

**18th Meeting of the Advisory Committee to the Director  
(ACD)**

# **Update on Ebola and Measles Outbreaks**

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**Director**

**National Institute of Allergy and  
Infectious Diseases**

**National Institutes of Health**

**June 13, 2019**



# **Ebola Update**

# **Outbreaks of Ebola Virus Disease**

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- **West Africa (Liberia, Sierra Leone, Guinea) – 2014-2016**
  
  
  
  
  
  
  
  
  
  
- **Democratic Republic of the Congo – 2018-2019**

# **Outbreaks of Ebola Virus Disease**

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■ **West Africa (Liberia, Sierra Leone, Guinea) – 2014-2016**

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# Reported Ebola Virus Disease Cases in Guinea, Liberia, and Sierra Leone, 2014-2016

**Guinea**  
3,814 cases / 2,544 deaths

**Sierra Leone**  
14,124 cases / 3,956  
deaths

**Liberia**  
10,678 cases / 4,810 deaths



**Total\*:**  
**28,616 cases**  
**11,310 deaths**

**40% mortality**

\*Confirmed, probable and suspected cases

Source: WHO, 12/2016

# Partnership for Research on Ebola Virus in Liberia (PREVAIL)

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## Liberia MOH-NIAID Collaboration

- **PREVAIL 1: Phase 2, two candidate vaccines vs placebos**
- **PREVAIL 2: ZMapp vs standard-of-care treatment**
- **PREVAIL 3: Study of Ebola survivors**
- **PREVAIL 4: GS-5734 vs placebo for persistent Ebola RNA in semen**
- **PREVAIL 5 (PREVAC): Phase 2, three vaccine strategies vs placebos**
- **PREVAIL 6: Genome-wide association study, genetic factors affecting Ebola**
- **PREVAIL 7: Cataract surgery in Ebola survivors and close contacts**



The  
New England  
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

VOLUME 377

October 12, 2017

NUMBER 15

## **Phase 2 Placebo-Controlled Trial of Two Vaccines to Prevent Ebola in Liberia**

SB Kennedy, HC Lane et al. for the PREVAIL I Study Group

VOLUME 375

October 13, 2016

NUMBER 15

## **A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection**

The PREVAIL II Writing Group, for the Multi-National PREVAIL II Study Team. RT Davey, Jr., D Malvy et al.

VOLUME 380

March 7, 2019

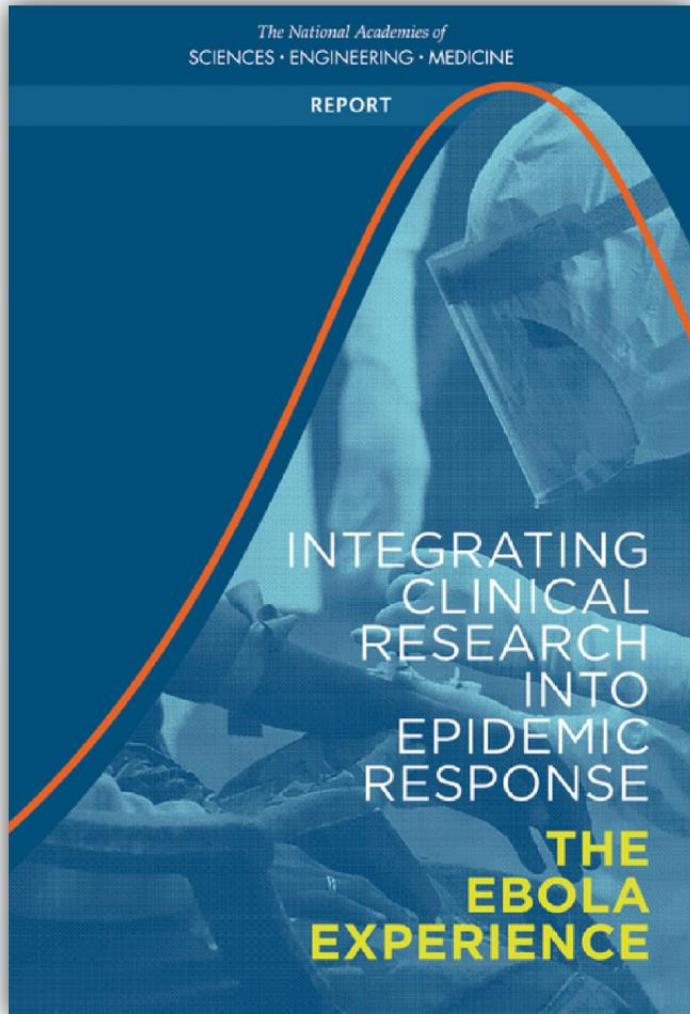
NUMBER 10

## **A Longitudinal Study of Ebola Sequelae in Liberia**

The PREVAIL III Study Group

# April 2017: NAS Report on the Ebola Clinical Research Experience

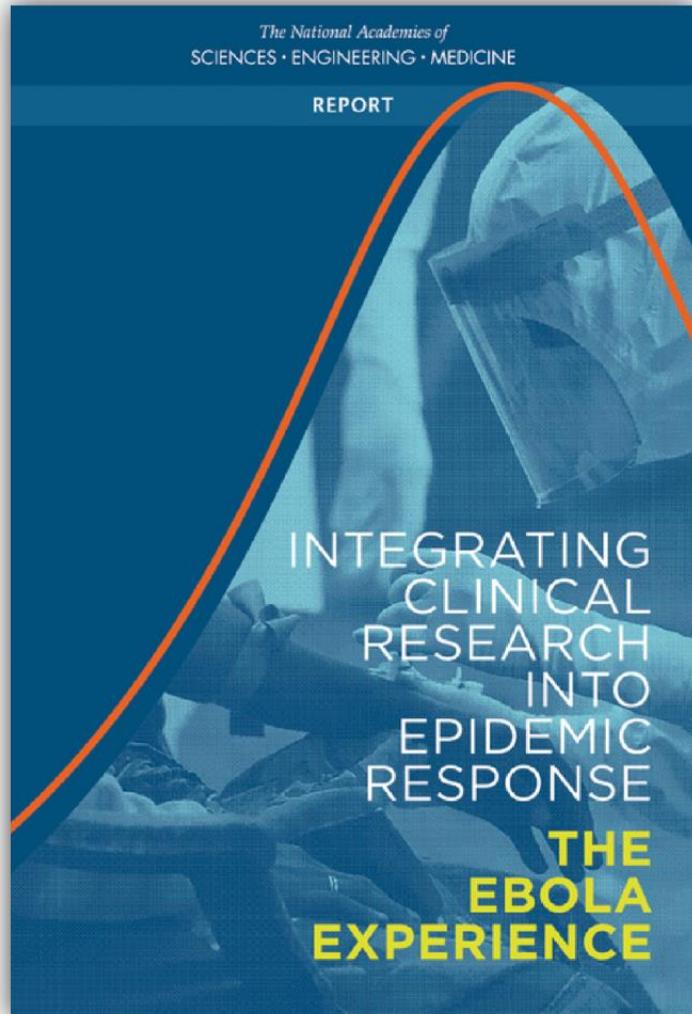
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- **Core principles of science and ethics in conducting clinical research should not change during an epidemic**
- **RCTs ethical and appropriate: most efficient, reliable way to determine safety and efficacy**
- **Clinical research studies must have**
  - Scientific and social value
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  - Post-trial access to candidate products proved safe/effective

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# **Outbreaks of Ebola Virus Disease**

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■ **Democratic Republic of the Congo – 2018-2019**

# **Two Ebola Virus Disease Outbreaks – Democratic Republic of the Congo, 2018-Present**

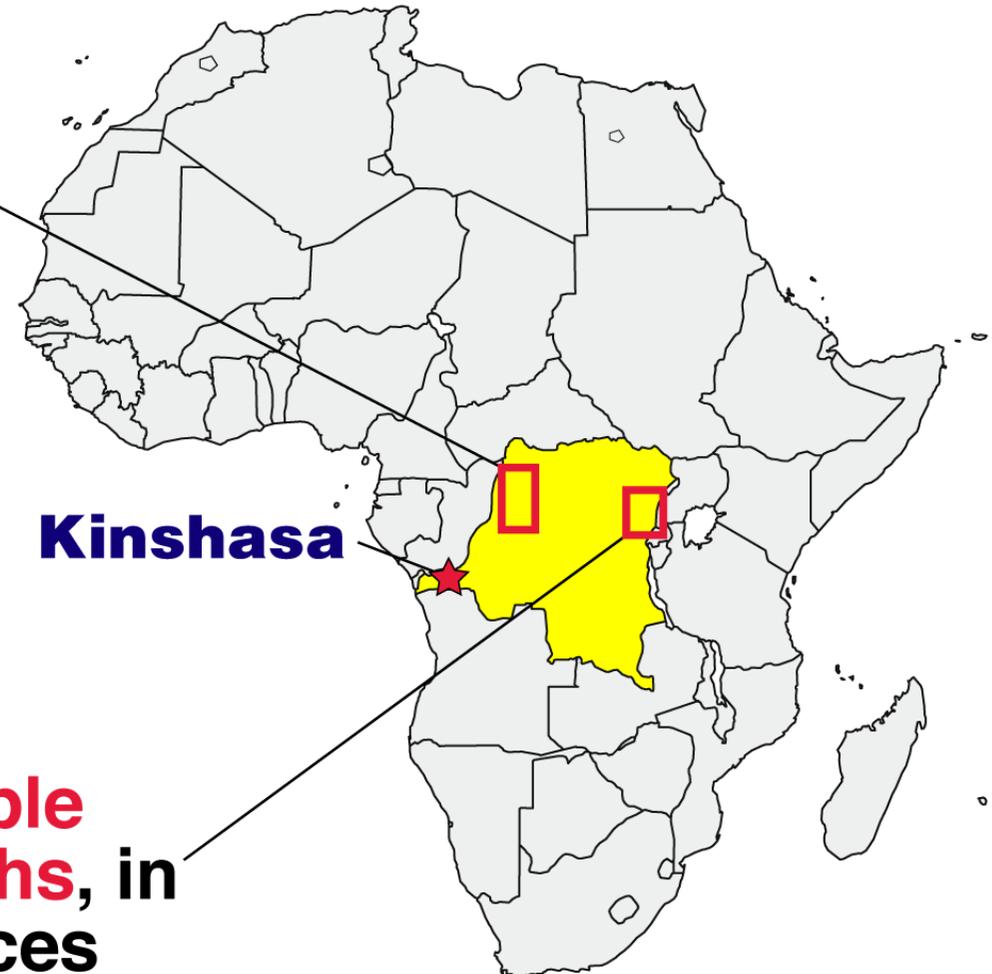
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## **April–July, 2018**

**54 cases, 33 deaths  
in three towns in  
Équateur Province**

## **August 1, 2018 through June 12, 2019**

**2,084 confirmed and probable  
cases, including 1,405 deaths, in  
North Kivu and Ituri Provinces**





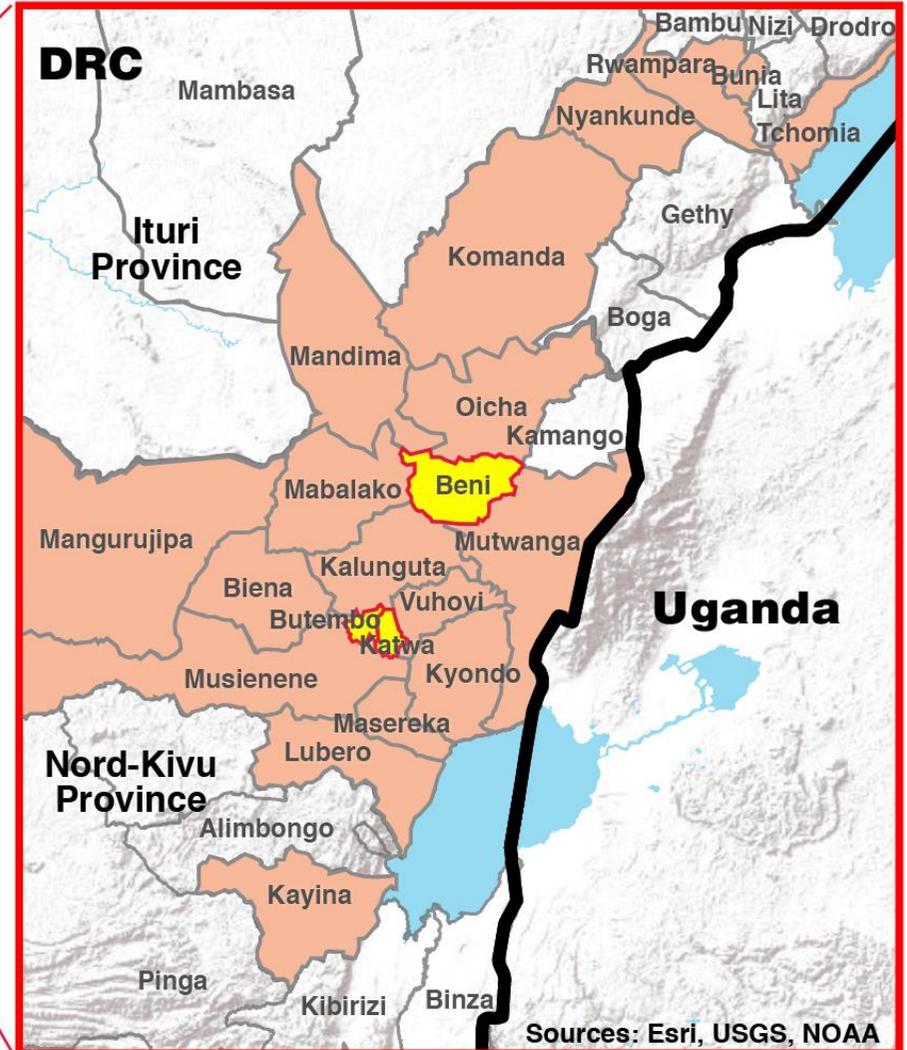
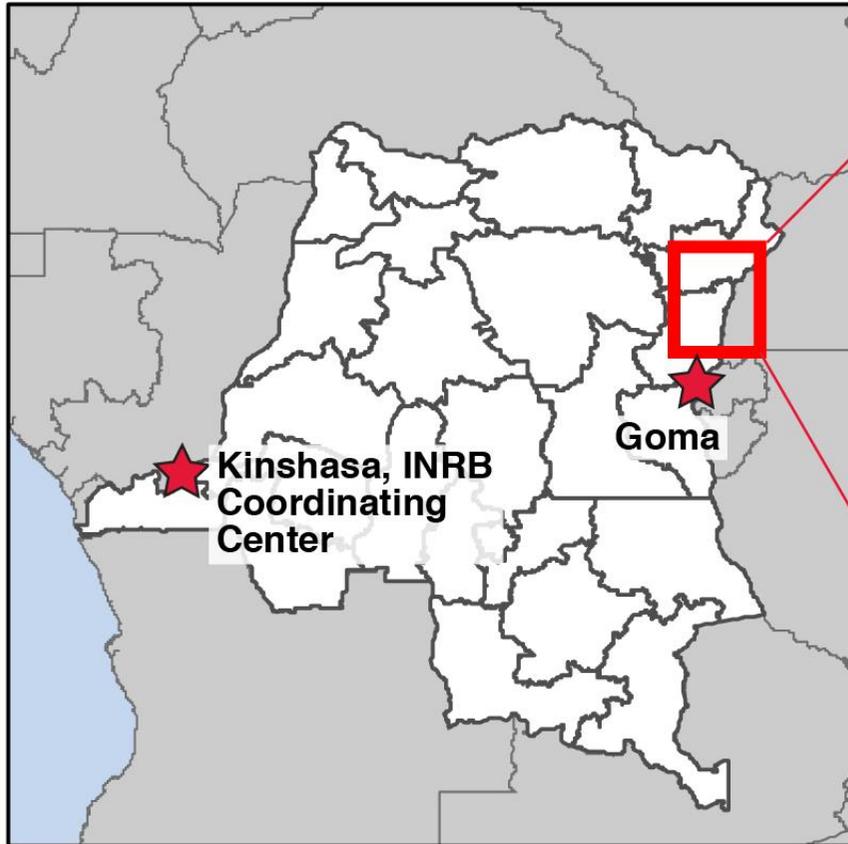
# Randomized, Controlled Trial of Ebola Therapeutics (PALM)

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- Opened November 2018 in the DRC
- Coordinated by WHO, led by DRC National Institute for Biomedical Research (INRB) & NIAID
- Four candidates: ZMapp, remdesivir, mAb114, REGN-3
- Target N = 500 (125 per arm)
- 323 patients enrolled as of 6/12/2019



# PALM RCT Sites, DRC



Sources: DRC Ministry of Health, WHO, CDC

# The New York Times

March 1, 2019

## 'Crippling' Attacks Force Doctors Without Borders to Close Ebola Centers in Congo

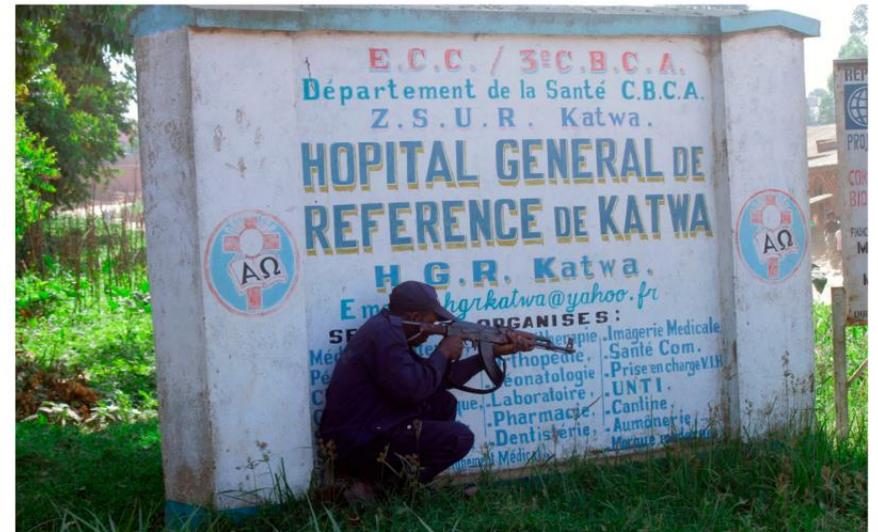


Ebola treatment center in Katwa, in northeastern DR Congo

# The Telegraph

April 23, 2019

## Ebola Doctor Killed As Violence Hampers Response to Outbreak in DRC



# Ring Vaccination with rVSV-ZEBOV in the Democratic Republic of the Congo

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- Per WHO policy, vaccinating contacts, contacts of contacts, frontline workers
- As of June 12, 2019, 132,679 people have received investigational rVSV-ZEBOV vaccine



Image credit: Sam Mednick/AP

# January 1, 2019: Vaccination Team Attacked Near Komanda, DRC

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# Associated Press

June 11, 2019

## Uganda Confirms First Ebola Case Outside Outbreak in Congo

**Kagando  
Hospital**



# The New York Times

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June 12, 2019

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## Two More Ebola Cases Diagnosed in Uganda as First Victim, 5, Dies



# THE HILL

June 7, 2019

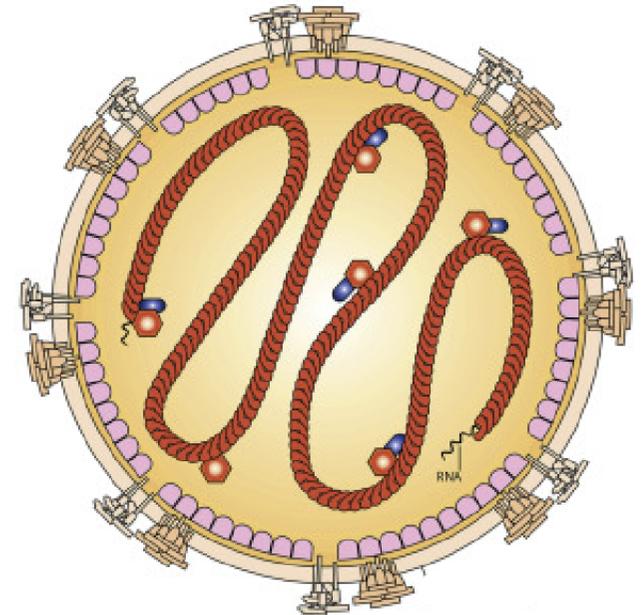
**Ebola Outbreak May Last Up  
to 2 Years, WHO Says**

# Measles

# Measles Virus

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- **Highly contagious airborne virus that survives up to 2 hours in the air after a cough or sneeze**
- **Paramyxovirus, Genus *Morbillivirus***
- **Genome sequencing helps identify origin of imported cases**
- **Potential for virus eradication:**
  - **Global eradication of closely related animal virus in 2011**



# Disease Progression of Measles

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- Initial symptoms include fever and cough
- Rash occurs 2-4 days later, lasts 5-6 days
- Contagious from 4 days before → 4 days after rash appears



# Measles Complications

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<b>Diarrhea</b>	<b>8%</b>
<b>Otitis media</b>	<b>7 – 9%</b>
<b>Pneumonia</b>	<b>1 – 6%</b>
<b>Hospitalized</b>	<b>1 in 4 cases</b>
<b>Encephalitis</b>	<b>1 per 1,000 cases</b>
<b>Death</b>	<b>1 – 3 per 1,000 cases</b>
<b>Subacute Sclerosing Panencephalitis (SSPE)</b>	<b>1 per 100,000 cases</b>

# **Groups at High Risk for Complications**

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- **Infants and children < 5 years old**
- **Pregnant women**
- **Immunocompromised people**
- **Adults > 20 years old**

# **Global Burden of Measles Before and After Vaccination**

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- **Pre-vaccine era: ~2.6 million deaths each year**
- **Dramatic decrease after vaccine introduced in 1963**
- **21.1 million deaths prevented from 2000 – 2017**
- **110,000 deaths in 2017, mostly in children < 5 years**

# **Pre-Vaccine Measles Burden in the U.S.**

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- **3,000,000 to 4,000,000 measles cases each year**
- **~48,000 hospitalizations each year**
- **~500 deaths each year**

# Measles Vaccine

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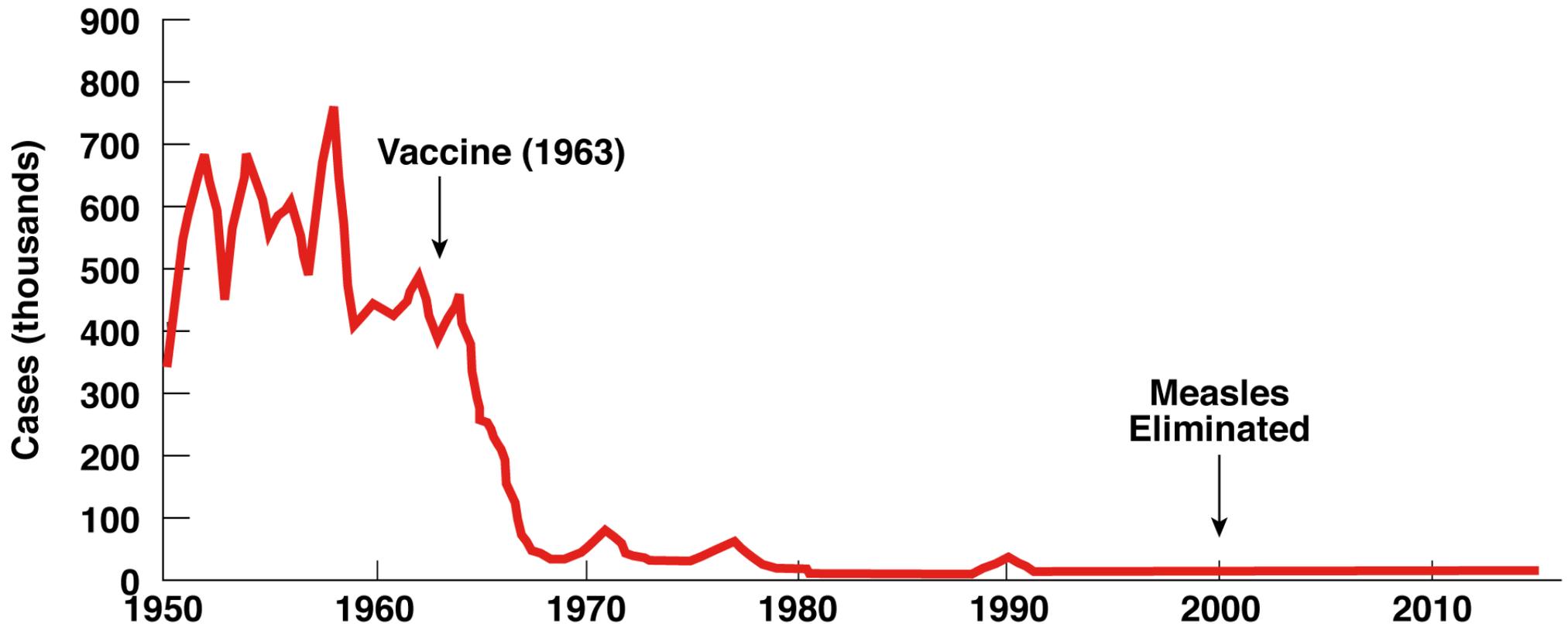
- Licensed in 1963 in the U.S.
- Combination measles-mumps-rubella (MMR) vaccine licensed in 1971
- Vaccine effectiveness:
  - 1-dose: ~93%
  - 2-doses: ~97%
- Excellent safety profile over last 50 years
  - Low risk of febrile seizures in children aged 12 – 23 months (1 in 3,000 doses)
  - Temporary pain/stiffness in joints (teenage or adult women)
  - Temporary low platelet count (1 in 30,000 doses)



# Success of U.S. Measles Vaccination

## ■ 2000: Elimination of measles in U.S.

- Absence of sustained transmission of virus for > 12 months





The  
New England  
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Published online April 17, 2019

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**Perspective**

**Measles in 2019 –  
Going Backward**

**CI Paules, HD Marston and AS Fauci**

May 15, 2019  
Volume 219  
Issue 10

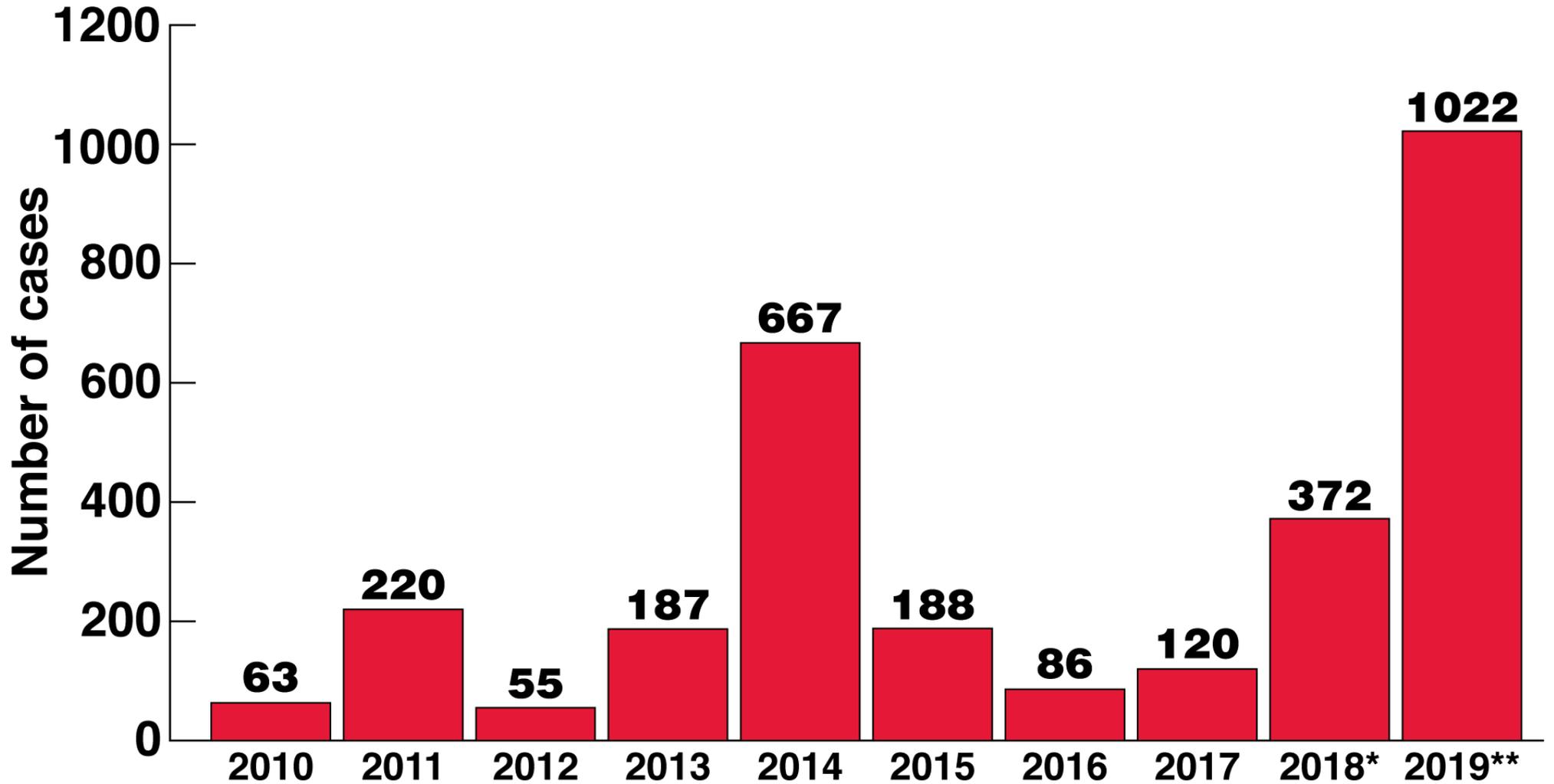
# The Journal of Infectious Diseases

## **International Importations of Measles Virus into the United States During the Postelimination Era, 2001–2016**

AD Lee, PA Gastanaduy et al.

- **553 imported cases-majority were U.S. residents who had traveled**
  - **87% unvaccinated or unknown vaccination status**

# Number of U.S. Measles Cases Reported By Year, 2010-2019



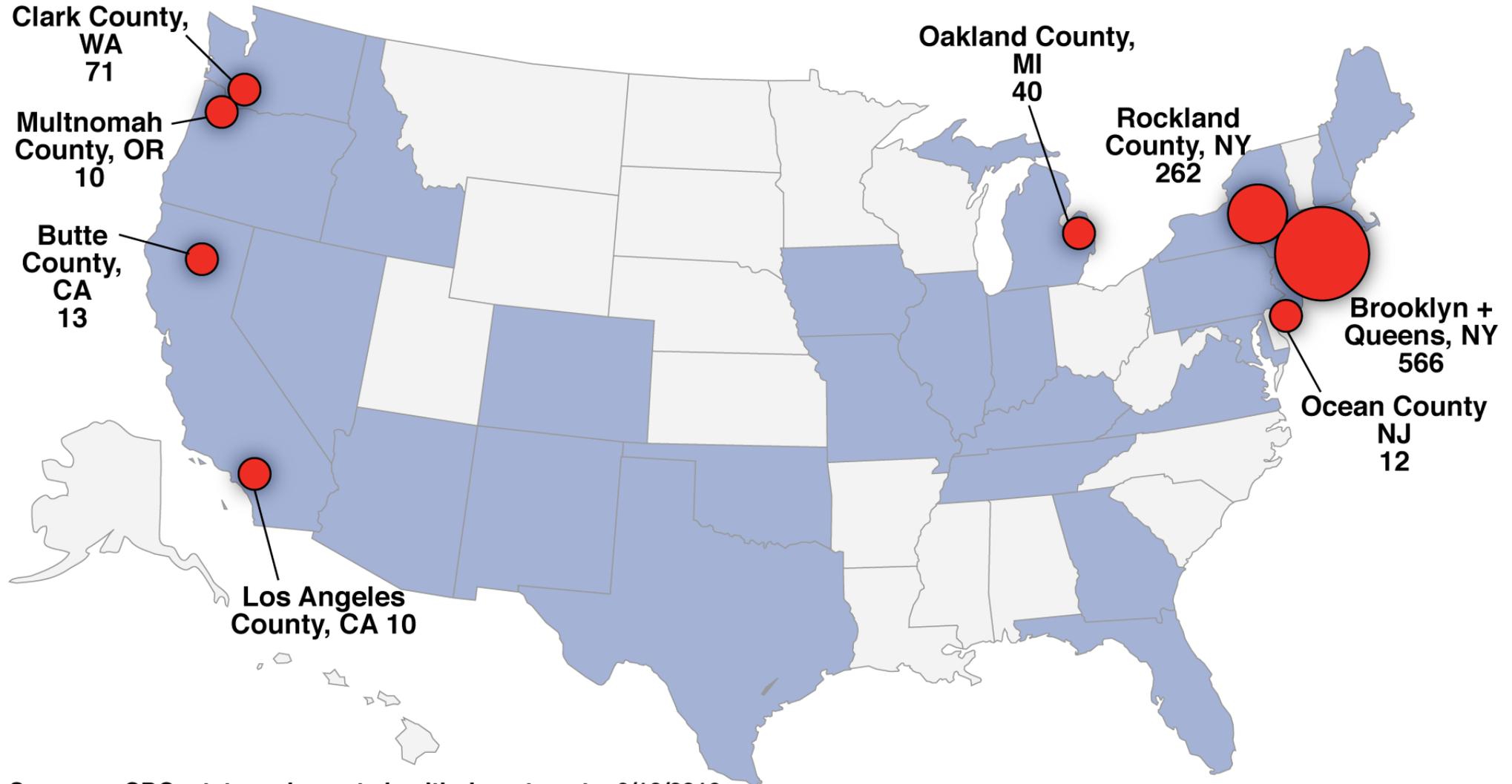
Source: CDC

\*Preliminary case count, as of December 29, 2018.

\*\*Preliminary case count, as of June 6, 2019.



# U.S. Areas with >10 Measles Cases, 2019



Sources: CDC; state and county health departments, 6/10/2019

# Reasons for Increase in Measles Cases

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- An increase in the number of travelers who contract measles abroad and bring it into the U.S.
- Further spread of measles in U.S. communities with pockets of unvaccinated people



# **Optimal Measles Vaccine Coverage for Herd Immunity**



**93% - 95%**

# Reasons for Increase in Measles Cases (cont.)

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- **Vaccine hesitancy**—the delay or refusal of vaccines despite their availability
  - Misconceptions/misinformation/lack of information about vaccines and their safety
  - Concerns the large number of injections; moral or religious objections; cost or other access problem; and concerns about side effects, particularly autism.
- **Nonmedical exemptions (NMEs) from vaccine mandates**
  - Tend to occur in geographic clusters and are associated with higher rates of measles
  - 47 states allow NMEs for religious beliefs; 16 states allow so-called philosophical or “personal belief” exemptions

January 16, 2019

# **WHO: Anti-Vaccine Movement a Top Threat in 2019**

**A refusal to vaccinate alongside air pollution and  
climate change as a top global threat**

**By Megan Trimble, Digital News Editor**