

# **Ebola in 2014: The Perfect Storm**

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Infectious Diseases**

**National Institutes of Health**

**December 11, 2014**



- **Ebola background**
- **Current outbreak in West Africa**
- **Ebola in the USA**
- **Role of research and development**
  - **Diagnostics**
  - **Vaccines**
  - **Therapeutics**



# ■ Ebola background

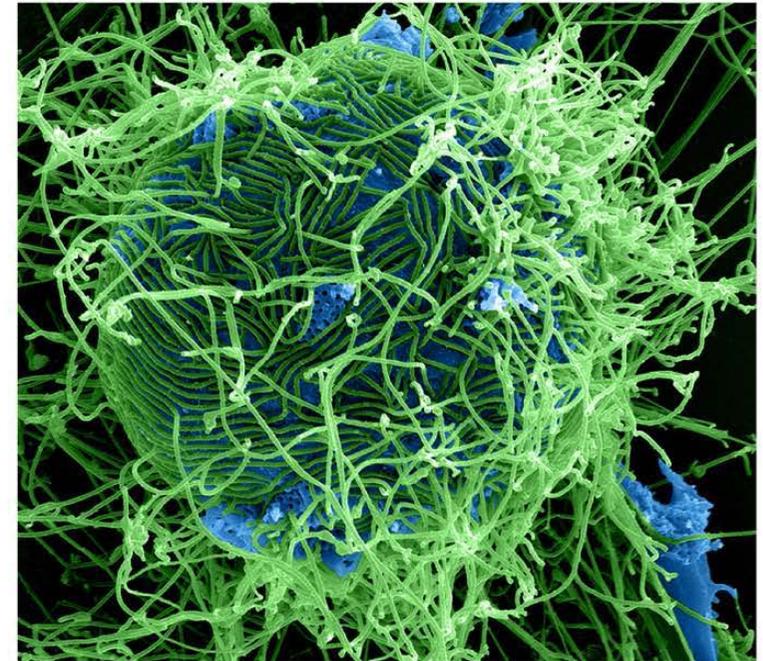
- **Current outbreak in West Africa**
- **Ebola in the USA**
- **Role of research and development**
  - **Diagnostics**
  - **Vaccines**
  - **Therapeutics**



# Ebola Virology

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- **Filovirus family**
- **Species and average fatality in the genus *Ebolavirus***
  - **Bundibugyo – ~30%**
  - **Zaire – 50-90%**
  - **Reston – animal disease**
  - **Sudan – ~50%**
  - **Tai Forest – 1 non-fatal human case**

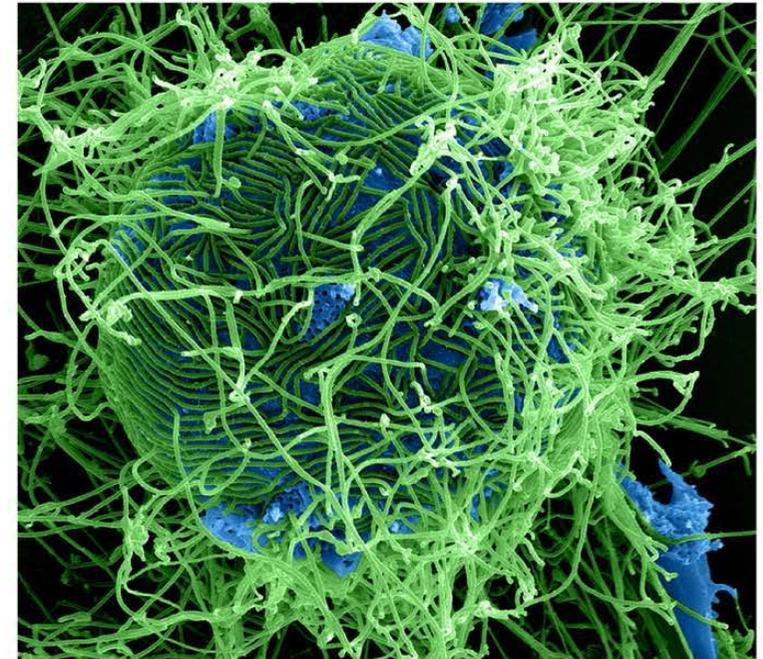


EM of Ebola virus particles (green) attached to Vero cell (blue). NIAID

# Ebola Virology

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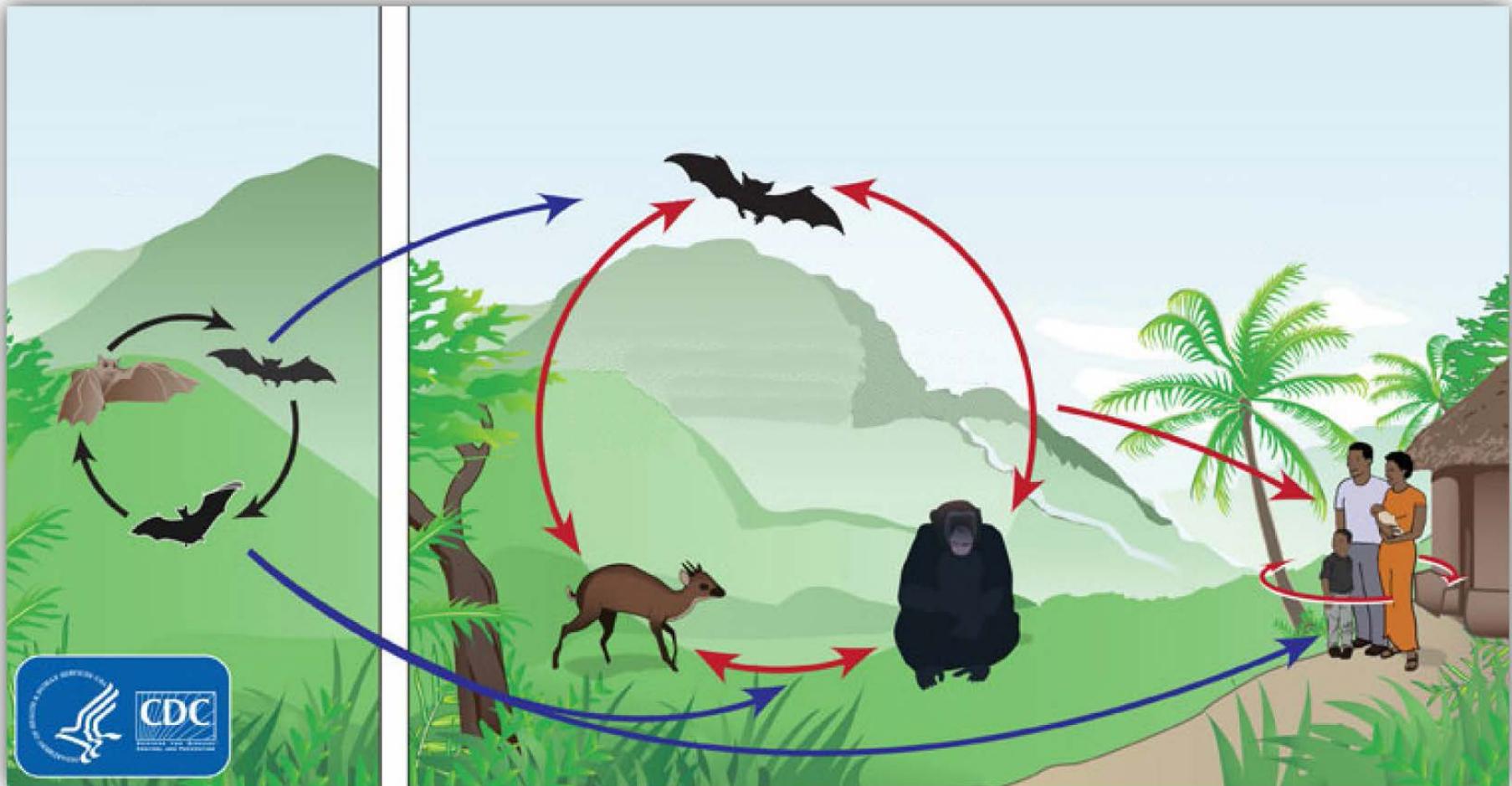


EM of Ebola virus particles (green) attached to Vero cell (blue). NIAID

# Ebola Transmission Cycle

Enzootic cycle

Epizootic cycle



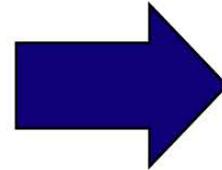
**Fruit bats putative reservoir; evidence inconclusive**

# **Ebola Transmission Routes**

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■ **Bodily fluids**

■ **Objects (fomites)**

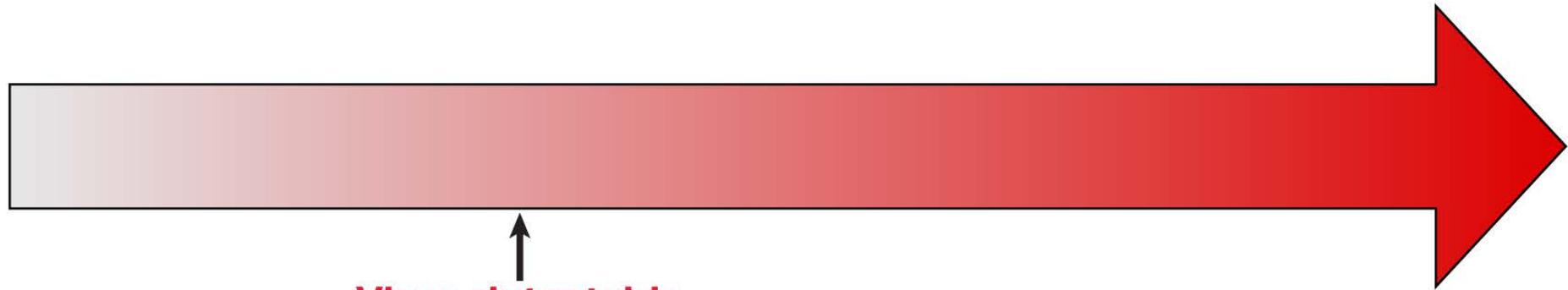


**Transmission  
occurs once  
symptomatic  
(viral load rises at  
symptom onset)**

■ **Infected animals**

# Typical Ebola Virus Disease Clinical Course

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Virus detectable  
and transmissible

<b>Exposure</b>	<b>Incubation period</b>	<b>Symptoms begin</b>			<b>Recovery or death</b>
	Average 8-10 days, range 2-21	<u>Days 1-3</u> Weakness, fever, influenza-like illness	<u>Days 4-7</u> Vomiting, diarrhea, hypotension	<u>Days 7-10</u> Confusion, possible bleeding (typically minor), shock	



The  
New England  
Journal of Medicine

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

Available online November 5, 2014

# **Ebola Virus Disease in West Africa – Clinical Manifestations and Management**

DS Chertow et al.

- **Experience with 700 Ebola Patients in Monrovia, Liberia**
- **August 23 - October 4, 2014**
- **Médecins sans Frontières Ebola Treatment Unit**

# **Evidence of Lack of Transmissibility During Early Febrile Stage of Ebola Virus Disease (EVD)**

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- **Early sx's of EVD – high fever, malaise, fatigue, body aches (“flu-like”)**
- **GI sx's begin 3-5 days later: epigastric pain, then nausea, vomiting and diarrhea**
- **Upon careful history, no patient contracted EVD from an infected person during early febrile illness**

## ■ Ebola background

## ■ Current outbreak in West Africa

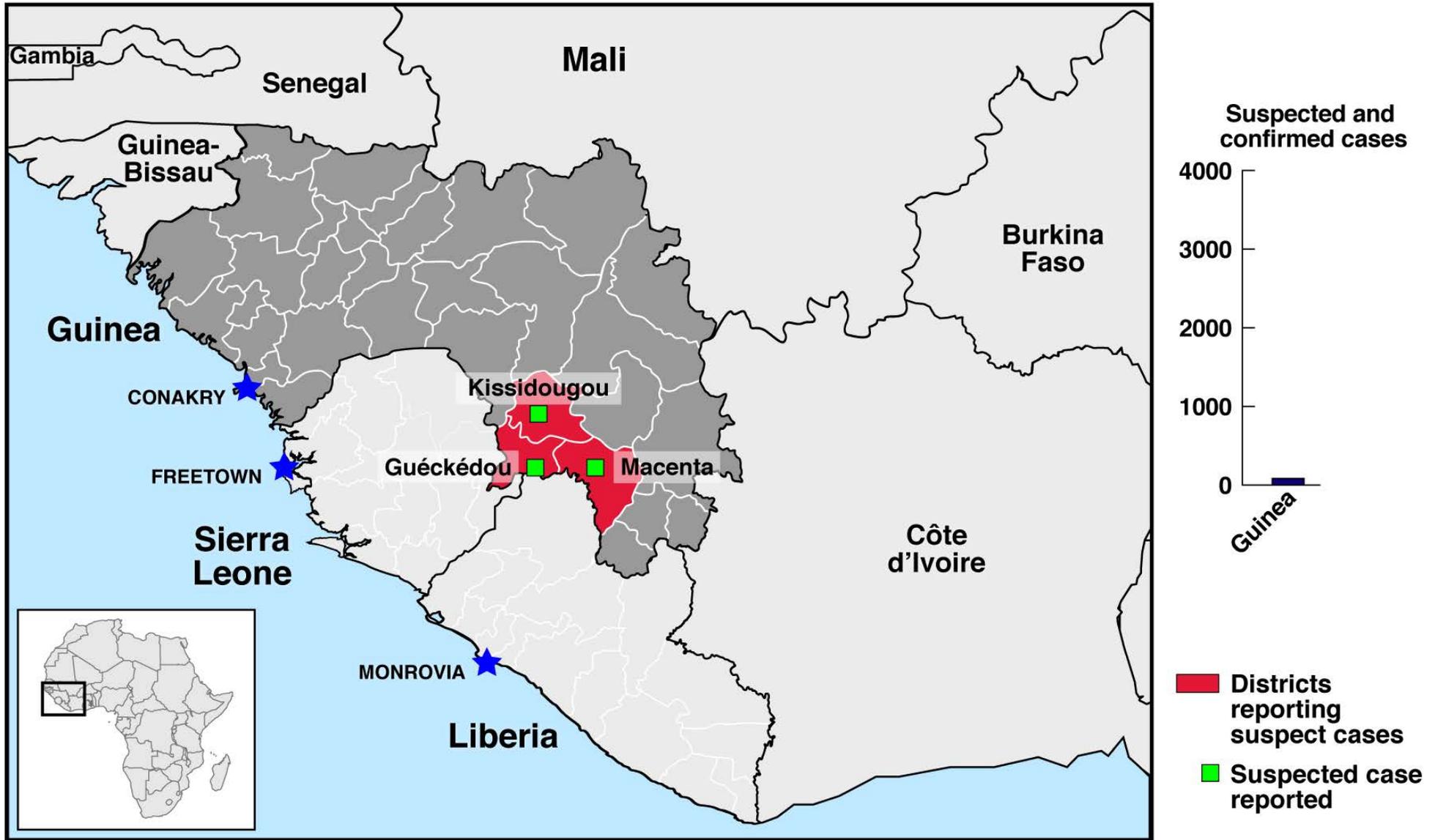
## ■ Ebola in the USA

## ■ Role of research and development

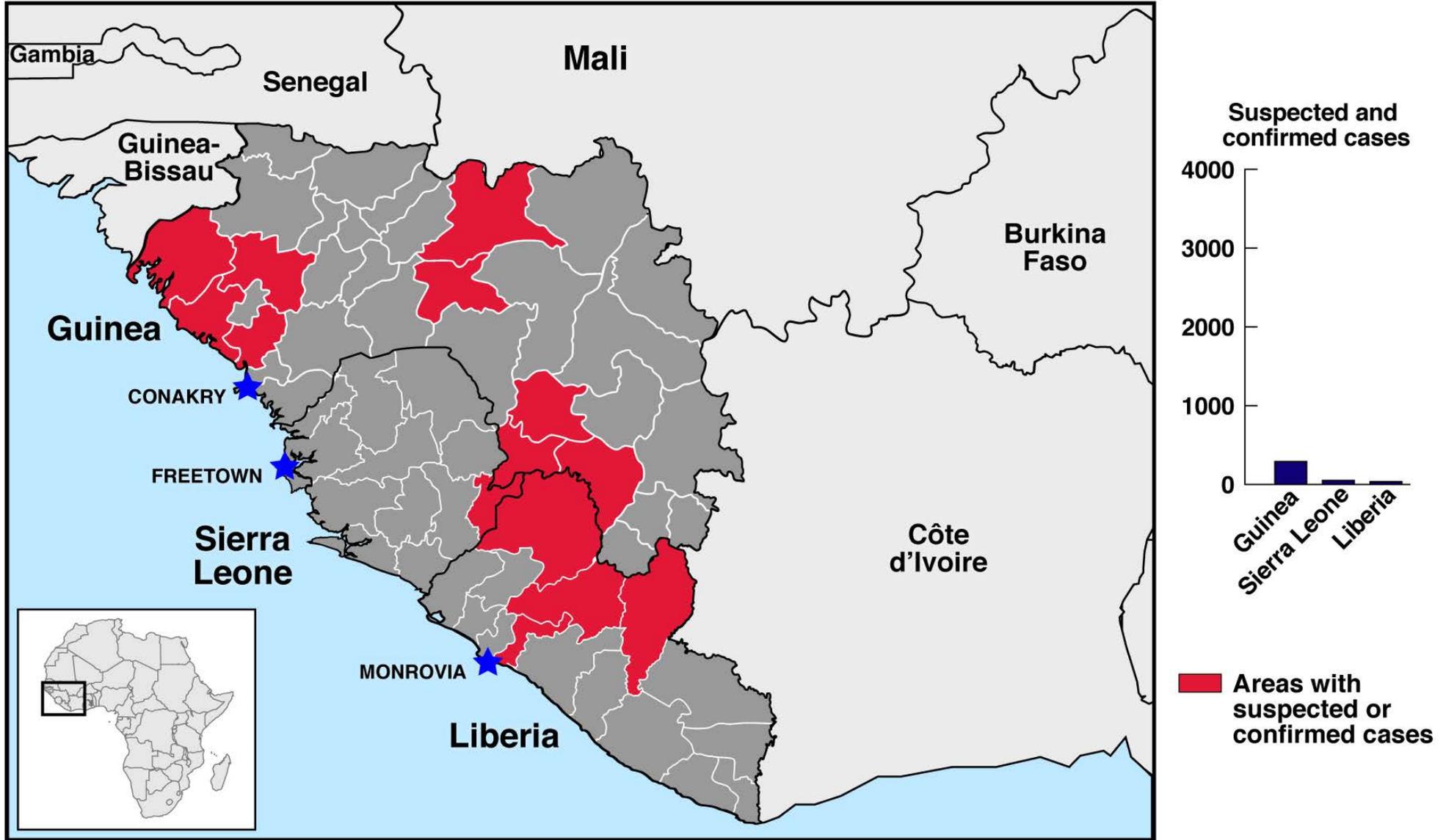
- Diagnostics
- Vaccines
- Therapeutics



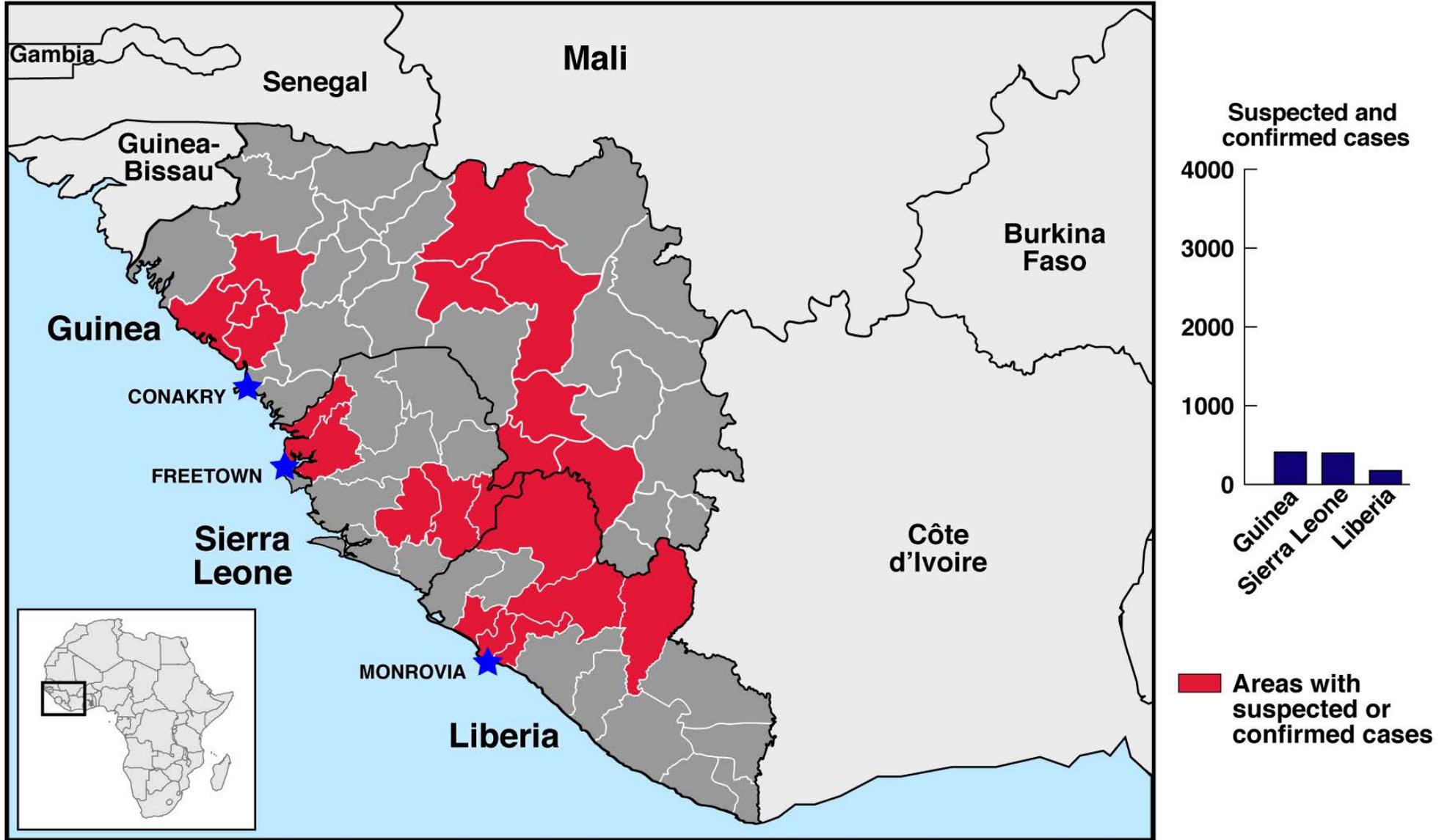
# State of the Outbreak: March 2014



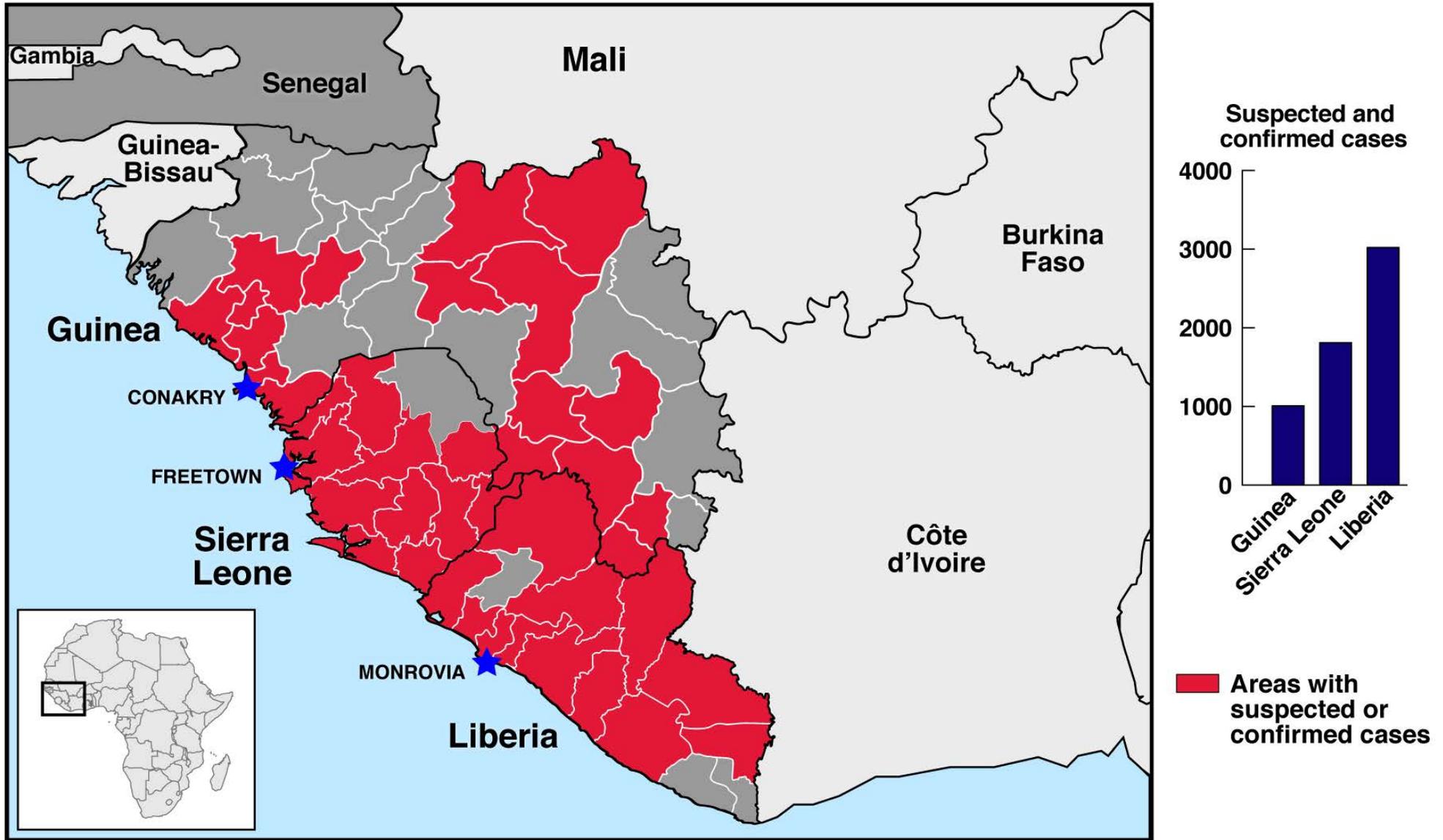
# State of the Outbreak: May 2014



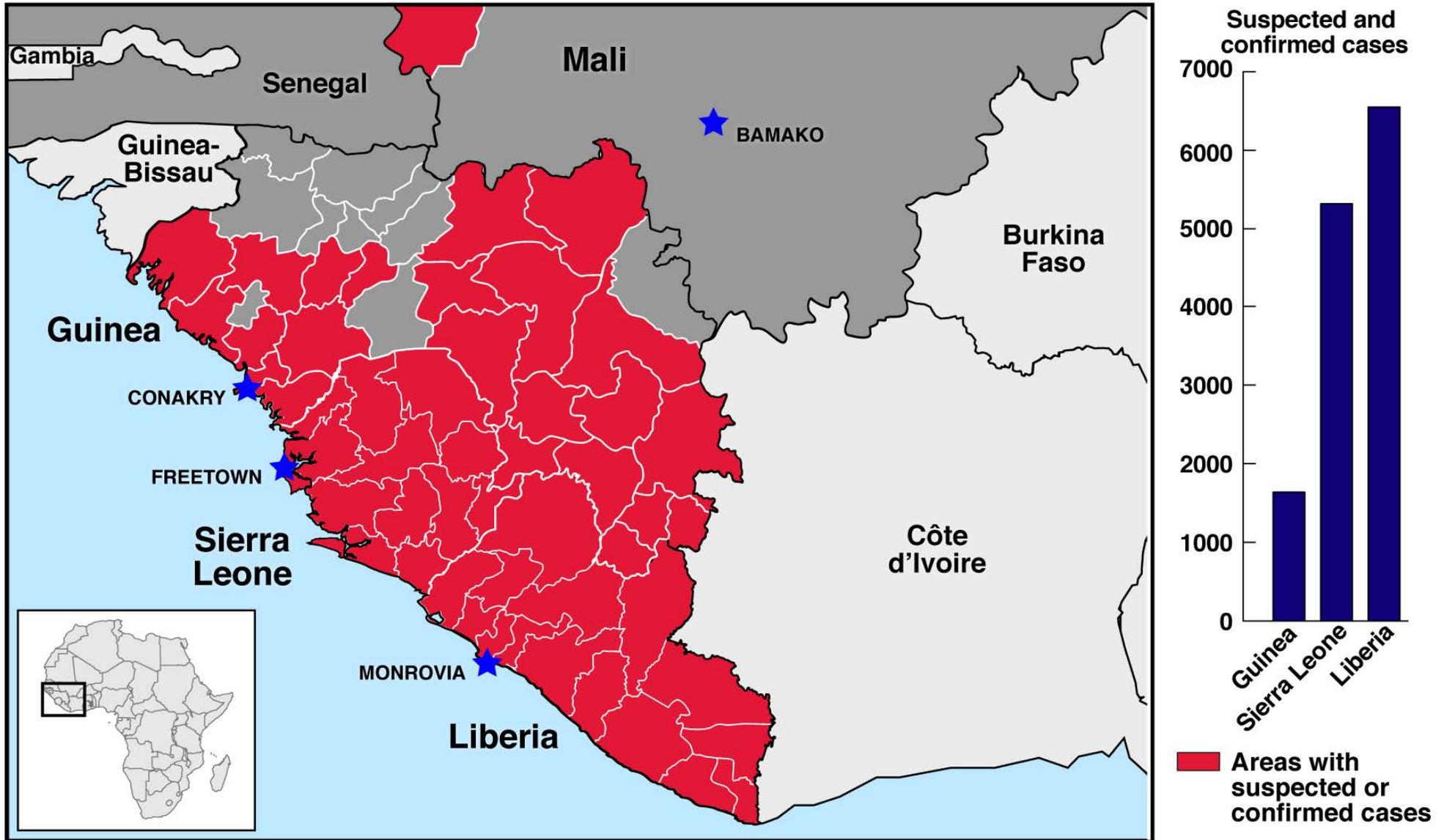
# State of the Outbreak: July 2014



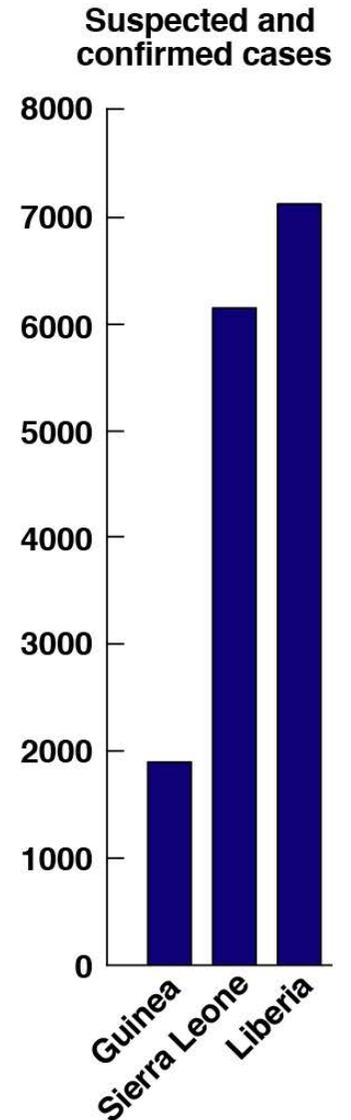
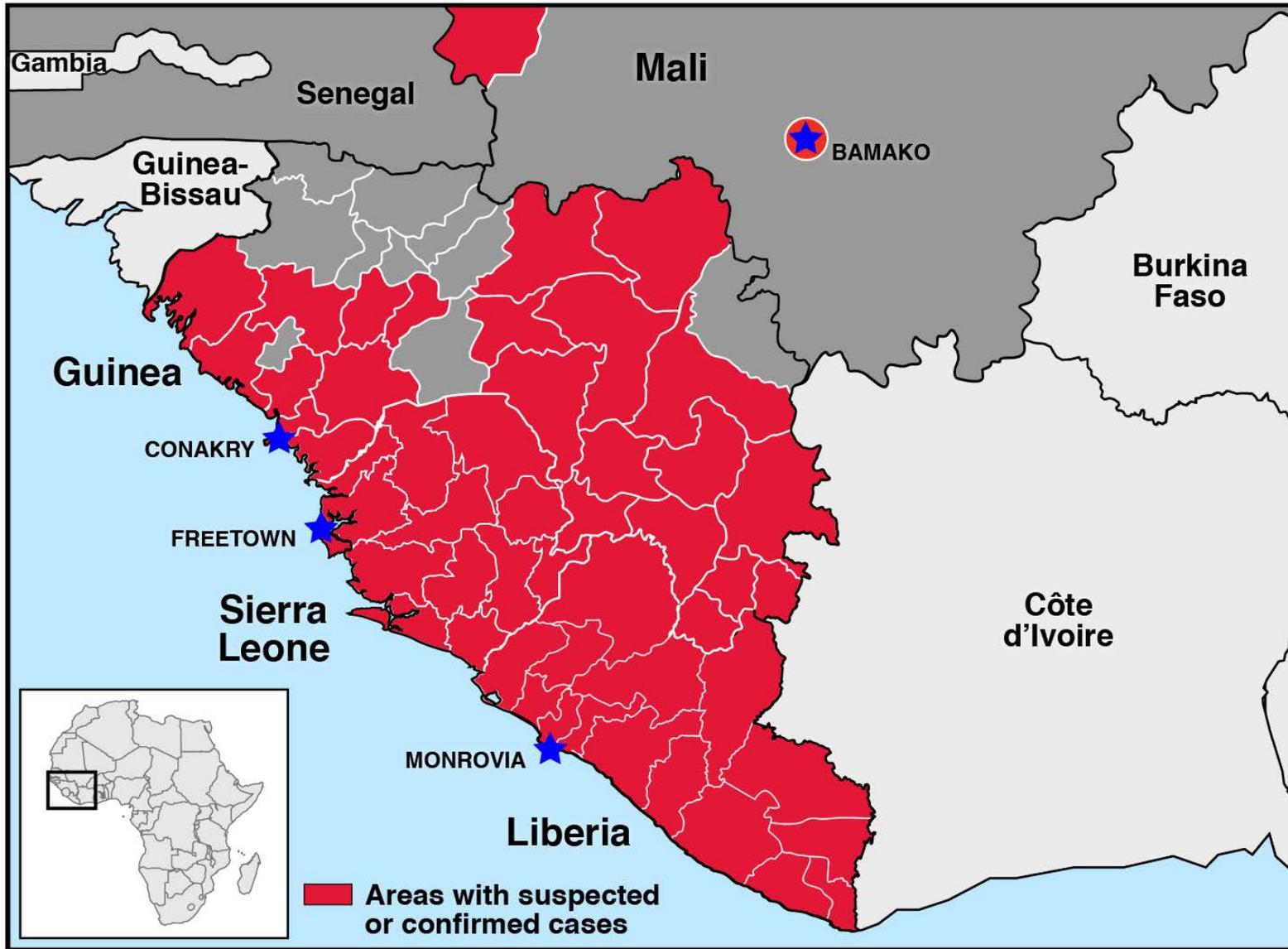
# State of the Outbreak: Sept. 2014



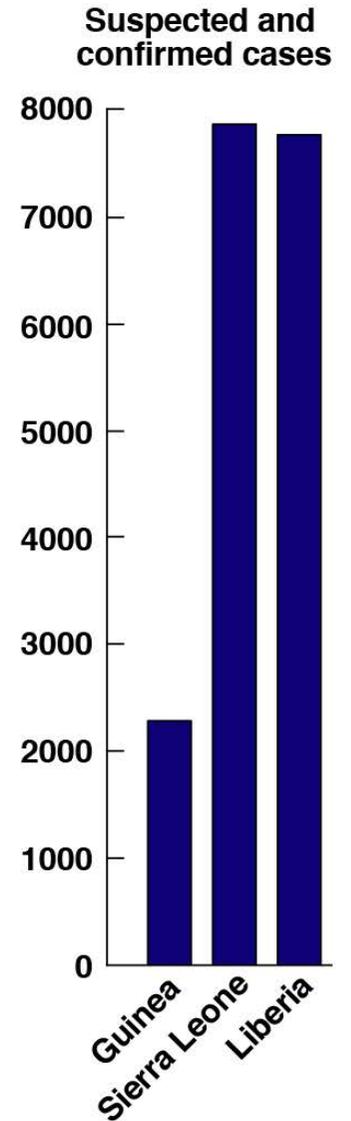
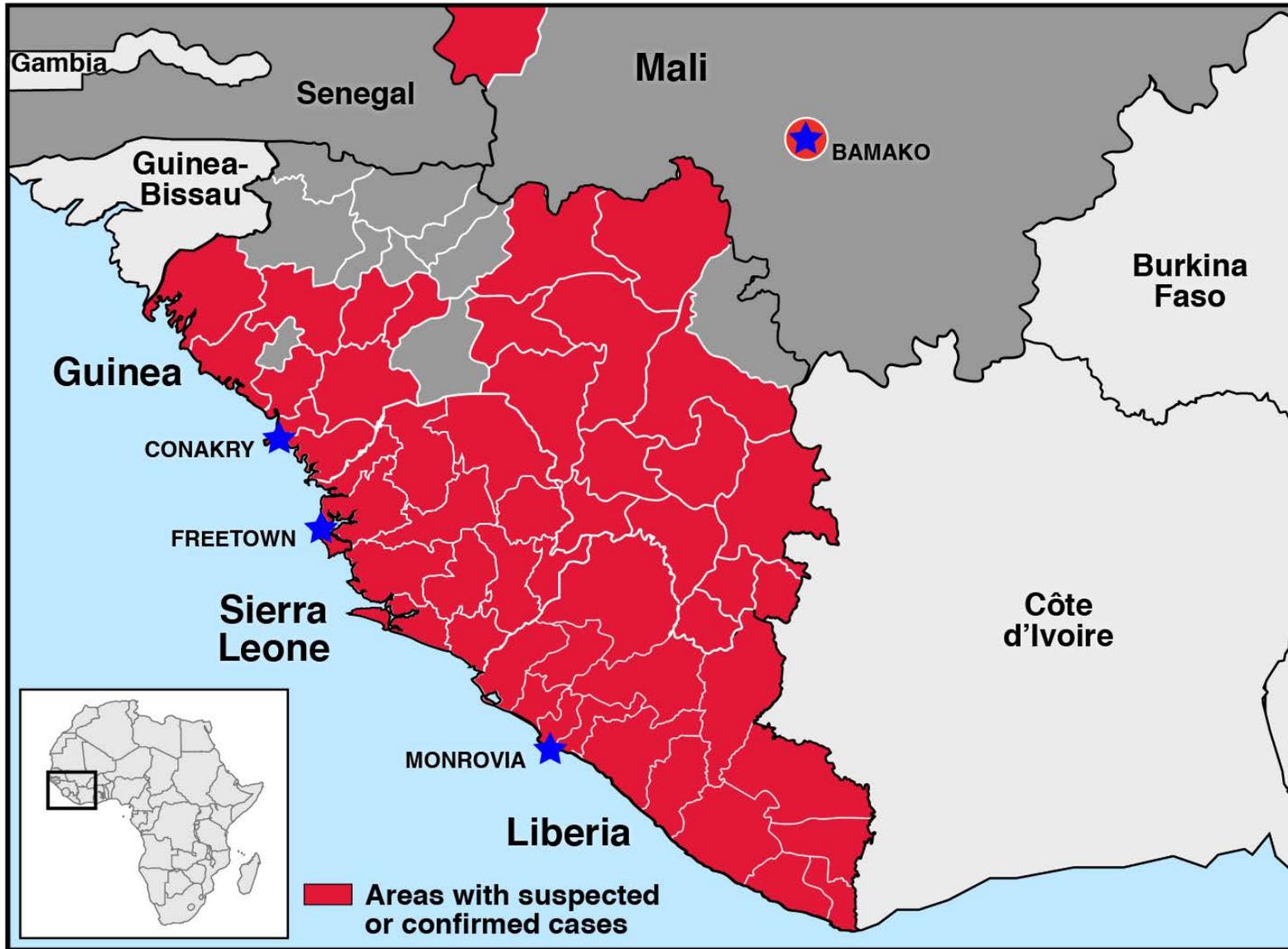
# State of the Outbreak: Oct. 2014



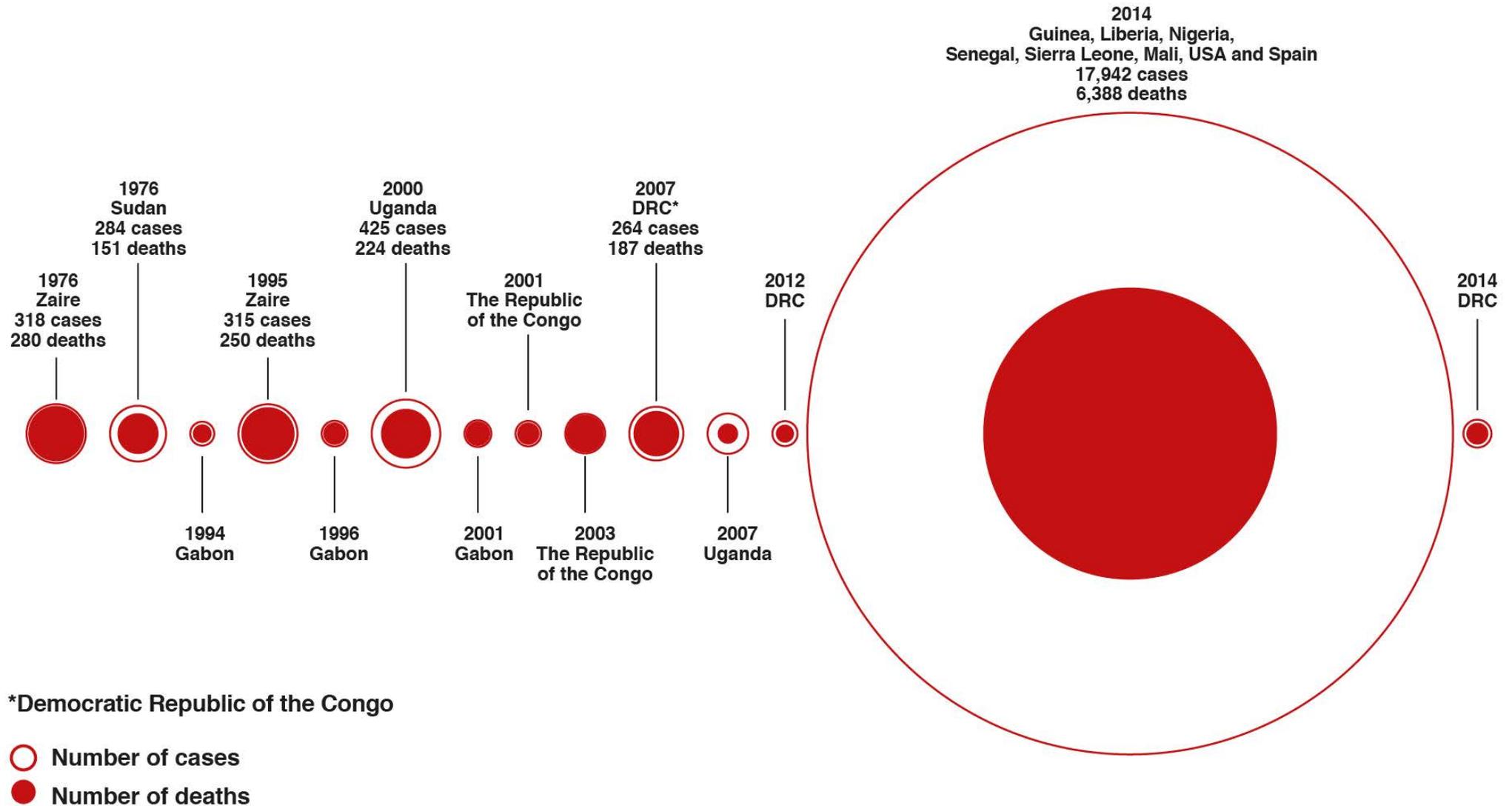
# State of the Outbreak: Nov. 2014



# State of the Outbreak: Dec. 2014



# Ebola Outbreaks 1976 to Present Day



# Factors Facilitating Spread

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- **Poor nations with limited health infrastructure**
- **No prior experience with Ebola**
- **Few health professionals; multiple health threats**
- **Frequent travel across porous borders**
- **Limited cooperation between neighboring governments**
- **History of regional conflicts**
- **Local customs, e.g., burial practices**



# Epidemiology and Genomic Sequencing of the Outbreak

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- 99 genome sequences from 78 individuals (May-June 2014): 395 mutations
- No evidence of significant functional change



## **Genomic Surveillance Elucidates Ebola Virus Origin and Transmission During the 2014 Outbreak**

SK Gire, PC Sabeti, et al.

# The Link between Viral Mutation and Transmissibility

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September 12, 2014

## **Ebola in the Air? A Nightmare That Could Happen**

Elizabeth Cohen



***“There really are no examples of a virus that has completely changed its method of transmissibility. It can get a little bit more virulent, a little bit less virulent... But to completely change its method of transmission would be unprecedented.”***

**- Anthony S. Fauci, M.D.  
Senate Appropriations Hearing, November 12, 2014**

Volume 179  
Suppl. 1  
February, 1999

The Journal of  
**Infectious  
Diseases**

# **Transmission of Ebola Hemorrhagic Fever: A Study of Risk Factors in Family Members, Kikwit, Democratic Republic of the Congo, 1995**

SF Dowell, CJ Peters et al.

- **173 household contacts of EVD patients**
- **No transmissions to those without *direct* physical contact with patient**

# Public Health Response to Ebola in Affected Countries

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- Education
- Hygiene practices
- Case identification
- Contact tracing
- Personal Protective Equipment for caregivers
- Prompt isolation
- Aggressive supportive care
- Safe burials



# International Response to Ebola Outbreak: U.S. Response

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*“Faced with this outbreak, the world is looking to us, the United States, and it’s a responsibility that we embrace... We are going to keep leading in this effort.”*

–President Barack Obama, Sept. 16, 2014

- 3,000+ troops
- Construction of Ebola Treatment Units (ETUs)
- 25-bed facility for healthcare workers
- Ongoing CDC and USAID support

- Ebola background
- Current outbreak in West Africa
- Ebola in the USA
- Role of research and development
  - Diagnostics
  - Vaccines
  - Therapeutics



# USA TODAY

October 14, 2014

## Fear Spreads Faster than Ebola: Our View

By USA Today Editorial Board



# **Ebola in the USA**

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- **Deliberate air evacuation of identified Ebola patients: Brantly, Writebol, Sacra, Mukpo, Salia, Crozier**
- **Inadvertent importation of infected persons:**
  - **Traveler – Thomas Duncan**
  - **Health care worker – Craig Spencer**
- **Health Care Worker infected in the USA – Nina Pham and Amber Vinson at Texas Presbyterian**

# Medevacs from West Africa



# August 2014: Infections Reported in American Aid Workers

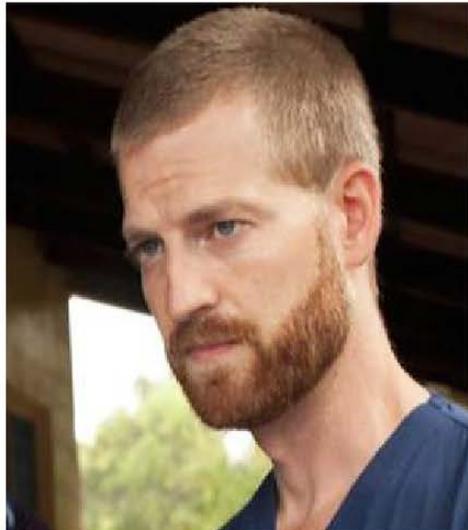
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The Washington Post

August 1, 2014

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## U.S. Confirms 2 Americans with Ebola Coming Home for Treatment



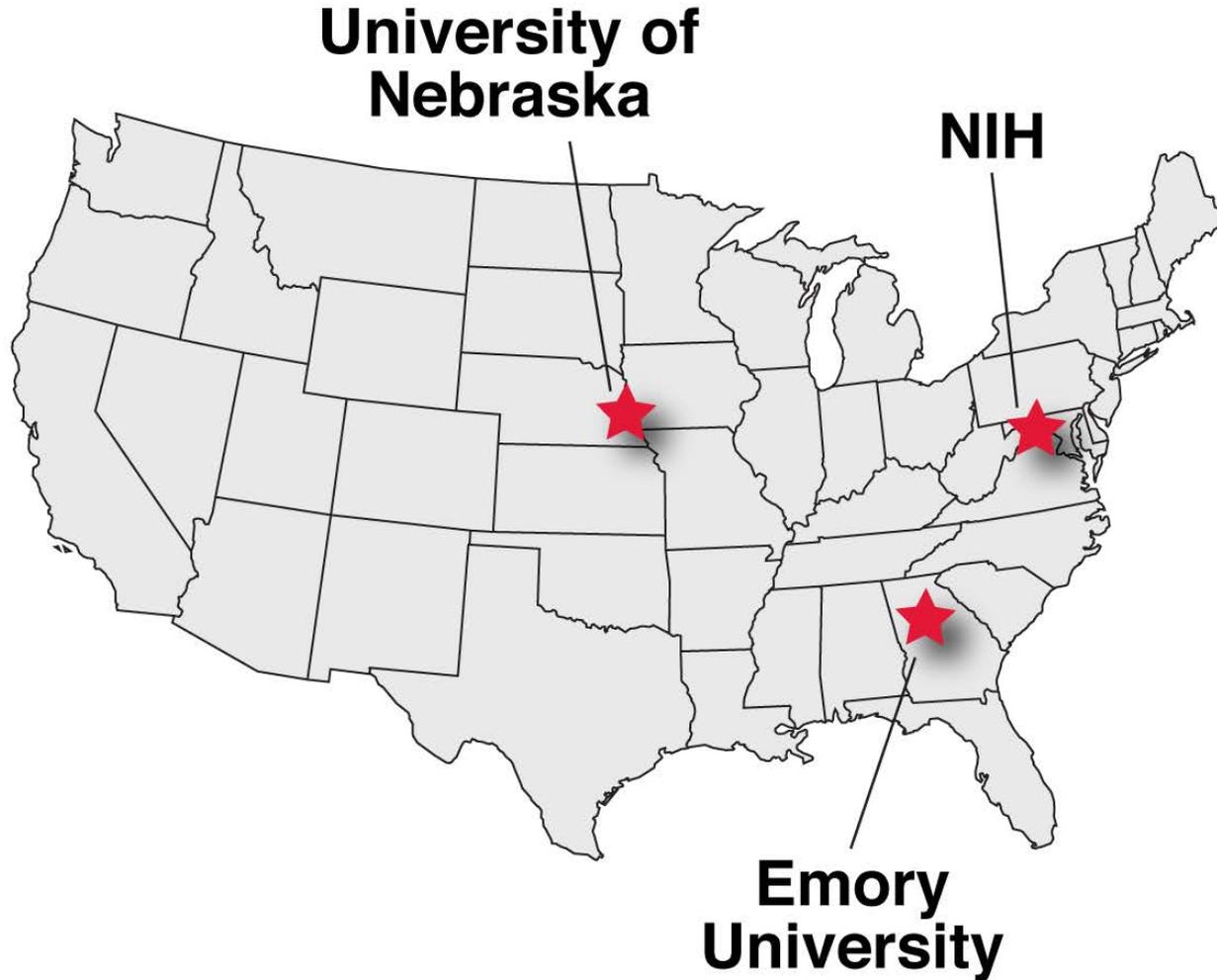
Kent Brantly, MD



Nancy Writebol

# Additional Medevac Cases

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- Richard Sacra, MD
- Ashoka Mukpo
- Lewis Rubinson, MD (Ebola exposure)
- Ian Crozier, MD
- Martin Salia, MD
- Unnamed patient monitored for Ebola exposure

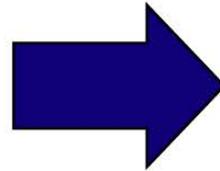
# Inadvertent Importation of Ebola: First Case Diagnosed in U.S

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THE WALL STREET JOURNAL

September 30, 2014

**First Case of Ebola in U.S. Is Confirmed**



# First Case Diagnosed in the U.S.:

## Timeline

**Sept 19**  
Subject  
departs  
Monrovia

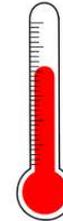


**Sept 20**  
Arrives  
and  
departs  
Brussels,  
Belgium

**Sept 20**  
Arrives in  
Dallas



**Sept 24**  
Develops  
symptoms



**Sept 26**  
Presents to ER,  
sent home



**Sept 28**

Patient transferred by  
ambulance, admitted



**Sept 30**

Tests positive for  
Ebola



**Oct 8**

Patient **dies**

# **First Two Ebola Transmissions Within the U.S.**

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**The New York Times**

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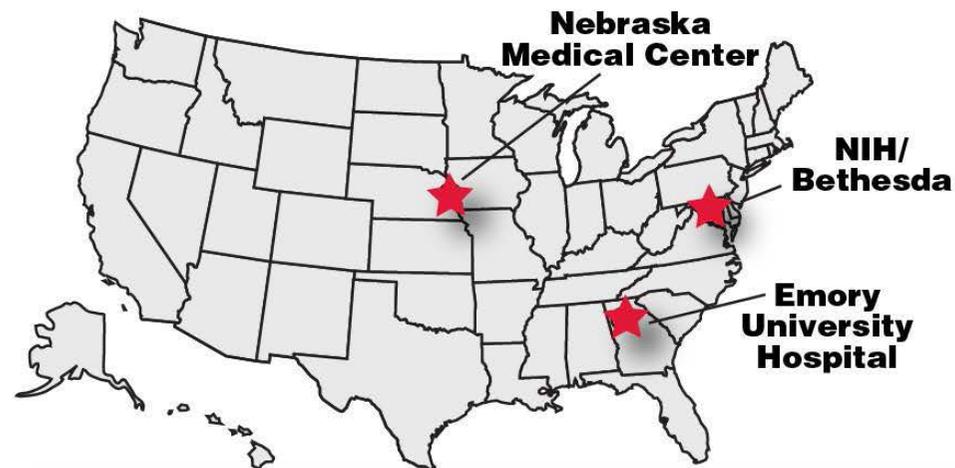
October 12, 2014

**Texas Health Worker Tests Positive for Ebola**

**2nd Ebola Case in U.S. Stokes Fears of Health Care Workers**

# NIH Special Clinical Studies Unit: Designated Ebola Treatment Facility

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# The Washington Post

October 25, 2014

## Nina Pham, Nurse Who Contracted Ebola, is Now Free of Virus and Leaves NIH



Photo: The Washington Post



Photo: Nina Pham

October 15, 2014

**FOX  
NEWS**

# **How to Stop Ebola in America: Ban Air Travel from West Africa**

**Dr. David B. Samadi**

# Airport Screening for Ebola Virus Infection

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## Exit screening:

- Fever
- Presence of symptoms
- Contact with Ebola patient
- Refuse exit if necessary



## Entry screening in the U.S.:

- All passengers routed through 5 airports
- Fever
- Presence of symptoms
- Contact with Ebola patient
- Isolate and further evaluate if warranted

# Exit Screening at West African Airports

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Centers for Disease Control and Prevention

**MMWR**

Morbidity and Mortality Weekly Report

Early Release / Vol. 63

December 9, 2014

## **Airport Exit and Entry Screening for Ebola – August–November 10, 2014**

- August–October 2014, 80,000 travelers screened on exit from Guinea, Liberia and Sierra Leone; 12,000 en route to U.S.
- Of passengers denied boarding due to symptoms or high-risk exposure, none diagnosed with Ebola

# Entry Screening in the United States

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Centers for Disease Control and Prevention

**MMWR**

Morbidity and Mortality Weekly Report

Early Release / Vol. 63

December 9, 2014

## **Airport Exit and Entry Screening for Ebola – August–November 10, 2014**

- **Oct 11–Nov 10, 2014: 1,993 persons screened for Ebola after arrival from Guinea, Liberia or Sierra Leone; none symptomatic during travel**
- **86 referred to CDC officers; 7 of 86 found to be symptomatic and referred for medical evaluation**
- **None had Ebola**

# **NEW YORK POST**

October 23, 2014

## **Doctor Who Treated Ebola Patients Rushed to NYC Hospital**



# The New York Times

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October 24, 2014

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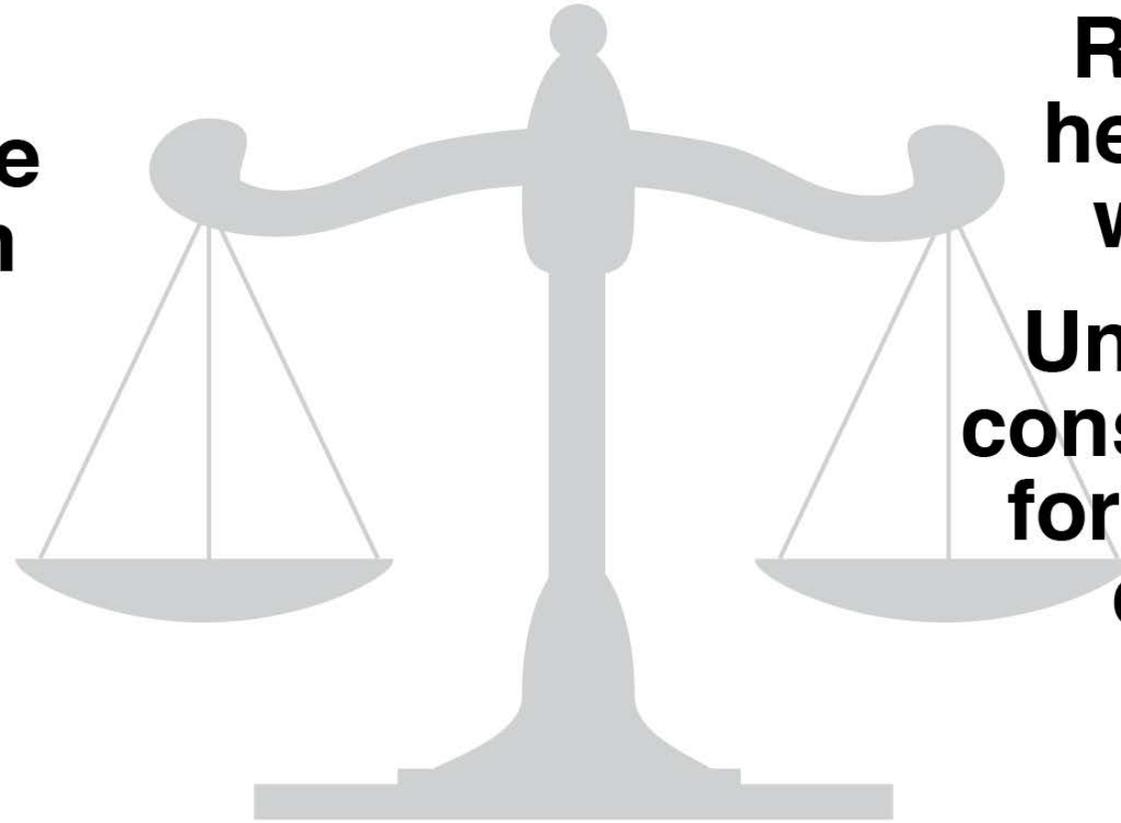
## New York and New Jersey Will Quarantine Medical Workers

# Isolation vs. Quarantine

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- **Isolation** separates sick people with a contagious disease
- **Quarantine** separates people exposed but not ill

**Risk to the  
American  
Public**



**Rights of  
healthcare  
workers**

**Unintended  
consequences  
for outbreak  
control**

**The right balance must be guided by  
scientific evidence**

## **High Risk**

- Direct contact without proper PPE with infected bodily fluids or with body of Ebola patient

## **Some Risk**

- Close contact with symptomatic patient without proper PPE
- Direct contact in proper PPE with symptomatic person in widespread-transmission area

## **Low Risk**

- Travel to widespread-transmission area within 21 days
- Brief contact e.g., shaking hands with symptomatic Ebola patient
- Same room or airplane with symptomatic Ebola patient
- Direct contact in proper PPE with symptomatic person in U.S.

## **No Risk**

- Contact with Ebola patient before symptoms

# CDC Guidelines for Individuals Potentially Exposed to Ebola

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<b>Risk Level</b>		<b>Monitoring</b>	<b>Public Activities</b>	<b>Travel</b>
<b>High Risk</b>		<b>Direct Active</b>	<b>Restricted</b>	<b>Restricted</b>
<b>Some Risk</b>		<b>Direct Active</b>	<b>Case-by-Case</b>	<b>Case-by-Case</b>
<b>Low Risk</b>		<b>Yes – Direct Active for some</b>	<b>No</b>	<b>No</b>
<b>No Risk</b>		<b>Self</b>	<b>No</b>	<b>No</b>

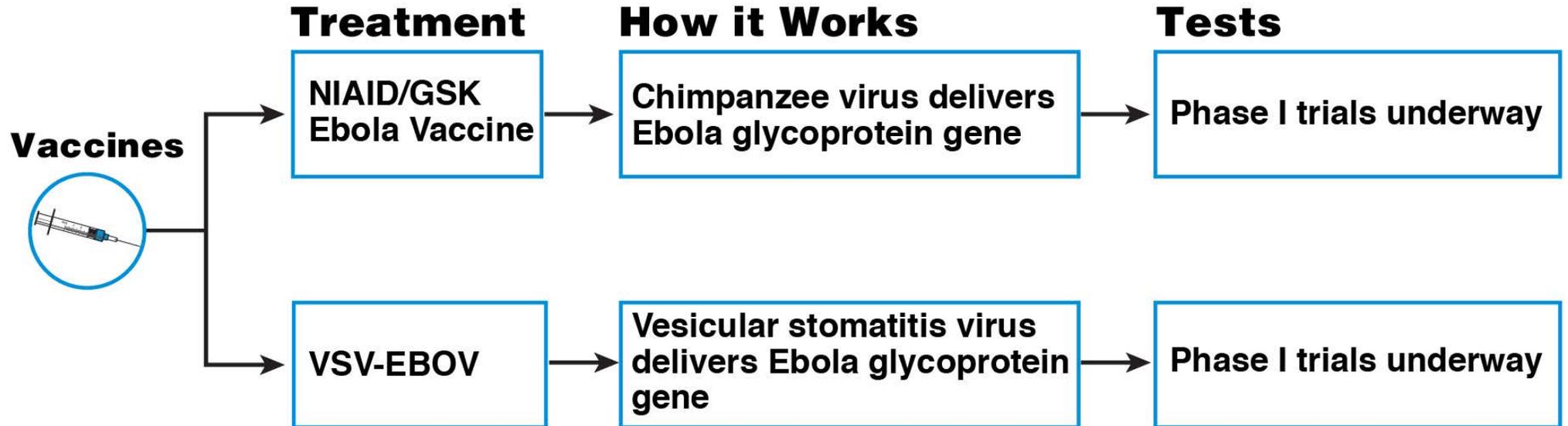
\* Direct Active for healthcare workers who have worked in ETUs in Sierra Leone, Liberia and Guinea with *no known exposure*

- **Ebola background**
  - **Current outbreak in West Africa**
  - **Ebola in the USA**
- **Role of research and development**
    - **Diagnostics**
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    - **Therapeutics**



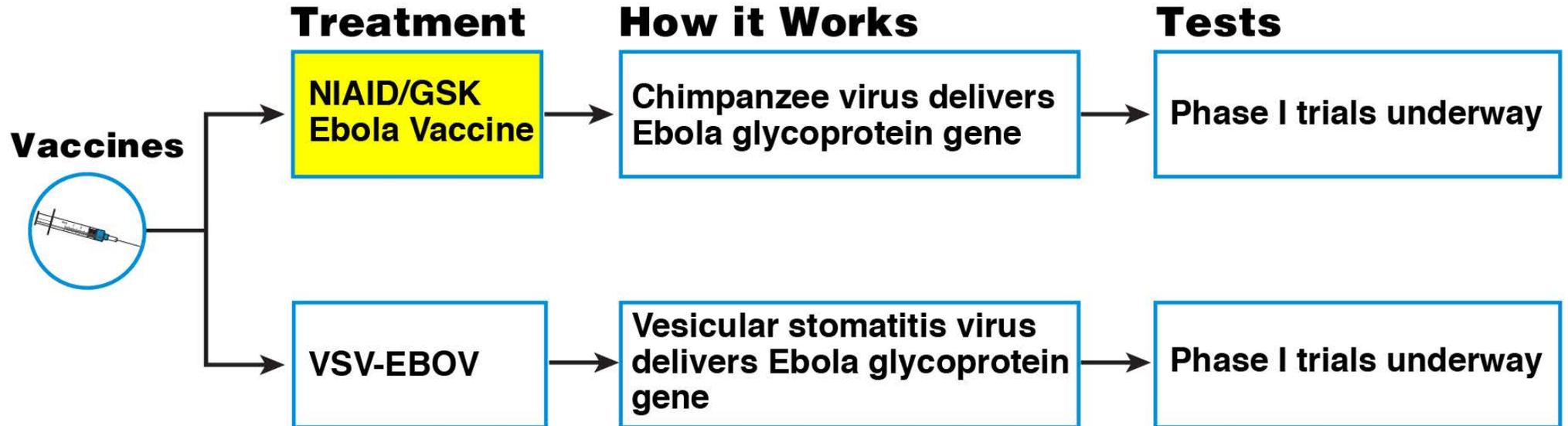
# Pipeline of Vaccines

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# Pipeline of Vaccines

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# **Chimpanzee Adenovirus Vaccine Generates Acute and Durable Protective Immunity Against Ebolavirus Challenge**

DA Stanley, NJ Sullivan et al.

- **Prime-boost Ebola vaccine tested: NIAID/GSK Chimp Ad3 vector + single MVA vector boost**
- **First demonstration of durable protection against Ebola in 4/4 rhesus macaques**



The  
New England  
Journal of Medicine

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Epub ahead of print November 26, 2014

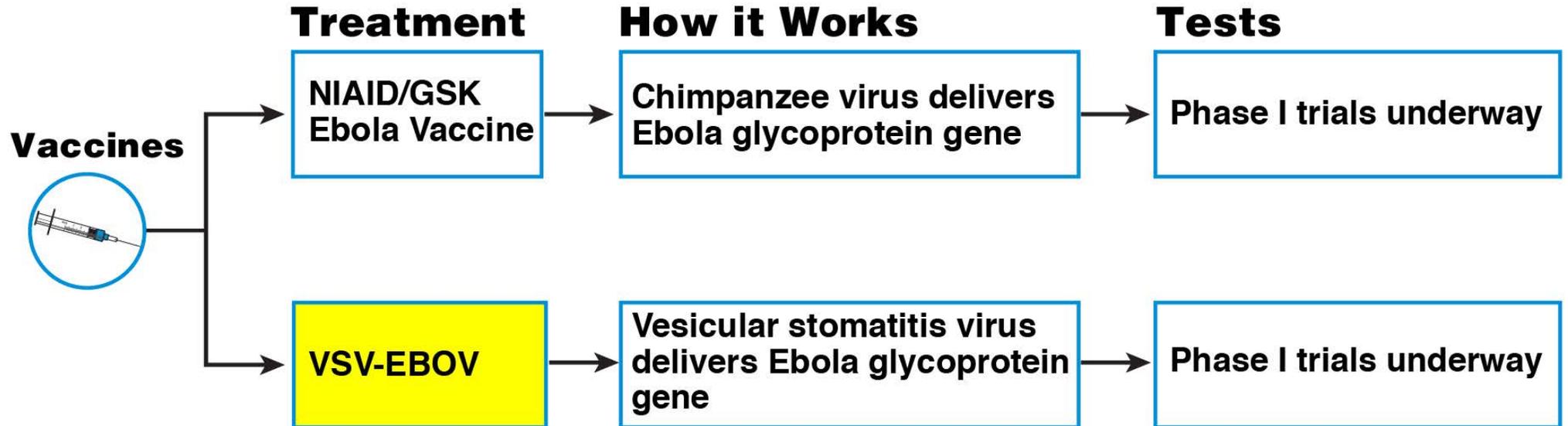
# **Chimpanzee Adenovirus Vector Ebola Vaccine – Preliminary Report**

JE Ledgerwood, BS Graham, the VRC 207 Study Team, et al.

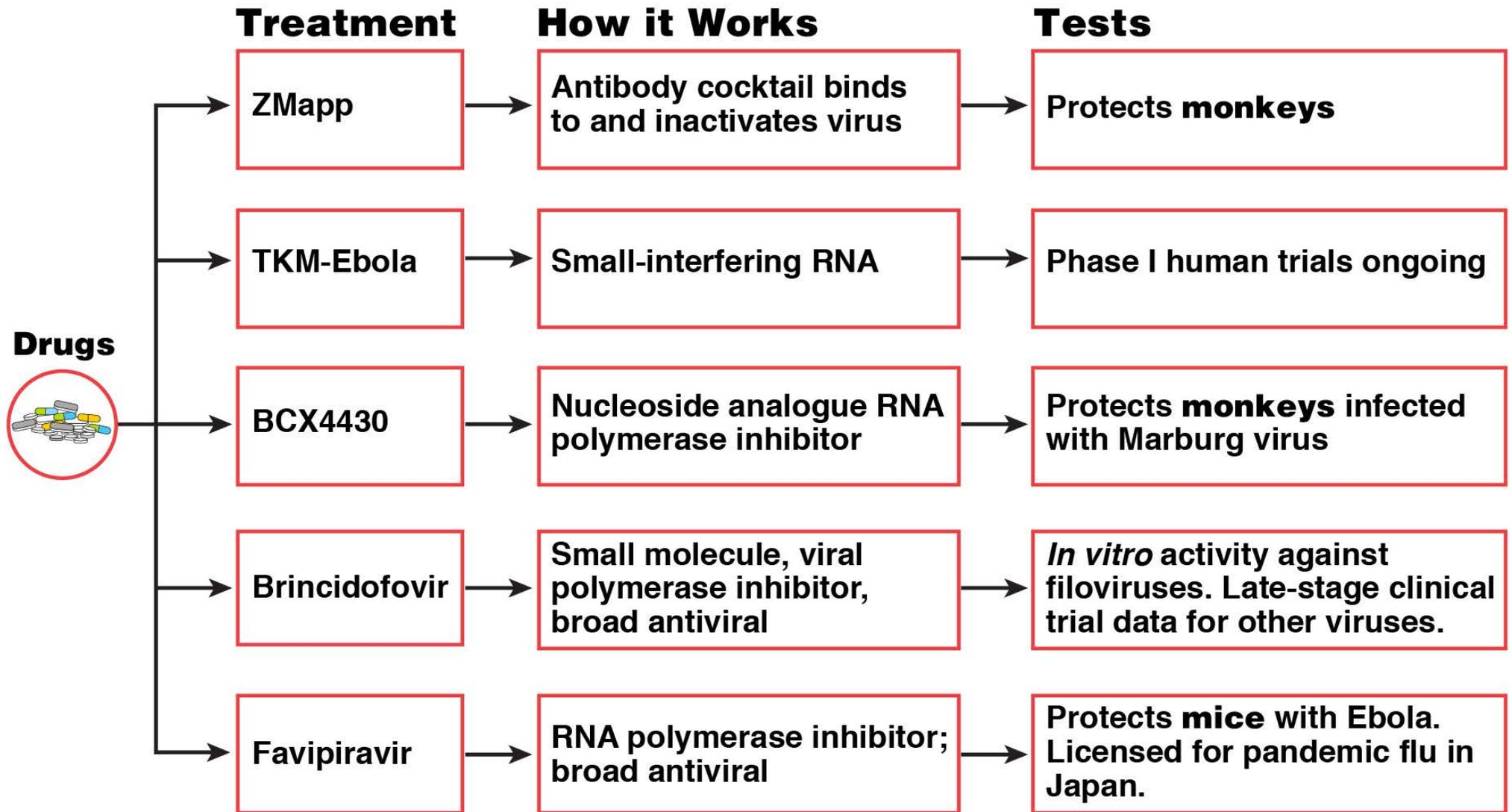
- **Phase I clinical trial of 20 healthy volunteers aged 18-50 yrs, two dose groups ( $2 \times 10^{10}$  and  $2 \times 10^{11}$ )**
  - Well tolerated (two fevers, both resolved in 24 hrs)
  - Antibody and CD8+ T cell responses at higher dose consistent with protective non-human primate response

# Pipeline of Vaccines

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# Pipeline of Therapeutics





**World Health  
Organization**

September 26, 2014

**Experimental Therapies: Growing  
Interest in the Use of Whole Blood or  
Plasma from Recovered Ebola  
Patients (Convalescent Therapies)**

**SCIENTIFIC  
AMERICAN**

December 1, 2014

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**Is the Blood of Ebola Survivors an  
Effective Treatment?**

# Looking Ahead

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- **Continue to focus on West Africa**
- **Prepare for future outbreaks: Global Health Security Agenda**
- **Move towards eliminating to the extent possible disparities of health care infrastructure in developing world**