



We Must Maintain Measles Elimination in the United States: Measles Clinical Presentation, Diagnosis, and Prevention

Clinician Outreach and Communication Activity (COCA) Call

Thursday, August 17, 2023

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Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Identify the clinical presentation of measles and other causes of febrile rash illness which may mimic measles.
2. Diagnose measles infection with appropriate laboratory diagnostics.
3. Identify measles vaccine adverse reactions.
4. Implement measles prevention and public health control strategies.

To Ask a Question

- Using the Zoom Webinar System
 - Click on the “Q&A” button
 - Type your question in the “Q&A” box
 - Submit your question
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- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

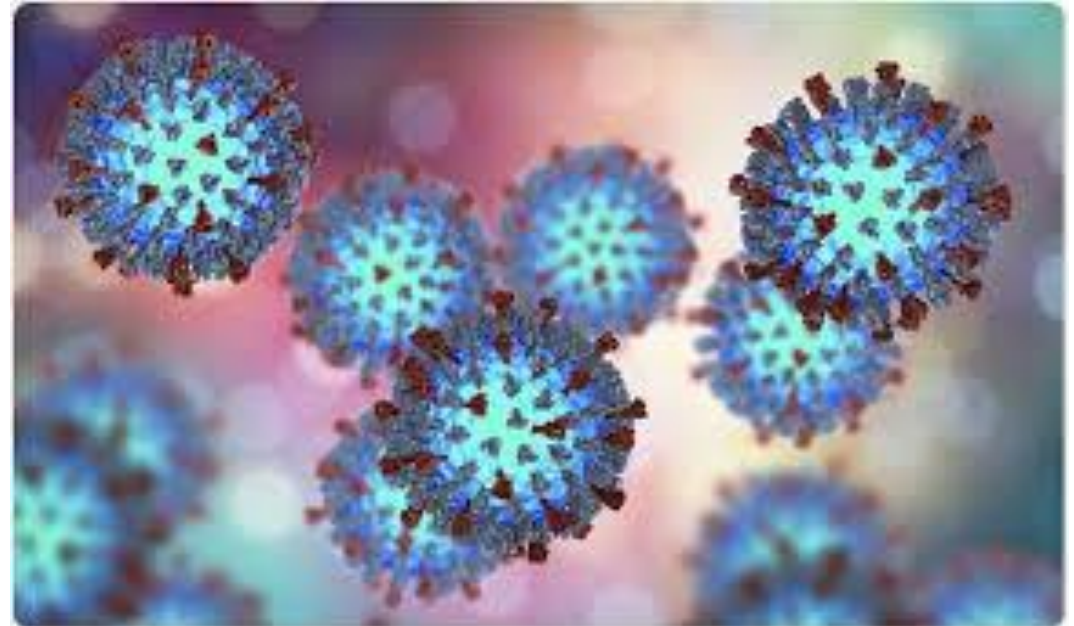
Today's Presenters

- **Adria Mathis, MSPH**
Epidemiologist
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
- **Dan Filardo, MD**
Medical Officer
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
- **Stephen Crooke, PhD**
Lead Research Microbiologist
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

We Must Maintain Measles Elimination in the United States: Measles Clinical Presentation, Diagnosis, and Prevention

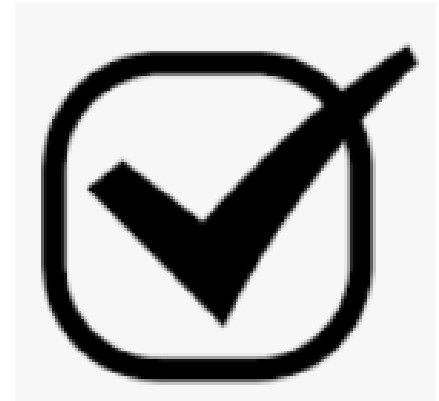
COCA Call

August 17, 2023



Objectives

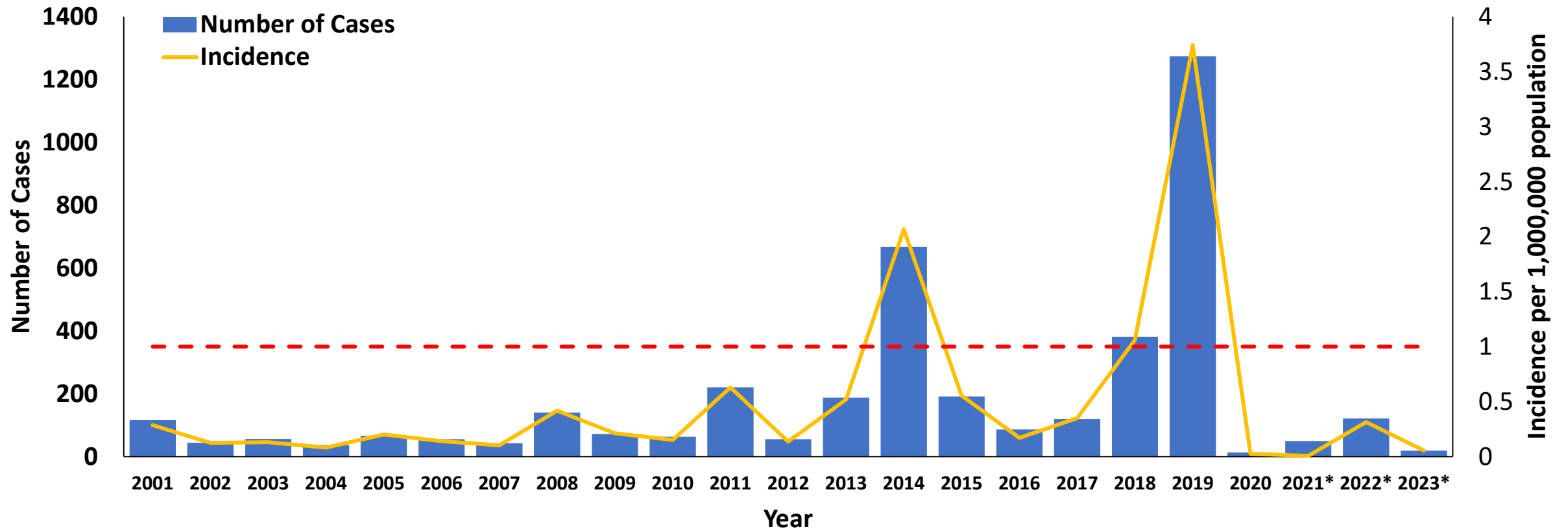
- Identify the clinical presentation of measles and other causes of febrile rash illness which may mimic measles.
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- Implement measles prevention and public health control strategies.



Measles Surveillance, 2023



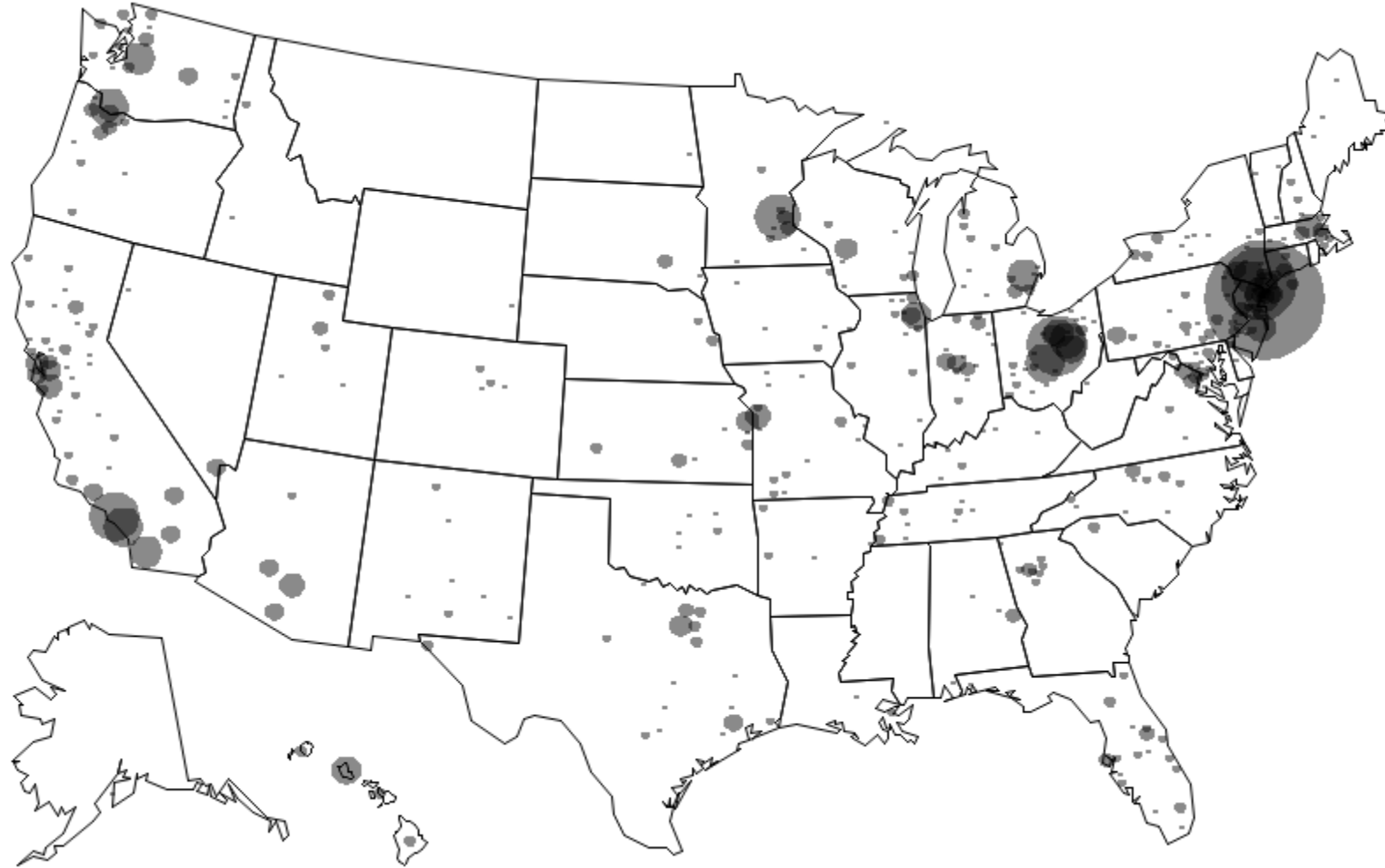
Number of reported measles cases, United States, 2001–2023



2001–2022: Median of 79 cases/year (range: 13–1,274)

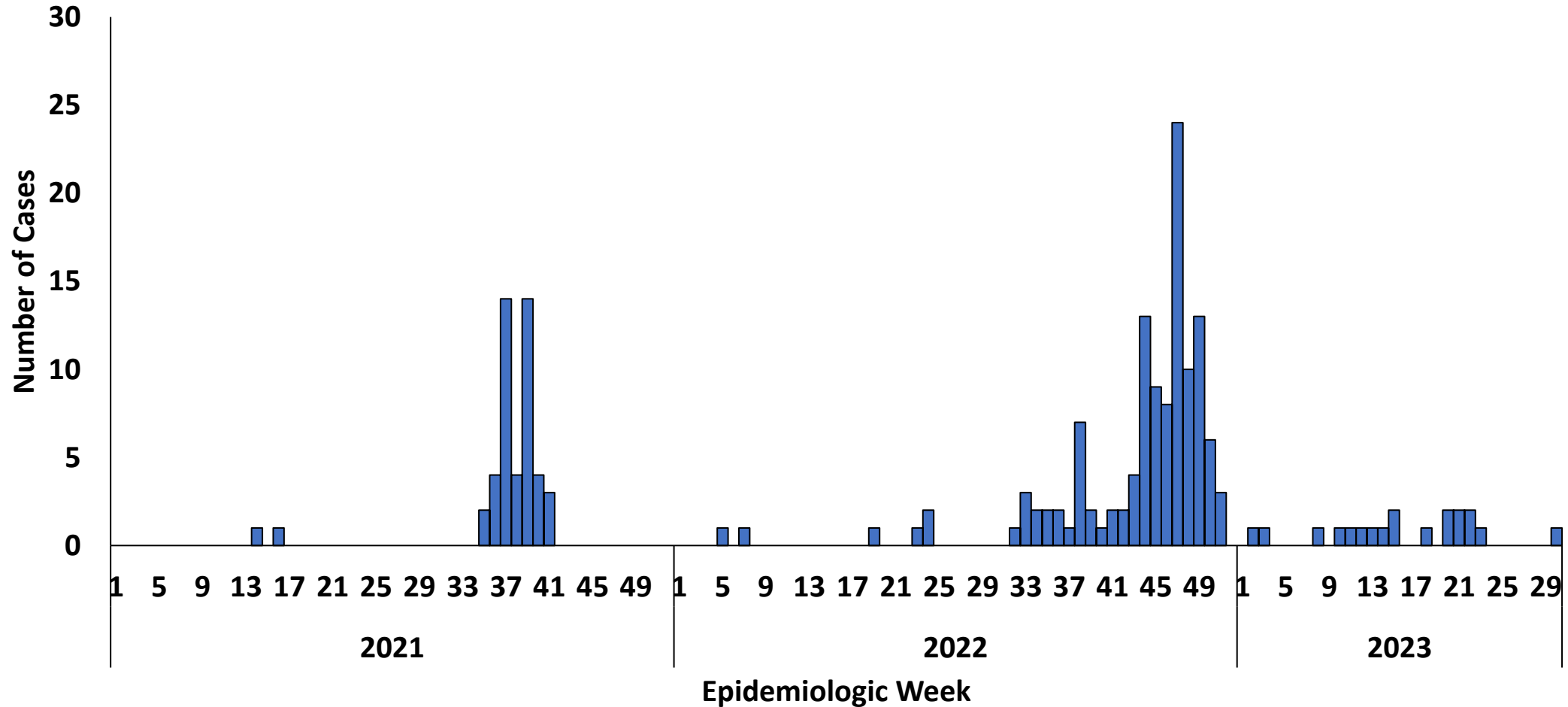
*2023 data as of August 3, 2023. 2021–2023 data are preliminary and subject to change

Measles has been reported from almost all U.S. jurisdictions since 2001



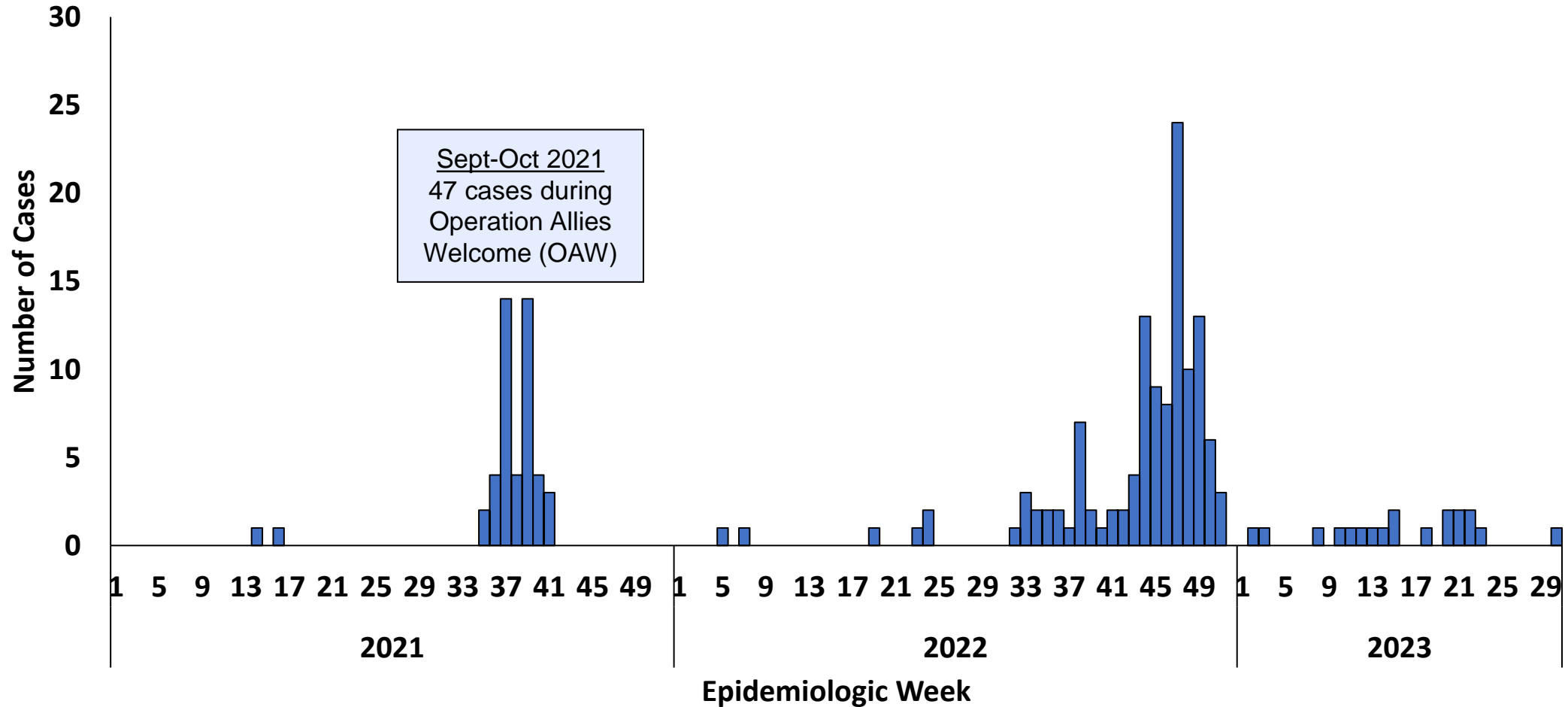
Smallest gray dot = 1 case

Measles cases by epidemiologic week, January 2021–July 2023



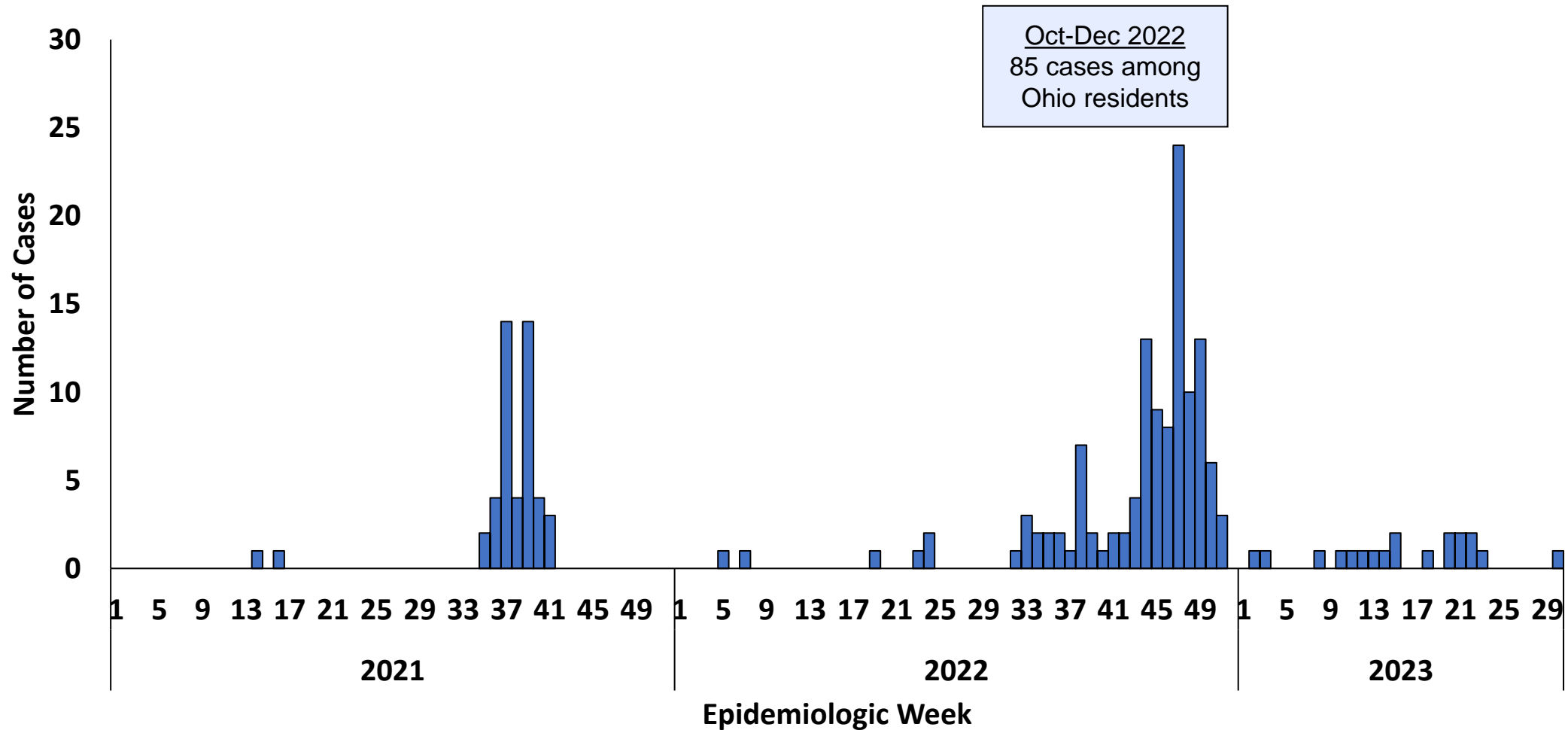
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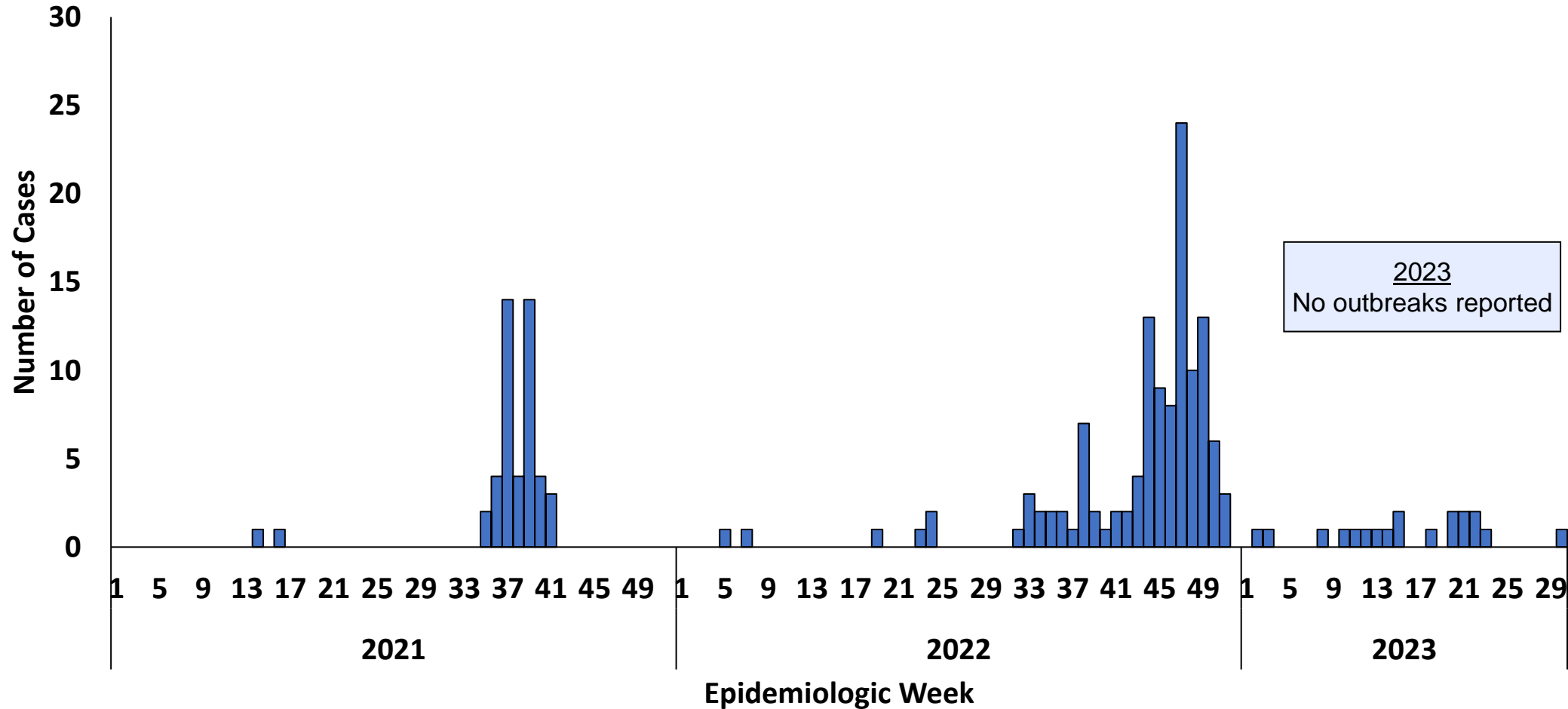
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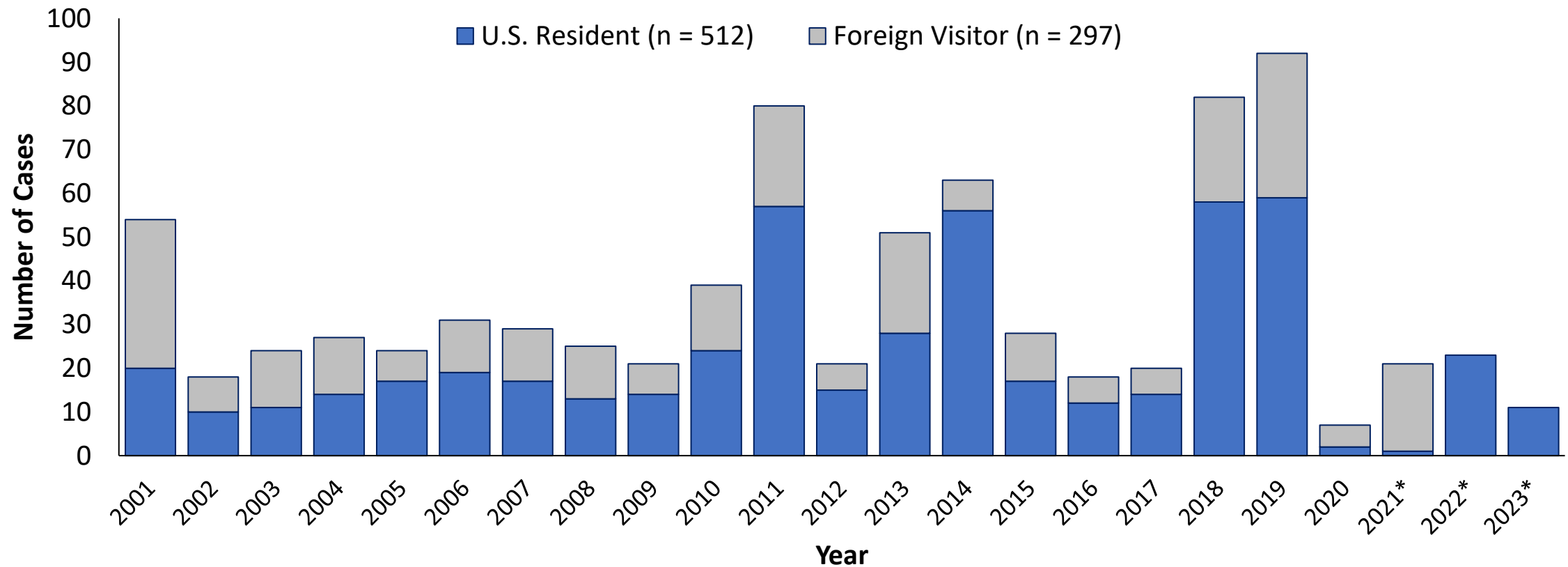
Measles cases by epidemiologic week, January 2021–July 2023



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Measles cases are imported primarily by unvaccinated U.S. residents traveling abroad

- Median 26 importations per year (range: 7–92)

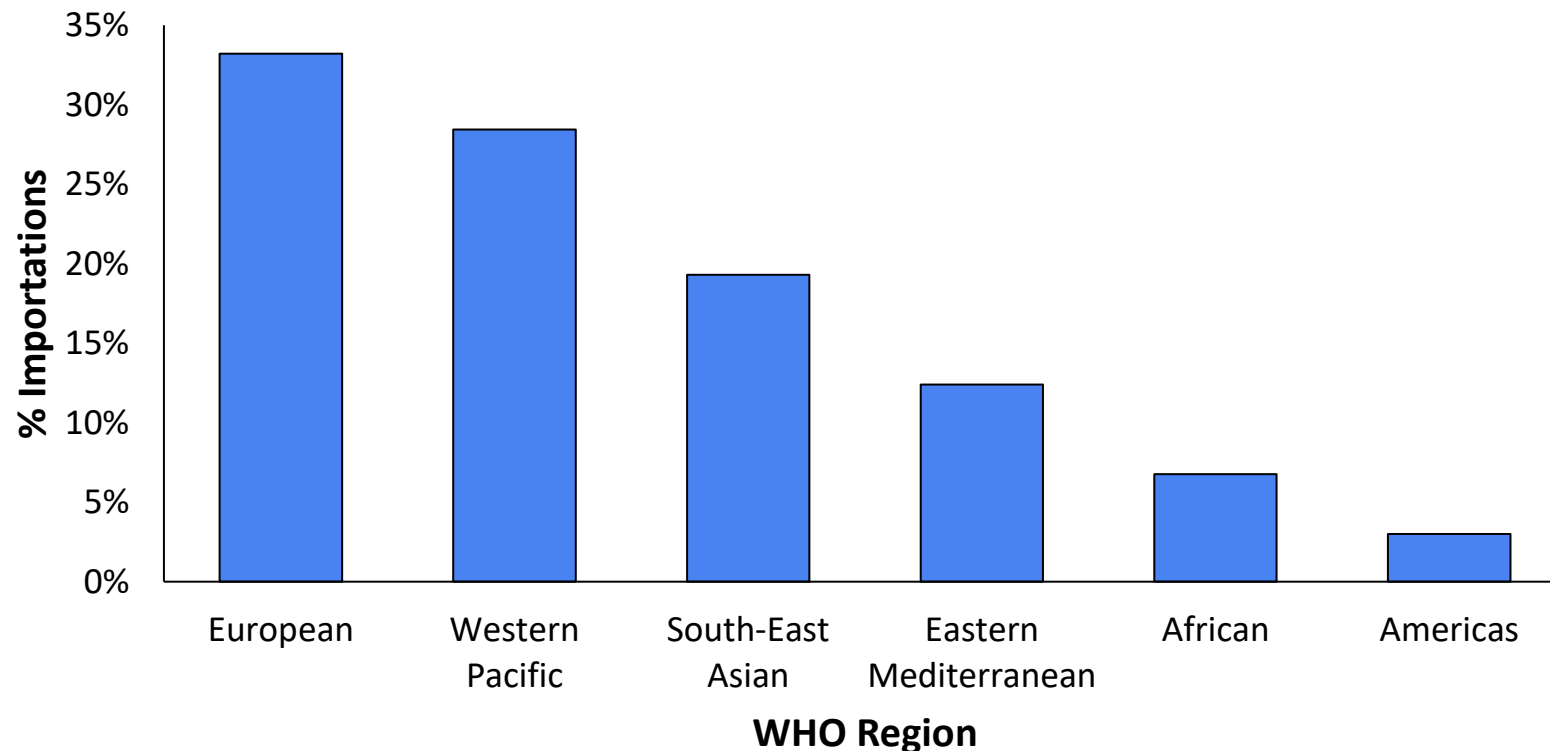


512 (63%) importations among US residents

*2023 data as of August 3, 2023. Data are preliminary and subject to change

International importations

- Among imported cases, 62% of patients reported travel to countries in the European and Western Pacific Regions during their exposure periods
- Top 5 source countries: India, the Philippines, China, Pakistan, and the UK



Knowledge Check #1

- Measles cases in the U.S. are most commonly the result of virus importation by unvaccinated foreign visitors
 - A: True
 - B: False

Knowledge Check #1

- Measles cases in the U.S. are most commonly the result of virus importation by unvaccinated foreign visitors
 - A: True
 - **B: False**

Clinical Overview of Measles

Measles

- An acute, febrile rash illness caused by the measles virus
- Transmitted by direct contact with infectious droplets or airborne route
- Measles is highly contagious
 - 90% of susceptible household contacts will develop illness
 - R_0 (the number of people who are infected by a single case) is estimated to be 12–16 in an unvaccinated population



Measles Notification

- Measles cases require a coordinated and robust public health response
- Measles is nationally notifiable and cases should be reported immediately to the appropriate health department
 - Health departments can assist with testing when measles is suspected



Measles – Clinical Case Definition

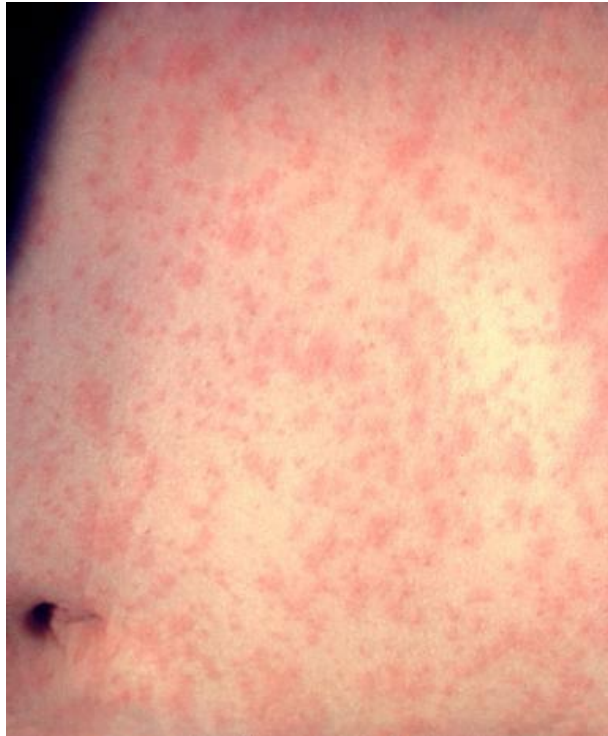
- Fever (up to 105°F)

AND

- Rash

AND

- At least 1 of “The 3 C’s”
 - Cough
 - Coryza (runny nose)
 - Conjunctivitis



Measles rash



Measles conjunctivitis

Measles Rash

- Typical presentation:
 - Starts on face, at hairline, or behind ears
 - Spreads downwards to neck, trunk, extremities
 - Maculopapular
 - › Small raised or flat red bumps
 - › Spots may join together as the rash spreads
 - Not usually itchy
 - Koplik spots may be present on buccal mucosa

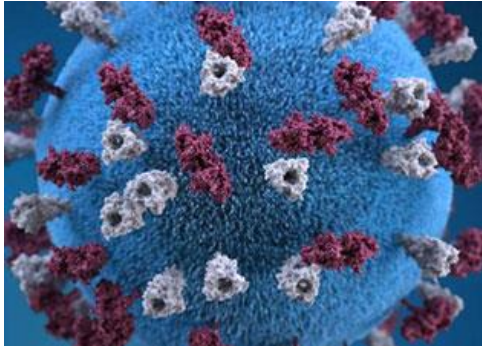


Koplik Spots

Measles Rash

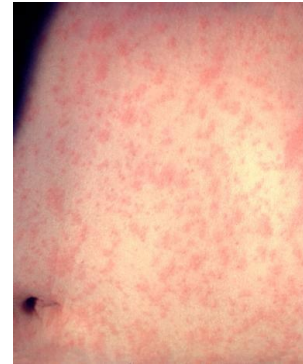
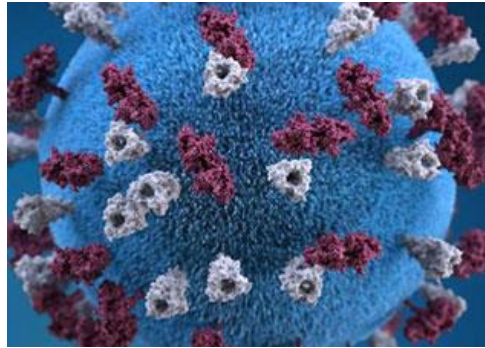


Measles – Typical Timeline



Incubation Period
10-14 days

Measles – Typical Timeline



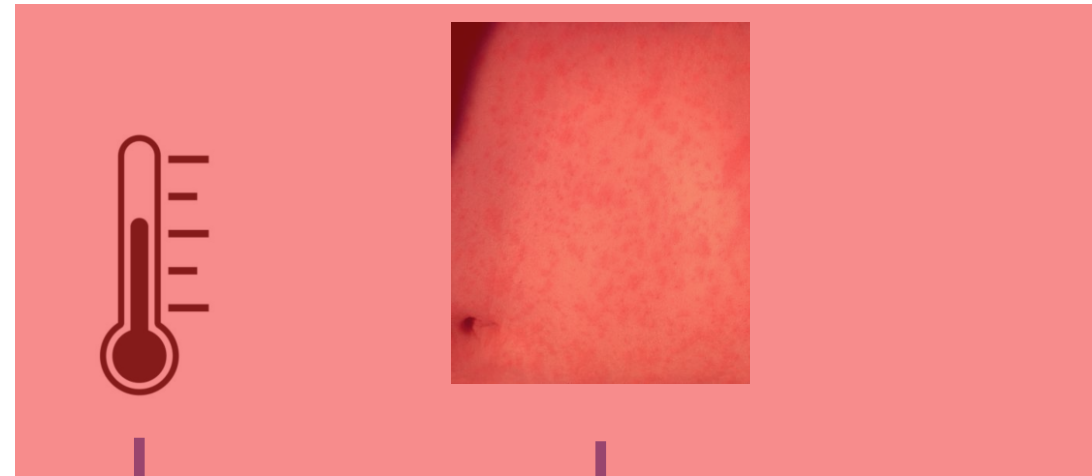
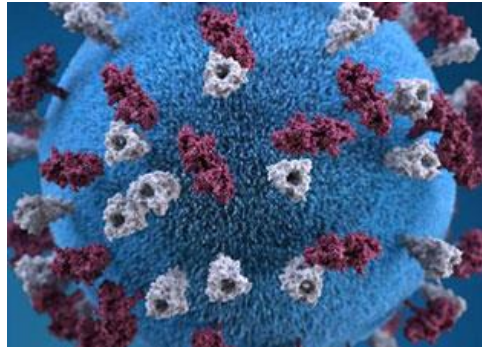
Day -4 to -2

Day 0

Prodrome

Measles – Typical Timeline

Contagious



Day -4 to -2

Day 0

Day 4

Infectious Period:

4 days before rash to 4 days after rash

Measles Complications

| | |
|--------------|--------|
| Diarrhea | 8% |
| Otitis media | 7 – 9% |
| Pneumonia | 1 – 6% |

Measles Complications

| | |
|---|-------------------------|
| Diarrhea | 8% |
| Otitis media | 7 – 9% |
| Pneumonia | 1 – 6% |
| Hospitalization | 1 in 4 cases |
| Encephalitis | 1 per 1,000 cases |
| Death | 1–3 per 1,000 cases |
| Subacute Sclerosing Panencephalitis (SSPE) | 7–11 per 100,000 cases* |

*Bellini WJ et al. J Infect Dis 2005;192:1686–93.

Other Common Causes of Maculopapular Febrile Rash

- **Parvovirus B-19 (Fifth Disease)**
 - “Slapped cheek” rash (photo) which can spread to trunk and extremities; more common in school-aged children than infants
- **Human Herpesvirus 6 (Roseola, Sixth Disease)**
 - Common cause of fever and rash in children; fever often resolves, and rash appears the next day starting on trunk and spreading outwards
- **Enteroviruses**
 - Rash can be maculopapular or urticarial
 - Often on hands/feet (Hand Foot Mouth, photo)
- **Antibiotic sensitivity reactions or allergies**



Slapped Cheek rash



HFM

Clinical Presentation of Measles

- Measles is a highly infectious acute febrile rash illness
- Measles cases should be reported to health departments immediately
- Clinical definition includes:
 - Fever + Rash + 3 C's (cough, conjunctivitis, coryza)
- Measles can cause severe complications, including pneumonia and encephalitis
- Measles has multiple mimickers (e.g., parvovirus, HHV-6)

Knowledge Check #2

- What is the typical presentation of a measles rash?
 - A. Starts on the trunk then spreads up to the hairline and extremities
 - B. Starts on the extremities and spreads everywhere on the body, including the palms and soles
 - C. Starts at the hairline or face then moves down to the trunk and extremities

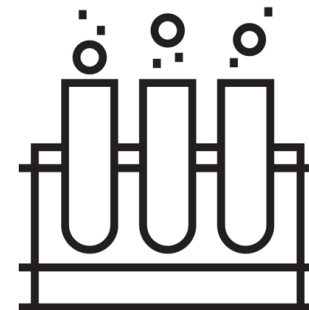
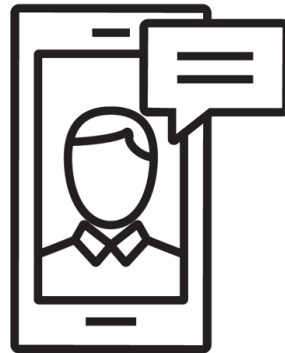
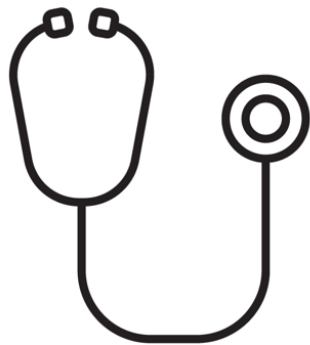
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 - C. Starts at the hairline or face then moves down to the trunk and extremities**

Laboratory Diagnosis of Measles

Bottom Line Up Front

- Clinical, epidemiologic, and laboratory data should all be considered when diagnosing measles infection
- Using serology (IgM) alone to test patients with low pre-test probability of having measles will result primarily in false positive results
- Both serum and NP/OP swabs should be collected for all suspect cases



Measles Serology

- Detection of measles antibodies is useful to help confirm the diagnosis
 - Serology can increase the window in which measles can be diagnosed, if diagnostic or reporting delays are encountered
 - IgM detection starts 1–3 days after rash onset and can be detected for up to 6–8 weeks
 - › May disappear rapidly, be delayed, or not appear at all in vaccinated persons
 - IgM testing alone can be problematic in settings with low measles incidence
 - › Cross-reactivity with other causes of febrile rash illness has been documented*
 - › False positive results are relatively common when the likelihood of measles is low:
 - » There isn't local active transmission and patients have not traveled[†]
 - » Patients have been fully vaccinated and have no known exposure

*Jenkerson SA et al. *N Engl J Med*. 1995;332(16):1103-1104.

[†] Ciccone FH et al. *Rev Soc Bras Med Trop*. 2010;43(3):234-239.

Hiebert J et al. *J Clin Microbiol*. 2021;59(6):e03161-20.

Measles PCR

- rRT-PCR testing can be performed on nasopharyngeal and throat swabs, as well as urine
 - Specimens are ideally collected within 3 days of rash onset, but can be positive up to 10 days after rash onset
 - › It is best to collect specimens for rRT-PCR as soon as possible after rash onset
 - Proper specimen collection, storage, and processing is critical to maintain the stability of viral nucleic acids. Most rRT-PCR assays include a control for specimen integrity (reference gene).
 - **rRT-PCR has much higher sensitivity and specificity than serology**
 - › False positive results can occur, but are **MUCH** less common
 - CDC and state public health labs can perform rRT-PCR

Commercial PCR Testing

- Some large commercial laboratories (e.g., Quest, Labcorp) are offering measles rRT-PCR testing, and others are in the process of onboarding tests
- Some issues that arise with commercial testing:
 - Loss of integration with public health departments
 - Specimens are not maintained appropriately or for long enough to allow for genotyping or additional testing if necessary

Additional Testing is Available

- Serology
 - Paired (acute and convalescent) IgG Testing
 - › Can provide additional evidence of measles infection if other data are inconclusive
 - Avidity Testing (IgG)
 - › Can provide information about breakthrough measles cases among previously vaccinated people

Additional Testing is Available

- Genotyping
 - Assists with outbreak detection and tracking, and should be performed ideally on all rRT-PCR positive specimens
 - Important to document sustained elimination of measles in the U.S.
- MeVA
 - A specialized rRT-PCR assay which can determine if detected measles virus is vaccine-derived or from community transmission
 - Among people recently exposed but also recently vaccinated, can differentiate a vaccine reaction from a measles case
- Both are performed at CDC and vaccine-preventable disease reference centers (CA, MN, NY, WI)

Key Laboratory Diagnostic Points

- Measles serology is a useful piece of diagnostic testing but is limited by:
 - Cross-reactivity with other causes of febrile rash
 - High dependence on disease prevalence
- Diagnostic evaluation of measles should include:
 - Both molecular testing (rRT-PCR) and serology
 - Consideration of the clinical and epidemiologic context (e.g., travel history, vaccination status)
- Additional testing is available at CDC and VPD reference centers, in coordination with state or local public health laboratories

Knowledge Check #3

- What testing is recommended for measles diagnosis?
 - A. Measles IgM only
 - B. Swab from nasopharynx / oropharynx (NP/OP) for rRT-PCR only
 - C. Both serology and a swab for rRT-PCR
 - D. None – measles is a clinical diagnosis

Knowledge Check #3

- What testing is recommended for measles diagnosis?
 - A. Measles IgM only
 - B. Swab from nasopharynx / oropharynx (NP/OP) for rRT-PCR only
 - C. Both serology and a NP/OP swab for rRT-PCR**
 - D. None – measles is a clinical diagnosis

Measles Vaccination



Measles Vaccine

- Measles vaccine was licensed in the U.S. in 1963, and combination MMR vaccine was licensed in 1971
- MMR is an attenuated (weakened) live virus vaccine
 - The vaccine cannot cause measles, mumps, or rubella and cannot be transmitted from person to person
 - However, transient side effects can occur which can mimic these diseases
- Vaccine is highly effective
 - 1 dose: ~93% protection
 - 2 dose: ~97% protection
- MMR vaccination has an excellent safety record



MMR Vaccine Routine Recommendations

- Pediatric vaccination schedule
 - First dose at 12–15 months
 - Second dose at 4–6 years of age
 - A dose between 6-11 months of age can be given for travel or outbreak response
 - › If a “zero” dose is given between 6–11 months of age, two more doses should be given on the usual schedule

MMR Vaccine Recommendations for Adults

- Adults who have presumptive evidence of immunity* include:
 - Birth before 1957
 - Laboratory evidence of immunity (positive IgG)
 - Prior laboratory confirmed measles diagnosis
- Adults without evidence of immunity generally should get one dose of MMR
 - Two doses are required/recommended for high-risk adults
 - › Healthcare personnel
 - › International travelers
 - › Postsecondary school students

2013 ACIP recommendations: <http://www.cdc.gov/mmwr/pdf/rr/rr6204.pdf>

2019 Adult Immunization schedule: <http://www.cdc.gov/vaccines/schedules/hcp/adult.html>

* Apart from written documentation of age-appropriate vaccination

MMR Recommendations for International Travelers

- CDC recommends that all U.S. residents older than age 6 months who will travel internationally receive MMR vaccine prior to departure if they are without evidence of immunity:
 - Infants 6–11 months of age: 1 dose of MMR vaccine
 - › Followed by two more doses on the typical pediatric schedule
 - Children 12 months of age or older: 2 doses of MMR vaccine, separated by at least 28 days
 - Teenagers or adults without evidence of immunity: 2 doses of MMR vaccine separated by at least 28 days

MMR Vaccine Contraindications

- Severe immunocompromising conditions (e.g., hematologic malignancy, receipt of chemotherapy, long-term immunosuppressive therapy)
 - HIV if CD4 % < 15% or absolute CD4 <200
- Family history suggestive of a congenital immunocompromising condition, unless assessed to be immunocompetent by a clinician or laboratory testing
- History of severe allergic reaction to MMR or to an MMR vaccine component (e.g., gelatin)
- Pregnancy

MMR Vaccine Adverse Events

- MMR vaccine is generally very well tolerated
- Common side effects include:
 - Fever (<15%)
 - Brief rash (5%)
 - Lymphadenopathy (5% of children, 20% of adults)
- Rare serious adverse events include:
 - Anaphylaxis (2–14 events per million doses)
 - Febrile seizures (1 event per 3–4,000 doses)
 - Low platelet count (1 event per 40,000 doses; may be higher risk if known ITP)

MMR Can Cause a Self-limited Rash

- MMR can cause a short-lived febrile rash syndrome that is not contagious to others
- Differentiating measles from an MMR reaction in the setting of an outbreak can be challenging, especially if MMR was given to prevent measles after an exposure
 - Serology cannot differentiate measles infection from measles vaccination
 - Molecular testing (MeVA) **can** differentiate measles from an MMR reaction



Rash or URI Panels May Detect Vaccine Reactions

- Some commercial labs nationally have begun offering measles rRT-PCR as part of a viral exanthem or upper respiratory infection panel
- Positive results for measles have so far only detected vaccine reactions
- Clinicians should be aware that measles PCR can detect vaccine-derived measles virus 14+ days after MMR vaccination



MMR Review

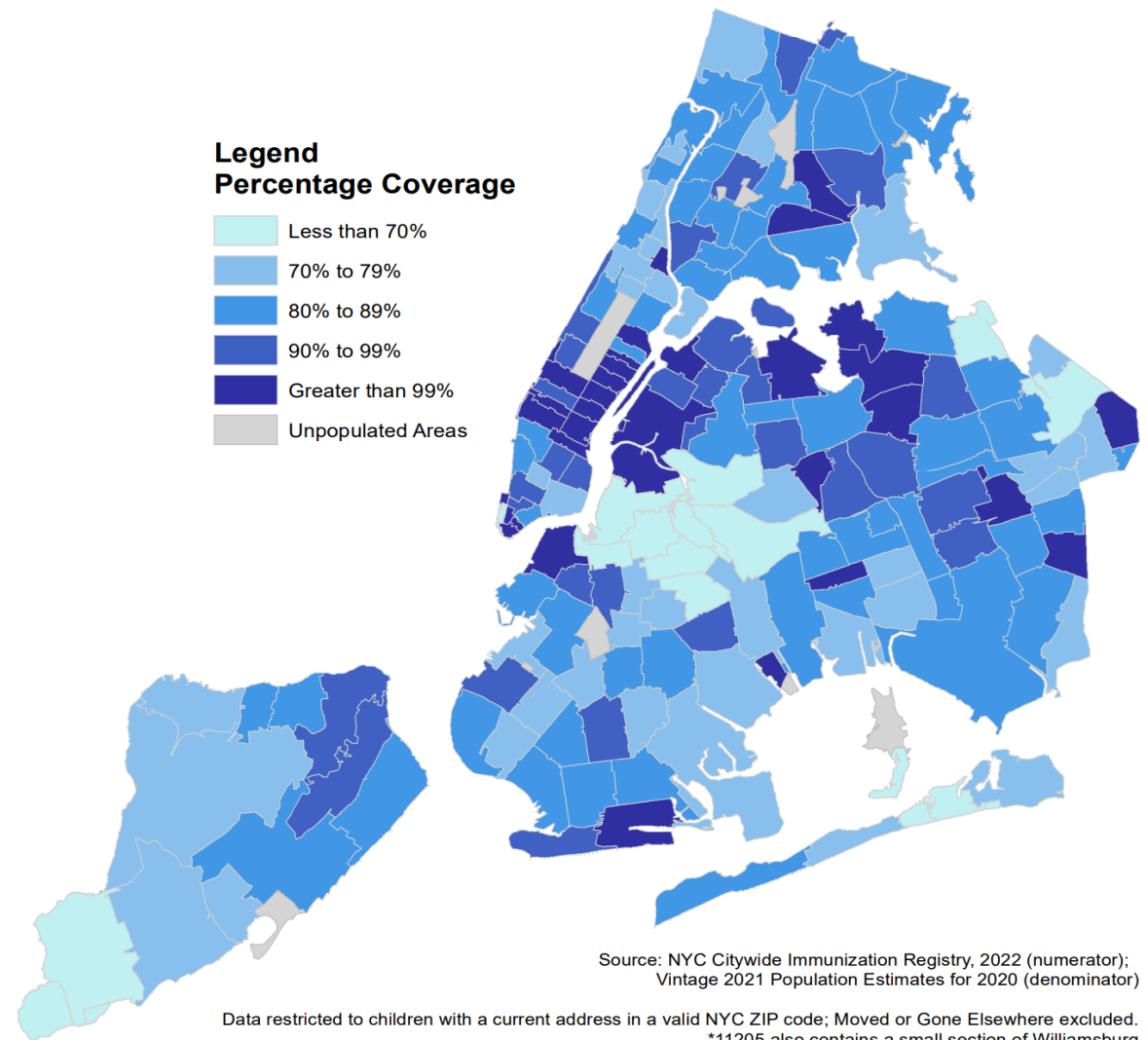
- MMR is a safe and effective vaccine
- MMR is contraindicated for pregnant people and people who are severely immunocompromised
- International travelers should be assessed for prior vaccination or evidence of immunity, and provided MMR if appropriate for protection
- MMR can cause a self-limited febrile rash, but molecular testing can distinguish between measles and a vaccine reaction if necessary

Measles Prevention



Regional Differences in Coverage Can Hinder Measles Control

- CDC is working to estimate fine-area coverage for measles vaccination to identify regions where measles may spread more easily



National Coverage with 2 Doses of MMR Fell <95%, and Disparities Persist

| Birth Year | MMR1 coverage (by age 24 months)* |
|-------------------|--|
| 2017–2018 | 91.6% |
| 2018–2019 | 91.6% |

| School Year | MMR2 (~5–6 years of age)[§] |
|--------------------|---|
| 2019–2020 | 95.2% |
| 2020–2021 | 93.9% |

*Estimates for MMR1 are from the National Immunization Survey–Child (NIS–Child) and represent the estimated national percent of children born in 2017 and 2018 with provider–reported receipt of at least one dose of MMR by age 24 months.

[§]MMR2 column includes the estimated national percent of children entering kindergarten who have received two MMR doses, as reported by state health departments. The 2020–21 data represent estimates from the 2020–21 school year (see <https://www.cdc.gov/mmwr/volumes/71/wr/mm7116a1.htm>).

National Coverage with 2 Doses of MMR Fell <95%, and Disparities Persist

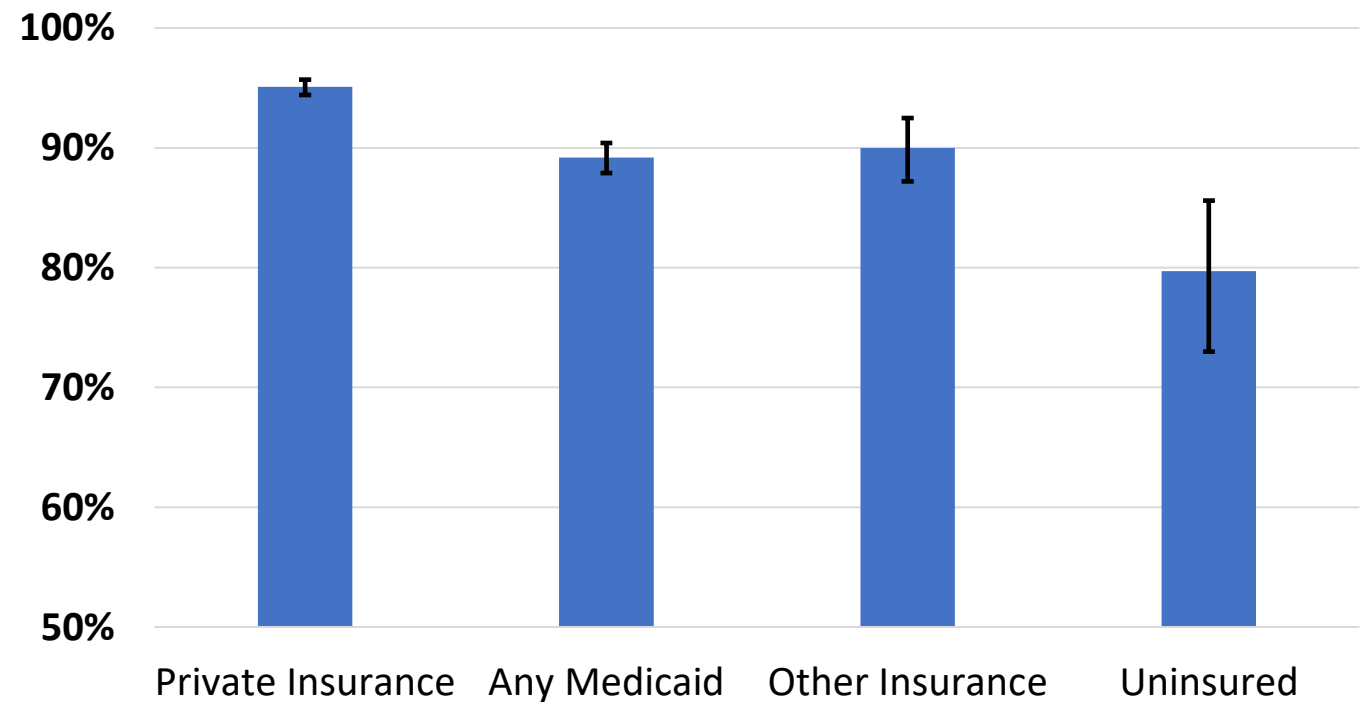
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MMR1 Coverage, 2019–2021



Routine Immunizations on Schedule for Everyone (RISE)



Initiative to get all Americans back on-schedule with their routine immunizations

Understand the size, scope and cause of declines in routine vaccinations resulting from COVID-19 pandemic

Devise an evidence-based strategy and operations plan to better direct CDC routine vaccination catch-up activities

Equip partners with evidence-based strategies and resources to get vaccination back on schedule

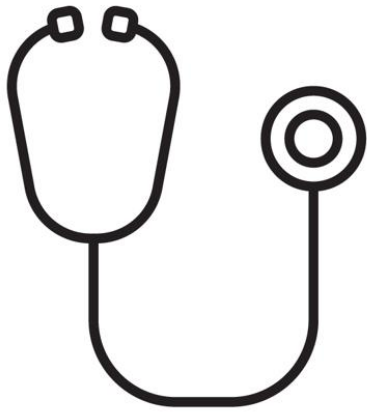
Share data and insights on trends in routine vaccination rates to find and protect communities that have fallen behind on vaccinations

Measles Outbreak Response

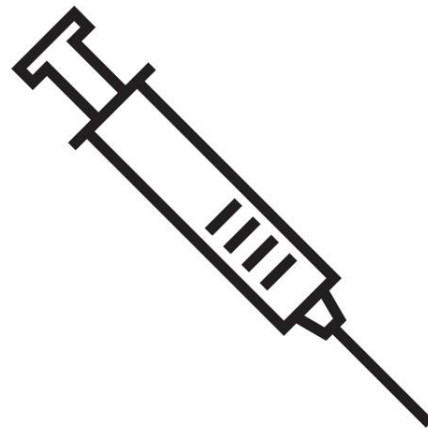
Overview of Measles Outbreak Response

- **Identify cases and establish the diagnosis**
- **Perform case and contact investigations**
 - Obtain accurate and complete immunization and travel histories
 - Identify and prioritize contacts without presumptive evidence of immunity
- **Implement Control Measures**
 - Community vaccination
 - Consider PEP for susceptible contacts
 - Isolation of cases and exclusion of susceptible contacts
 - Implement specific precautions in healthcare settings

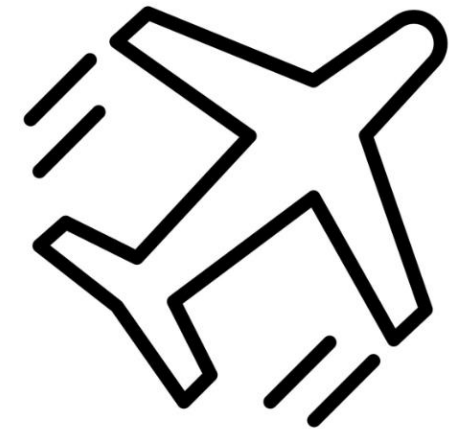
Identify cases and establish the diagnosis



Clinical Case Definition



Vaccination History



Travel or Exposure
History in Prior 21 days

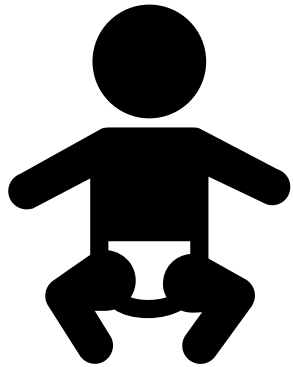
Identify cases and establish the diagnosis

- Public health departments can help advise on the need for testing and on the appropriate routing for specimens
 - Early involvement of public health departments can help prevent measles outbreaks



Identify and Prioritize Susceptible Contacts

- Contacts without presumptive evidence of immunity are at high risk to develop measles
- Exposed persons who are at high risk for serious disease include:



Infants aged <1 year



Pregnant people



People with
immunocompromising
conditions or medications

Control Measures: Community Vaccination

- Providers can ensure patients are up to date with MMR vaccine requirements
- If preschool-aged children are at risk due to outbreak location and transmission settings:
 - A 2nd dose early between age 1 and 4 years could be considered*
- If infants <12 months of age are at risk:
 - A “zero-dose” between age 6 and 11 months could be considered
 - Repeat vaccination should be pursued according to the routine schedule

*Any MMR dose should be given at least 28 days after a prior dose. 2 MMR doses is considered fully protective, but some states or territories may require an additional dose between ages 4–6 years in accordance with the usual schedule

Control Measures: Post Exposure Prophylaxis (PEP)

PEP within the target window may provide measles protection or modify the clinical course of disease among susceptible people



MMR

- Should be given within 72 hours (3 days) of initial measles exposure
- Vaccination can be given after this window, but would only be expected to protect from future exposures and is not considered “adequate PEP”



Immunoglobulin

- Needs to be given within 6 days of initial exposure
- Can be given intramuscularly (IMIG) or intravenously (IVIG)
 - IVIG should be prioritized for adults at high risk of severe disease

Control Measures: Isolation

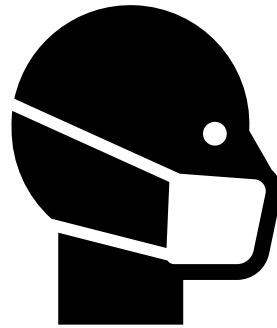
- Case-patients should be isolated for four days after rash onset
 - People with immunocompromising conditions with measles may require more prolonged isolation
- Susceptible contacts without evidence of immunity should be offered PEP or otherwise excluded from congregate settings



Control Measures: Health care settings



Encourage patients to contact health care facility before arrival, if known (e.g., if they contact health department prior to seeking care)



Provide facemask to patient and promptly isolate the patient in a room with the door closed



Use standard and airborne precautions including patient placement in an airborne infection isolation room (AIIR) (if unavailable, a single room with closed door may be used pending transfer to an AIIR)

Resources for Clinicians

- **MMR Vaccine Information for Parents | CDC**
 - <https://www.cdc.gov/vaccines/parents/diseases/measles.html>
- **Healthcare Professionals Patient Education | CDC**
 - <https://www.cdc.gov/vaccines/hcp/patient-ed/index.html>
- **Measles Outbreak Toolkit for Healthcare Providers | CDC**
 - <https://www.cdc.gov/measles/toolkit/healthcare-providers.html>
- **Vaccinate with Confidence | CDC**
 - <https://www.cdc.gov/vaccines/covid-19/vaccinate-with-confidence/community.html>

Thank you!

For more information, contact CDC
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Joining the Q&A Session

David Sugerman, MD, MPH

Medical Officer

CAPT, U.S. Public Health Service

National Center for Immunization and Respiratory
Diseases

Centers for Disease Control and Prevention

James T. Lee, MD, MSc

Medical Officer

National Center for Immunization and Respiratory
Diseases

Centers for Disease Control and Prevention

Andrew Beck, PhD

Microbiologist

National Center for Immunization and Respiratory
Diseases

Centers for Disease Control and Prevention

Raydel Anderson, MS

Microbiologist

National Center for Immunization and Respiratory
Diseases

Centers for Disease Control and Prevention

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