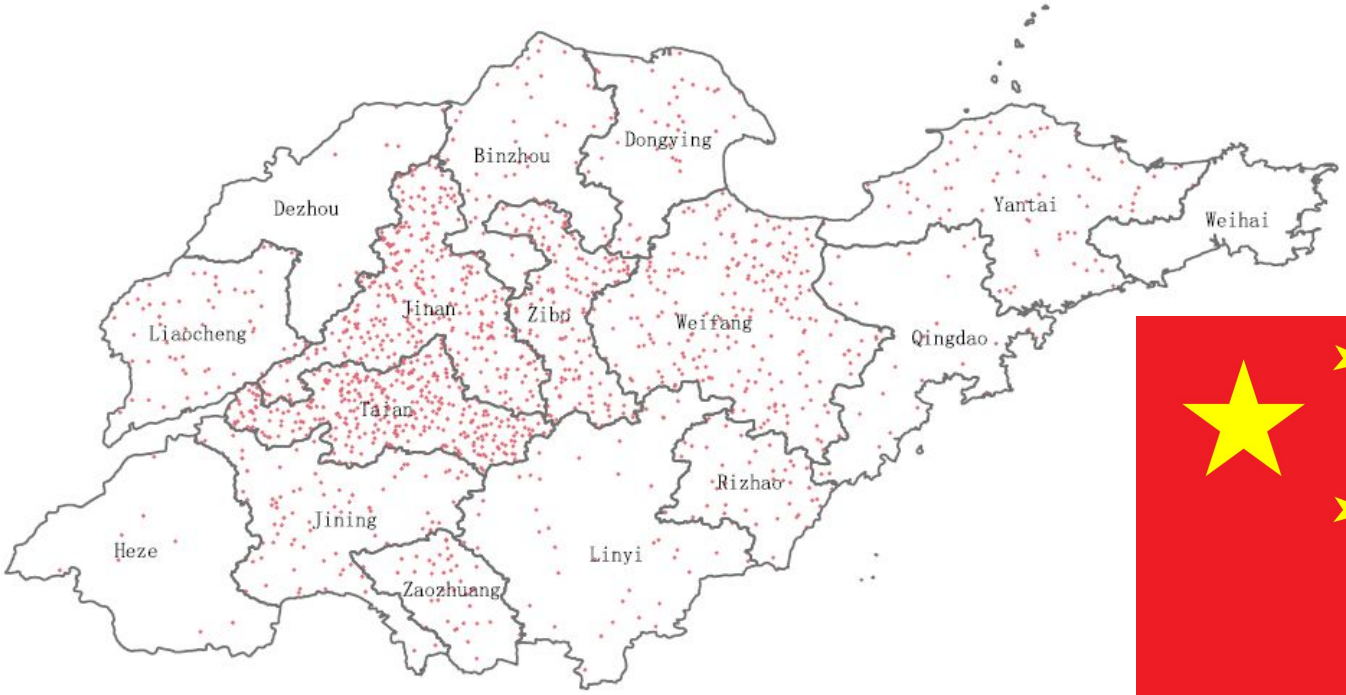

Figure 2: Wang et al [**11**]

Cui et al [10]

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Large study from China from 2011 to 2018

- **Surveillance Data**: The study utilized data from the **Measles Surveillance System** (MSS) and the Chinese Measles Laboratory Network (CMLN)
- **Case Identification**: identified 15,169 cases **confirmed by genotyping**
  - **14,902 wild-type** measles cases
  - Only **101 VARI** cases

Cui et al [10]

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Temporal distribution after vaccination

- VARI onset: The number of cases **peaks on the 8th day**
  - 97% of cases occur within 14 days of vaccination
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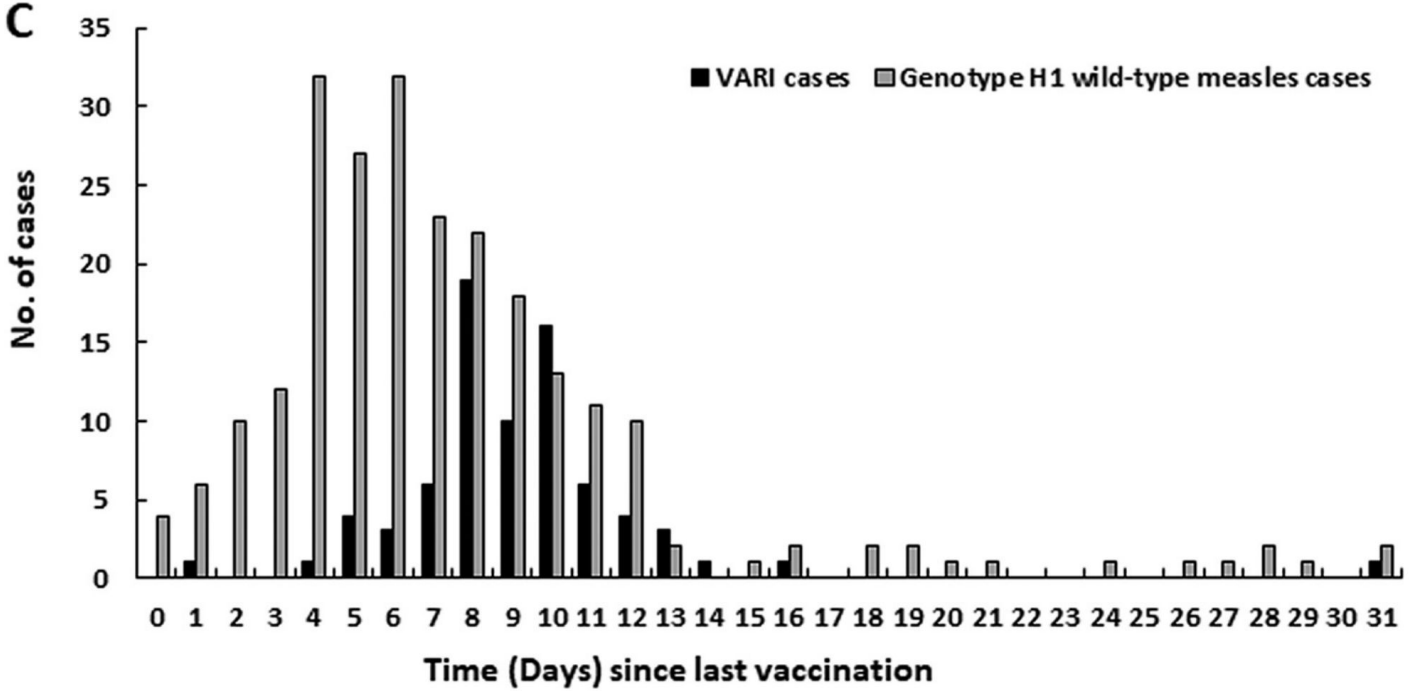
- C



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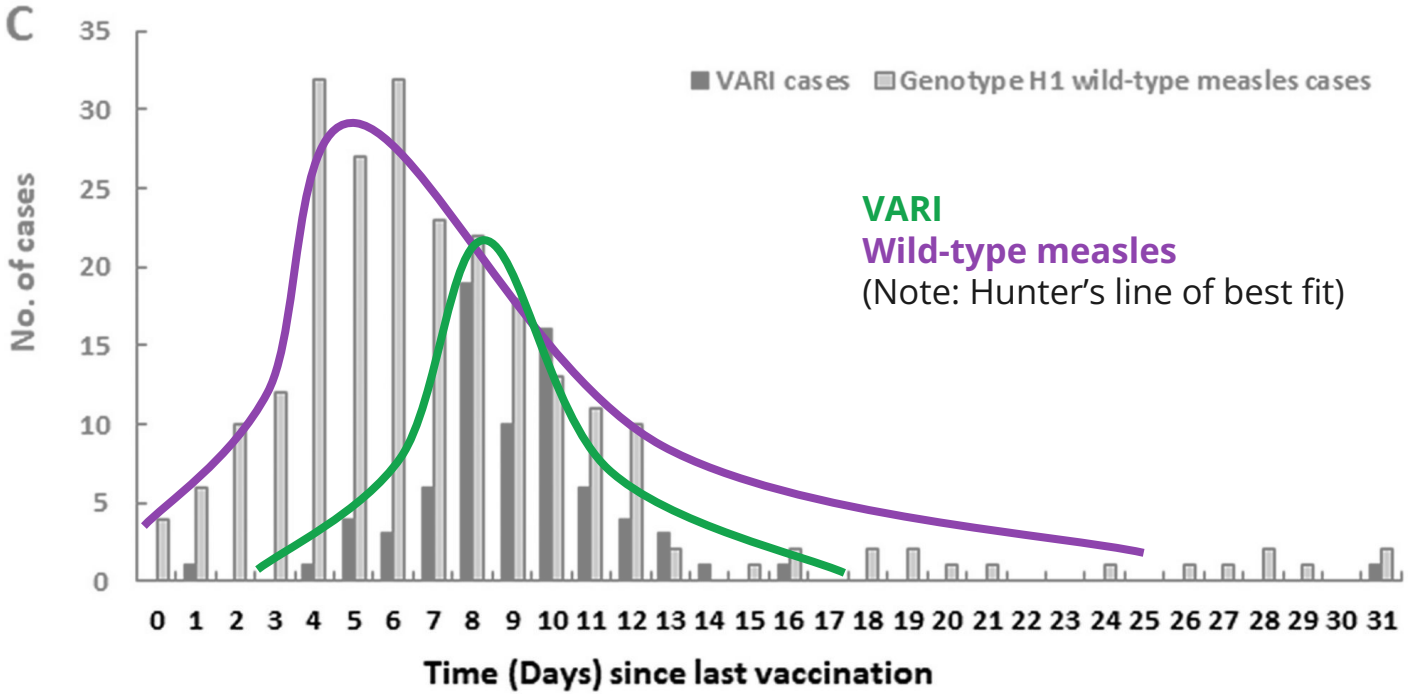

VARI
Wild-type measles
(Note: Hunter's line of best fit)

Cui et al [10]

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Clinical Symptom	**VARI Cases** (n=76)	**Wild-Type** (n=9,533)	P-Value
Fever	99%	99%	0.516
Rash	100%	99%	1.000
"3Cs" (any)	**49%**	**92%**	<0.001
Cough	39%	91%	<0.001
Coryza	26%	67%	<0.001
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Complications	**4%**	**13%**	0.020

100% of the “complications” (n=3/76) in the **VARI group** was diarrhea

Cui et al [10]

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No evidence of human-to-human transmission of the measles vaccine virus (they looked for mutations in the VARI cases, beyond the scope of this talk)

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Both groups had **similar symptoms** (moderate fever, rash, and one of the "3Cs"), so **difficult to distinguish VARI** from wild type measles

As **wild-type measles increased**, so **did cases of VARI**

- Again, highlights the public health importance of VARI during outbreaks

Wang et al [11]

Quite similar to Cui [10], used data from China's MSS (Measles Surveillance System) from 2015-2021. Unlike Cui, the study by Wang

Wang et al [11]

Quite similar to Cui [10], used data from China's MSS (Measles Surveillance System) from 2015-2021. Unlike Cui, the study by Wang

- Only on the **Shandong province**
- Also included "**clinically diagnosed**" VARI cases

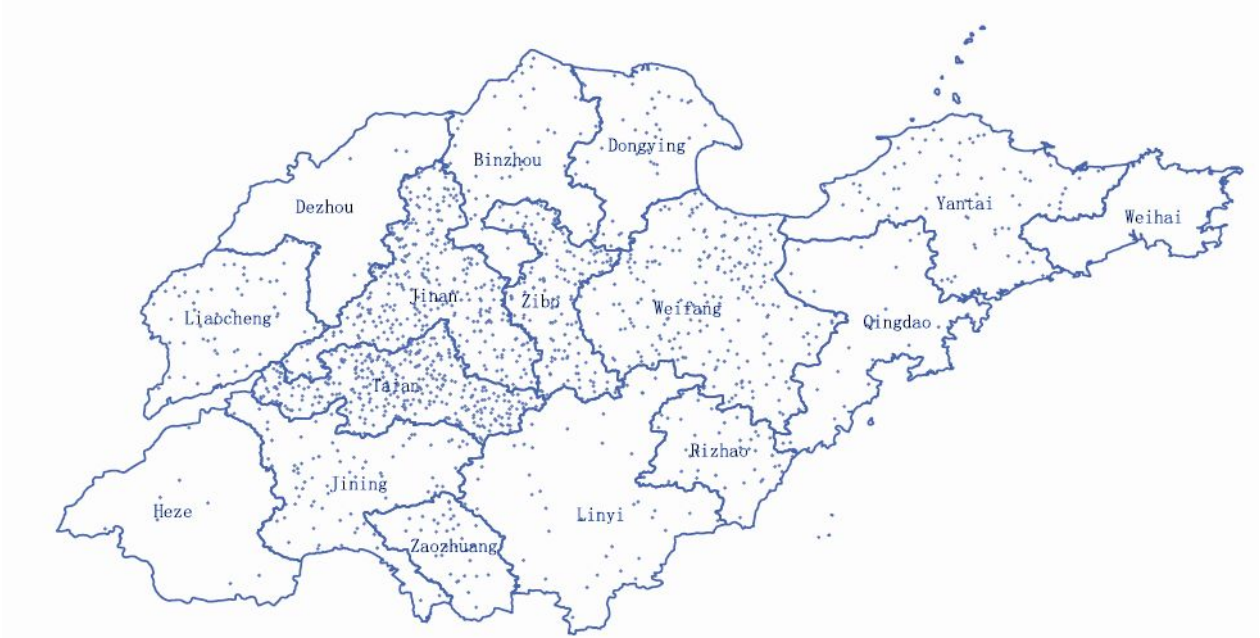
Wang -vs- Cui

	Wang [11]	Cui [10]
Geography	**Only Shandong**	All of China
How did they identify VARI?	Genotype –**or**– **clinical criteria**	**Only via genotyping**
Number of cases		
VARI	189	101
Measles	9,928	14,902

Wang is approaching it from very similar angle as the Minnesota DOH authors (CID article [**7**])

Wang et al [11]

- In their geographic information system analysis, found **VARI cases are geographically clustered**



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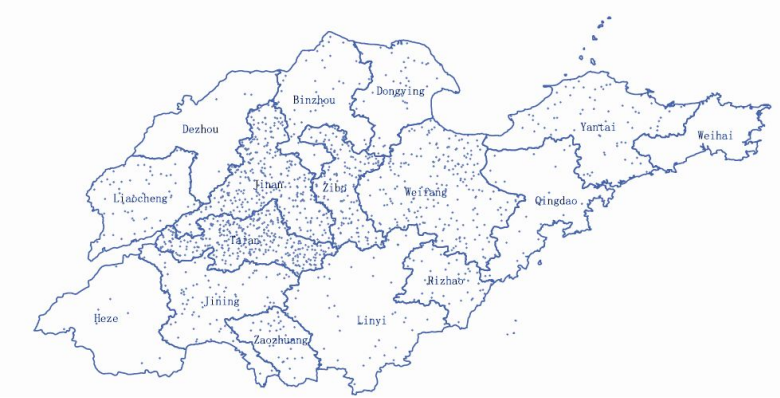

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- Also found **fever and rash** are typical in VARI, with a **median onset of fever at 8 days** after MMR
  - Same results as Cui [**10**]
  - Also falls in line with **original MMR studies** (9 days) [**5**]

Table 2 from Lancet study in 1986 [**5**]

	Days after injection									
	1–6		7–8		9–10		11–12		13–21	
	No	Rate	No	Rate	No	Rate	No	Rate	No	Rate
Moderate fever (38·6–39·5°C rectal):										
MMR	9	8	34	29	42	36	21	18	7	6
Placebo	9	7	13	11	10	9	10	9	9	8
Difference	0	1	21	18	32	27	11	9	−2	−2

Wang et al [11]

- In their geographic/GIS analysis, found **VARI cases are geographically clustered**
- Also found **fever and rash** are typical in VARI, with a **med**
  MMR

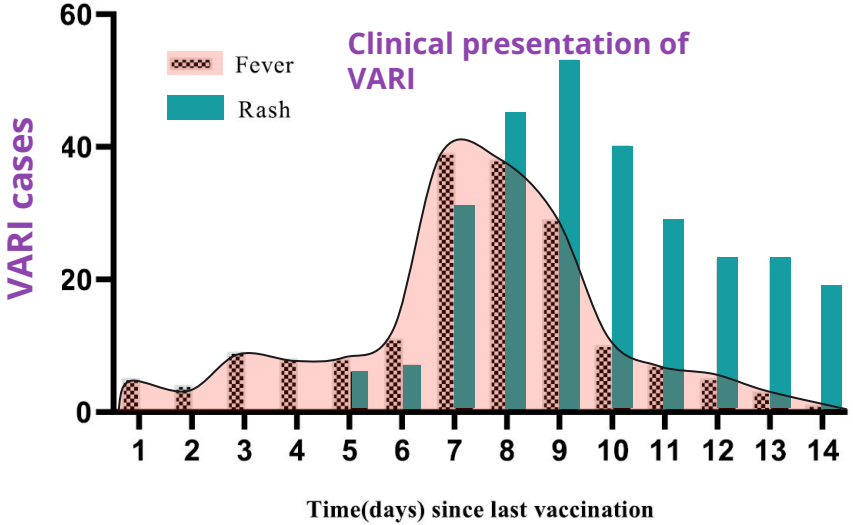
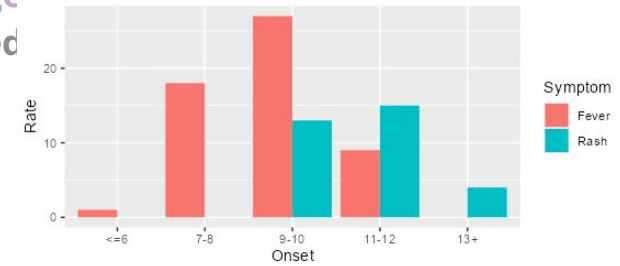


Figure 3 from Wang (2025) [11]



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Generalised rash:										
MMR	22	19	28	24	49	43	56	48	27	24
Placebo	23	20	29	25	35	30	39	33	24	20
Difference	−1	−1	−1	−1	14	13	26	15	3	4

Wang et al [11]

- In their geographic/GIS analysis, found **VARI cases are geographically clustered**
- Also found **fever and rash** are typical in VARI, with a **median onset of fever at 8 days** after MMR
  - Same results as Cui [10]
  - Also falls in line with **original MMR studies** (9 days) [5]
- VARI timing is pretty consistent across studies…

- **One in ten VARIs** had **Koplik spots** (20/189)
  - This is lower than Cui's [10] estimate of 25%
  - But there is likely cross over (since both using MSS)

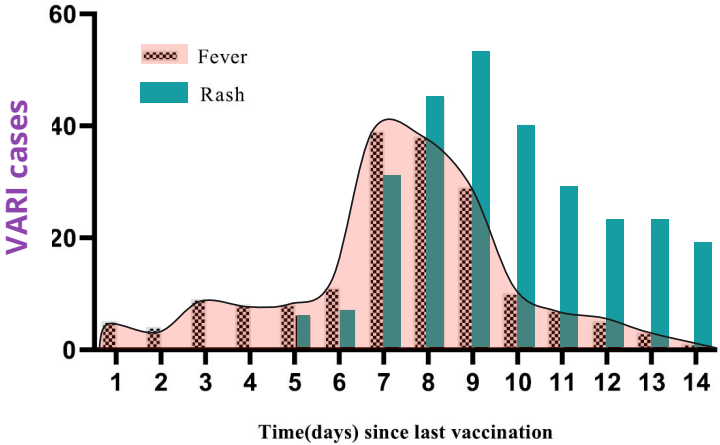

Figure 3 from Wang (2025) [11]

Wang et al [11]

Of their 189 VARI cases, 109 (57%) had throat swabs collected

- They were **only able to genotype 30%** of these cases (33/109)
- Likely due to **delayed sample collection** and **low viral load**

	BMC **Wang [11]**	AMERICAN SOCIETY FOR MICROBIOLOGY **Cui [10]**
Geography	**Only Shandong**	All of China
VARI criteria	Sequencing –**or**– **clinical**	**Only via genotyping**
# **VARI**	n=189	n=101
# **Measles**	n=9,928	n=14,902

Learning points & take aways

Learning points & take aways

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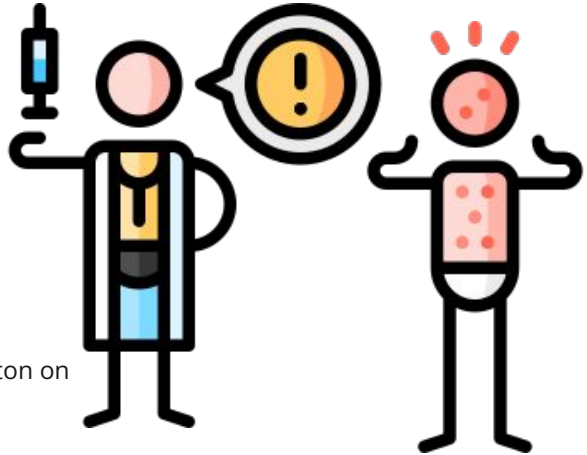

Slides available on hunterratliff1.com/talk/; Citations available via QR code or via the “citations” button on the website

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BG subtle (#e2eaf7)

Emphasis (#b03d50)
Danger (#DC4C64)
BG subtle (#fae4e8)

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Pink (#FF6F61)
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Info (#54B4D3)
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Emphasis (#0c622e)
Success (#14A44D)
BG subtle (#dcf1e4)

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BG subtle (#f1f2f3)

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Emphasis (#6C3483)
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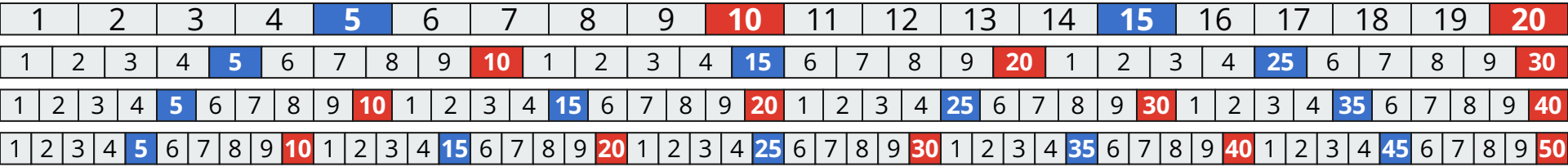

To scale these, select the entire row, go to format options, and make the width the desired width