

Ebola in 2014: The Perfect Storm

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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

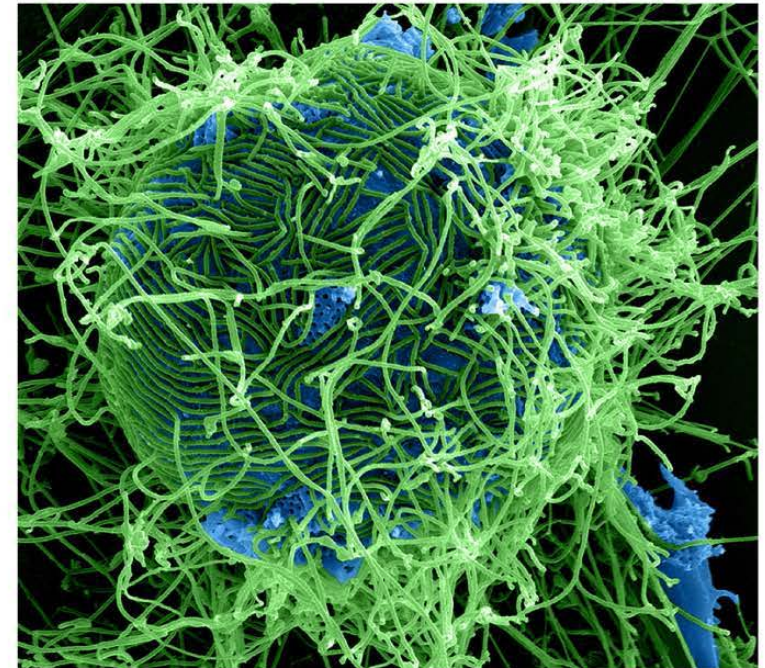
■ Role of research and development

- Diagnostics
- Vaccines
- Therapeutics



Ebola Virology

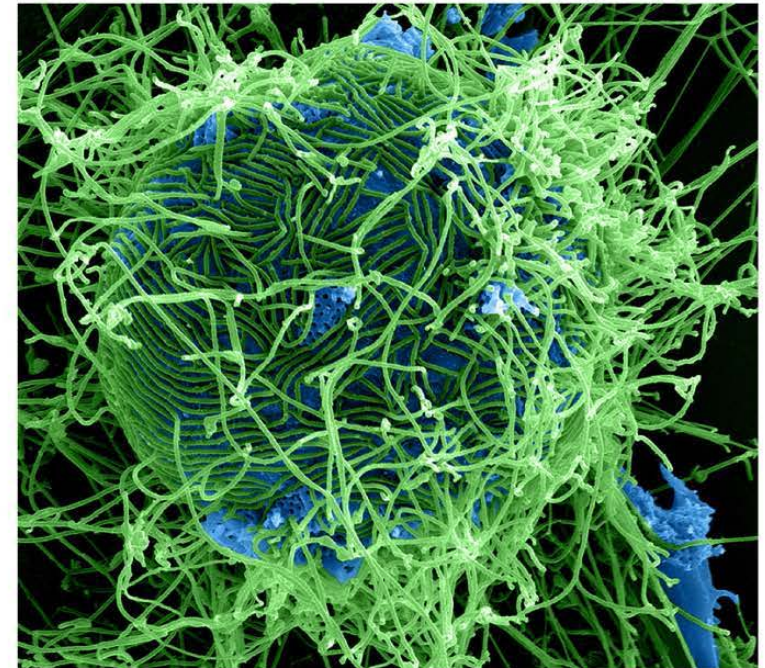
- Filovirus family
- Species and average fatality in the genus *Ebolavirus*
 - Bundibugyo – ~30%
 - Zaire – 50-90%
 - Reston – animal disease
 - Sudan – ~50%
 - Taï Forest – 1 non-fatal human case



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

Ebola Virology

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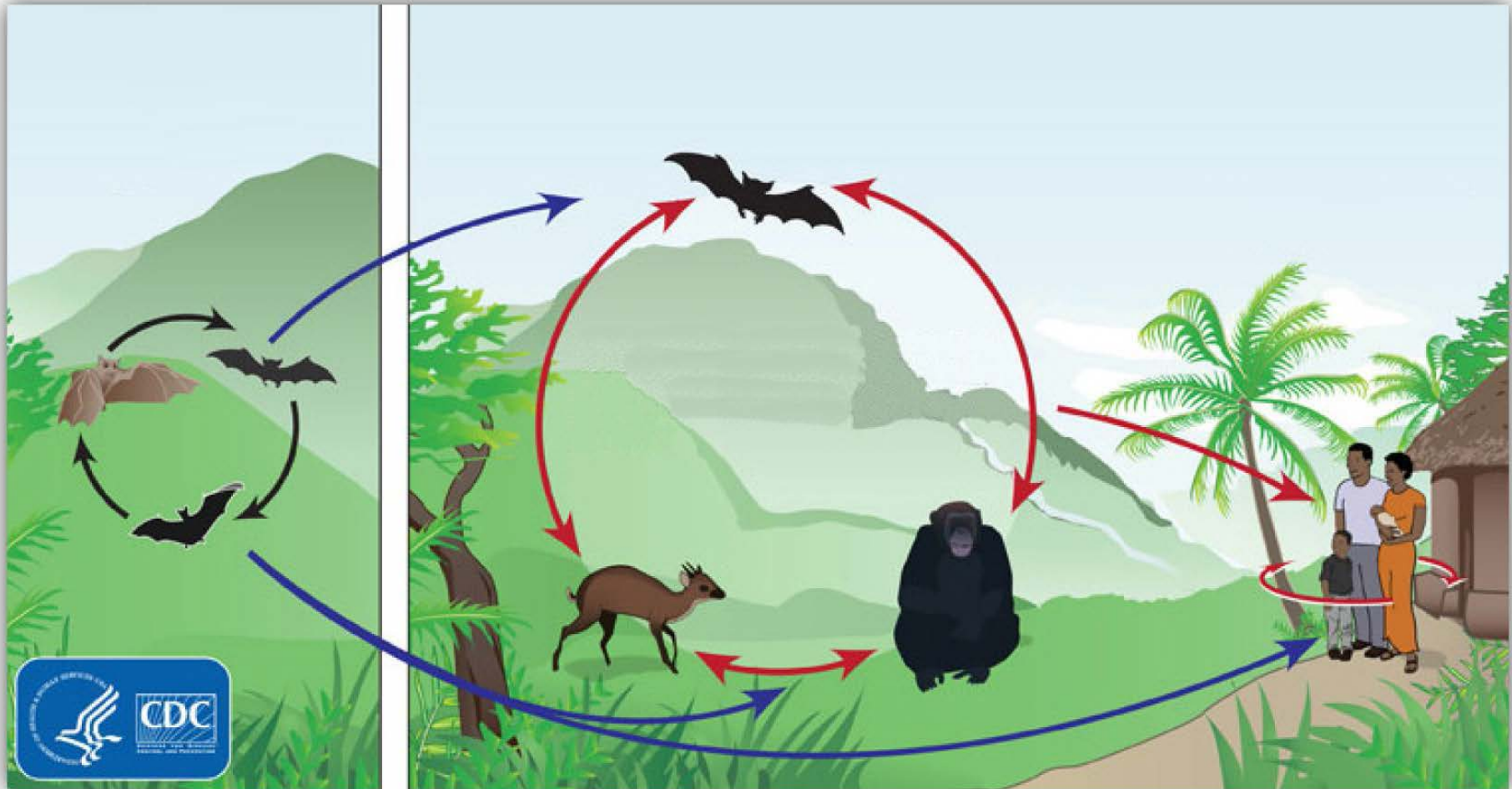


EM of Ebola virus particles (green) attached to Vero cell (blue). NIAID

Ebola Transmission Cycle

Enzootic
cycle

Epizootic cycle

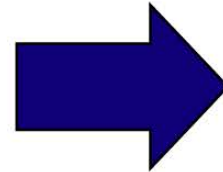


Fruit bats putative reservoir; evidence inconclusive

Ebola Transmission Routes

■ **Bodily fluids**

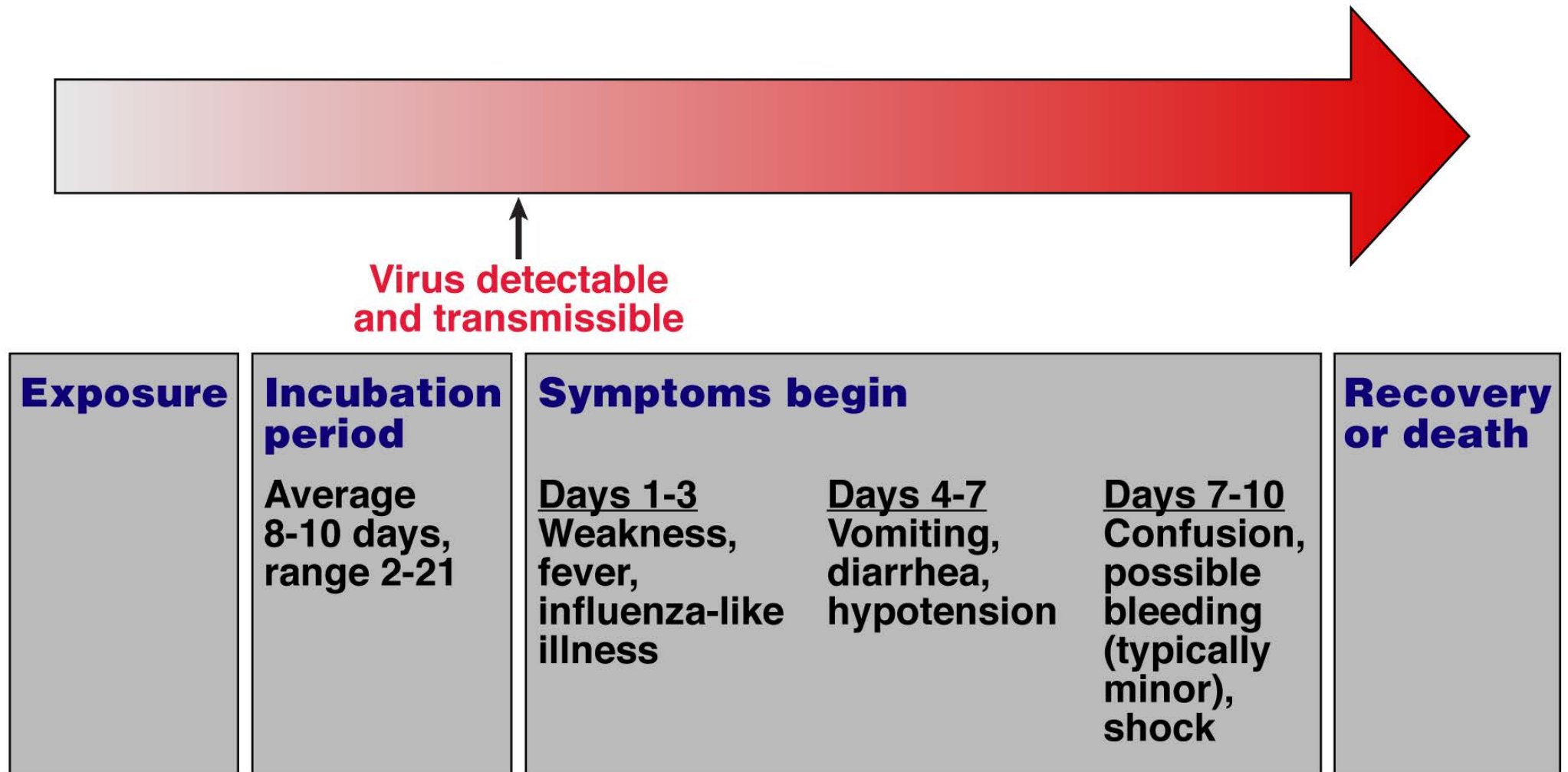
■ **Objects (fomites)**



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

■ **Infected animals**

Typical Ebola Virus Disease Clinical Course





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**

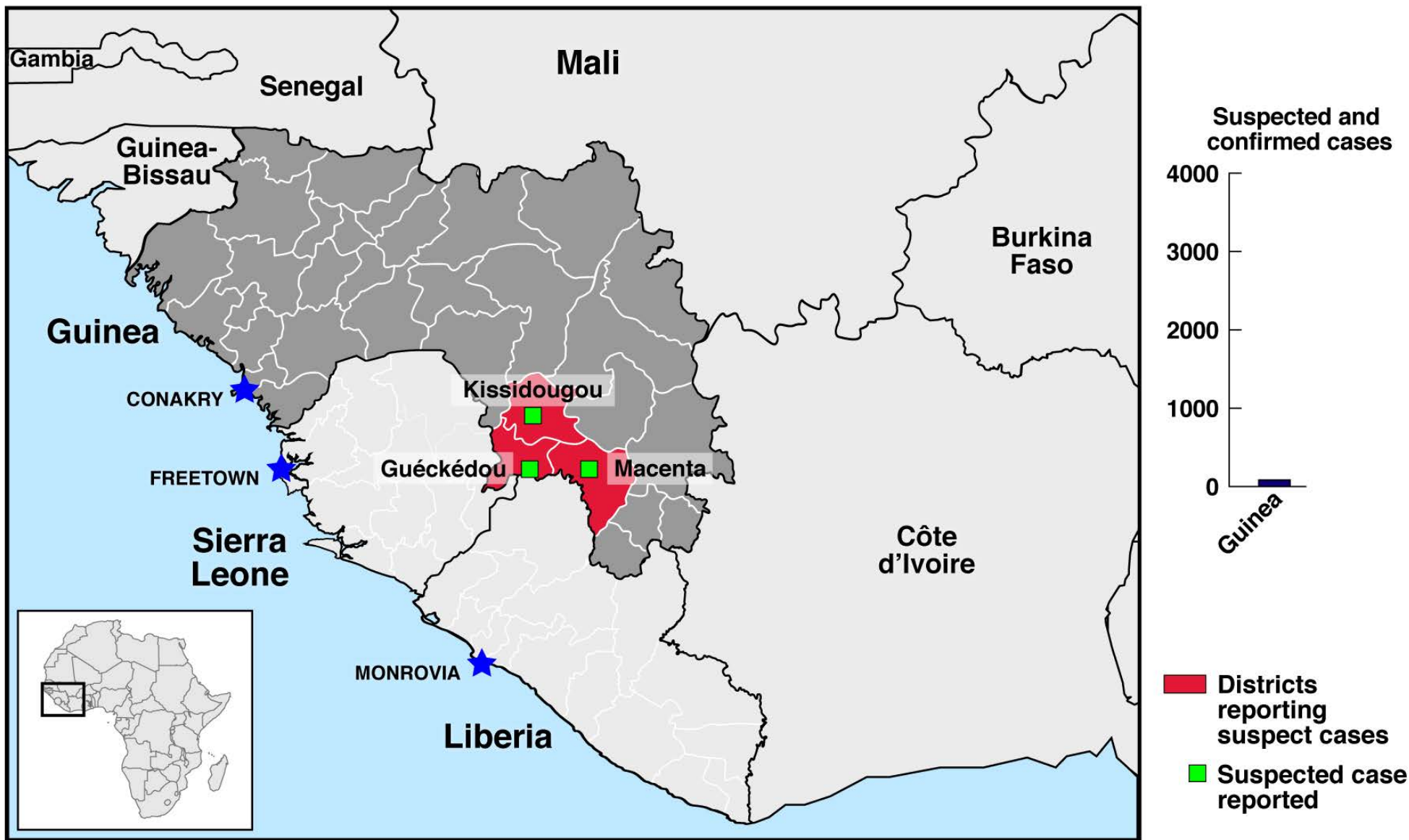
Evidence of Lack of Transmissibility During Early Febrile Stage of Ebola Virus Disease (EVD)

- **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**

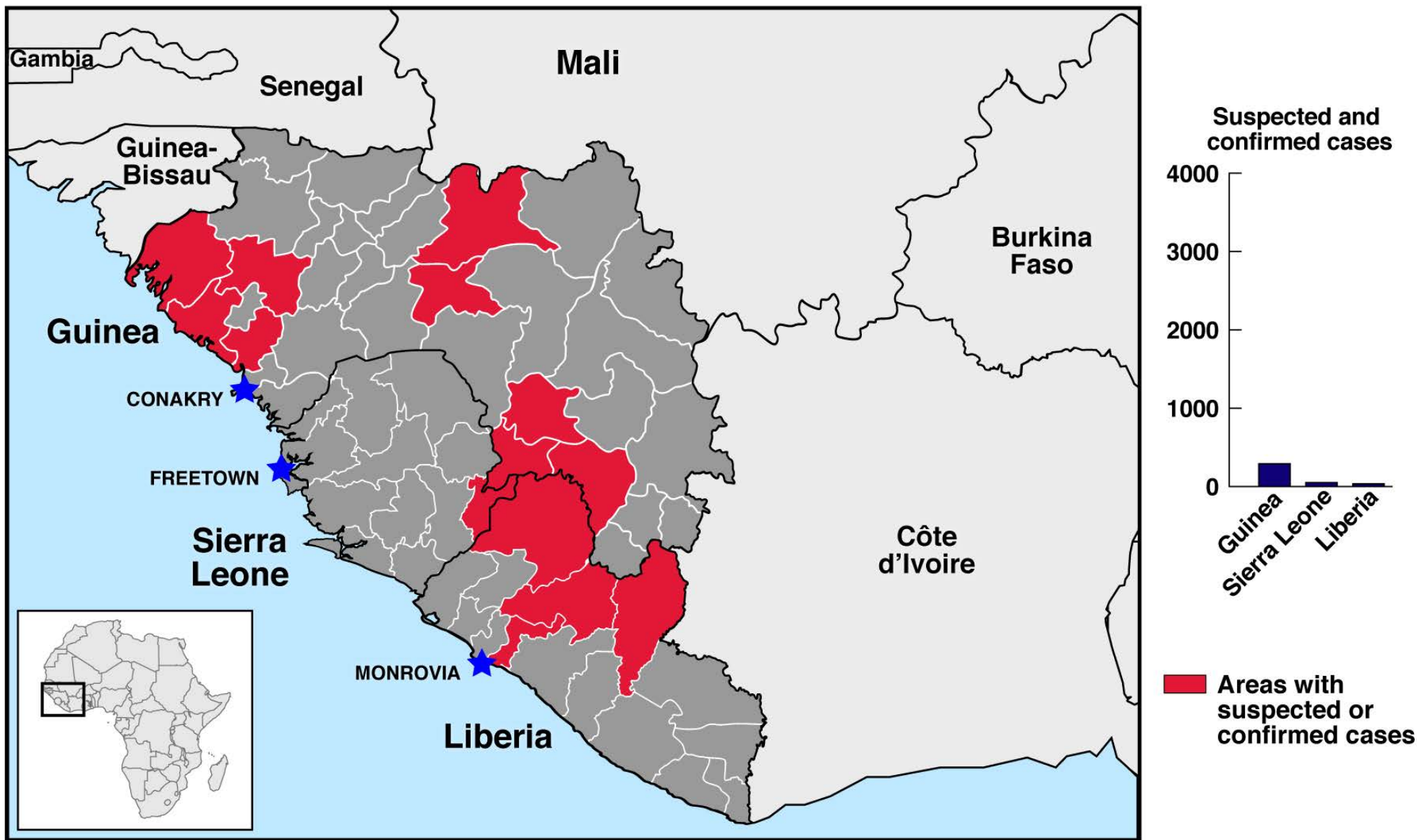
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State of the Outbreak: March 2014

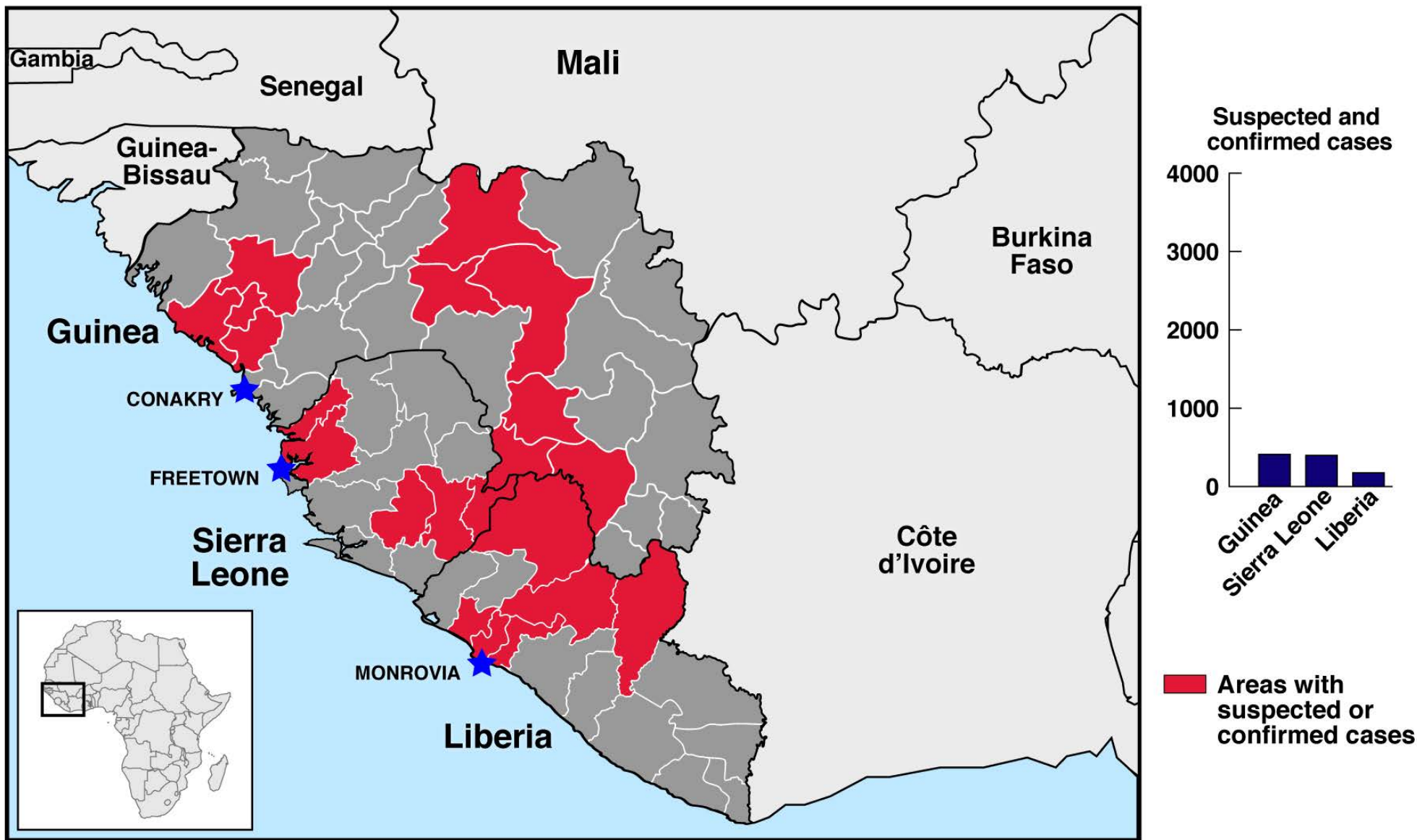


State of the Outbreak: May 2014



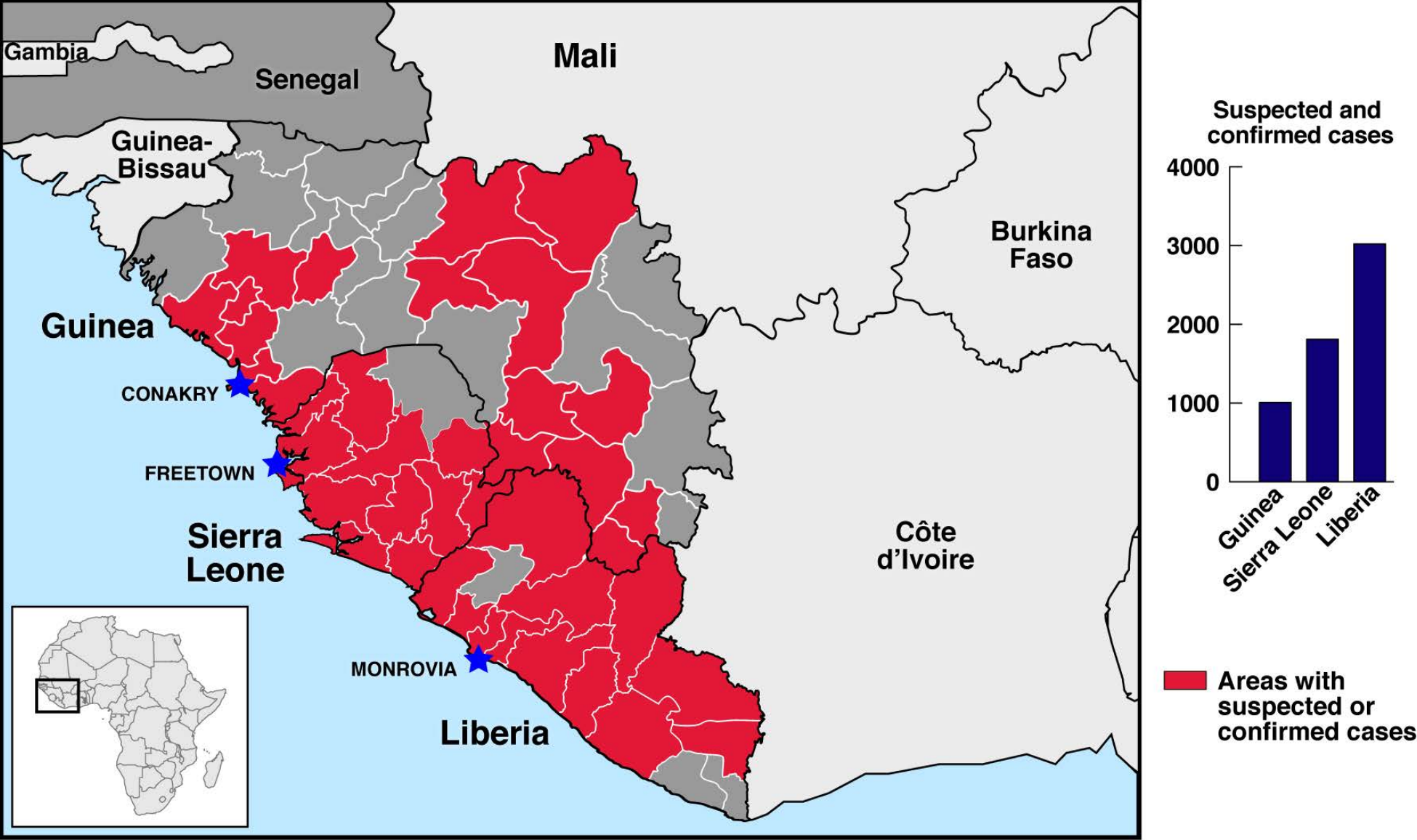
Source: E Ervin, CDC, WHO

State of the Outbreak: July 2014

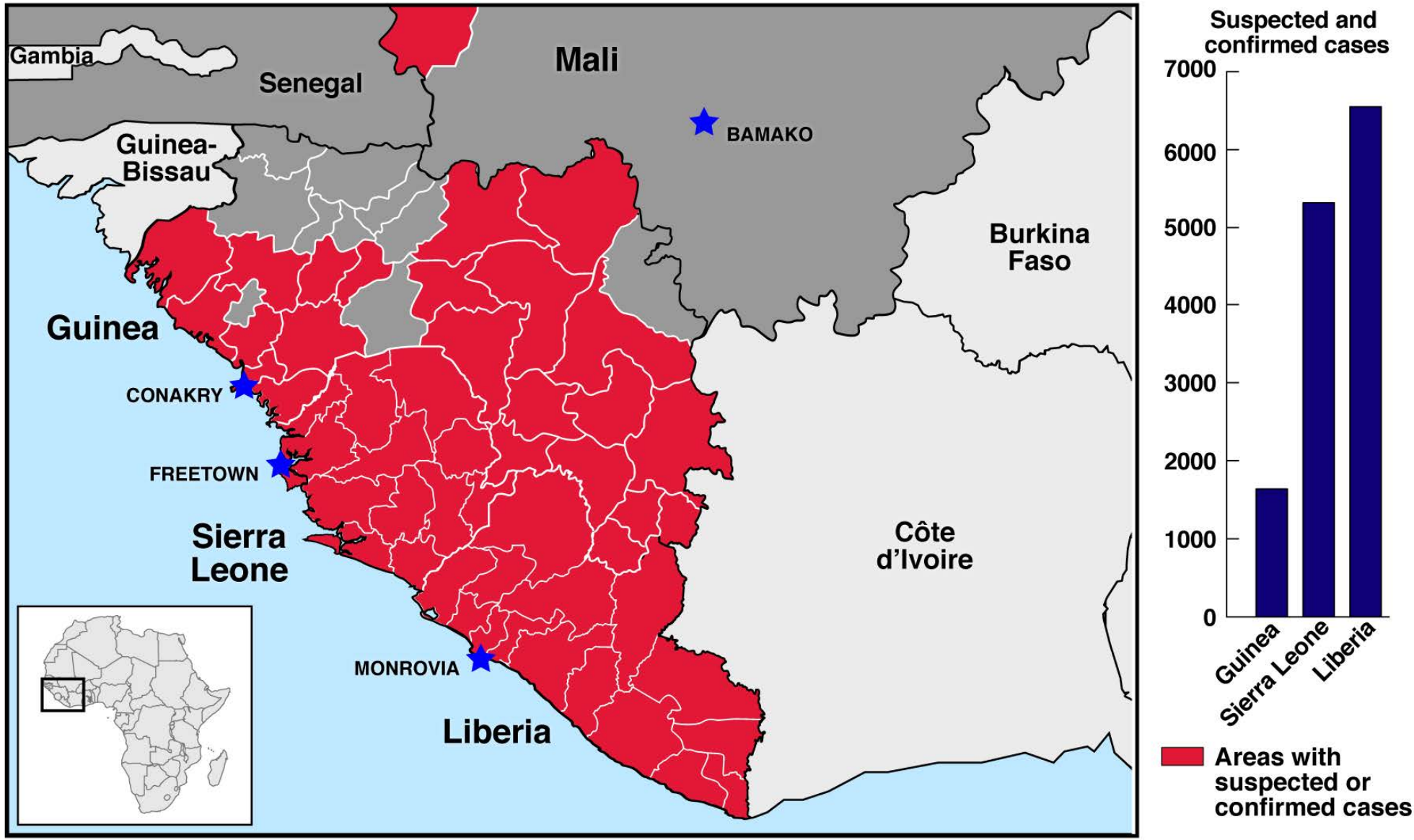


Source: E Ervin, CDC, WHO

State of the Outbreak: Sept. 2014

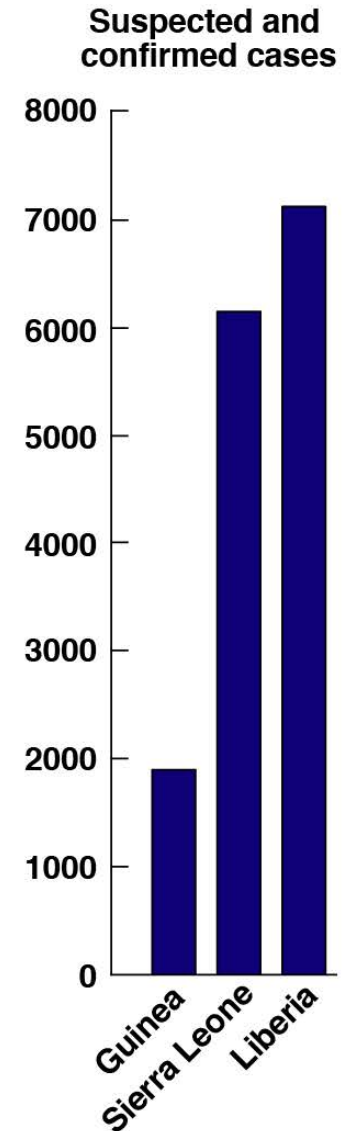
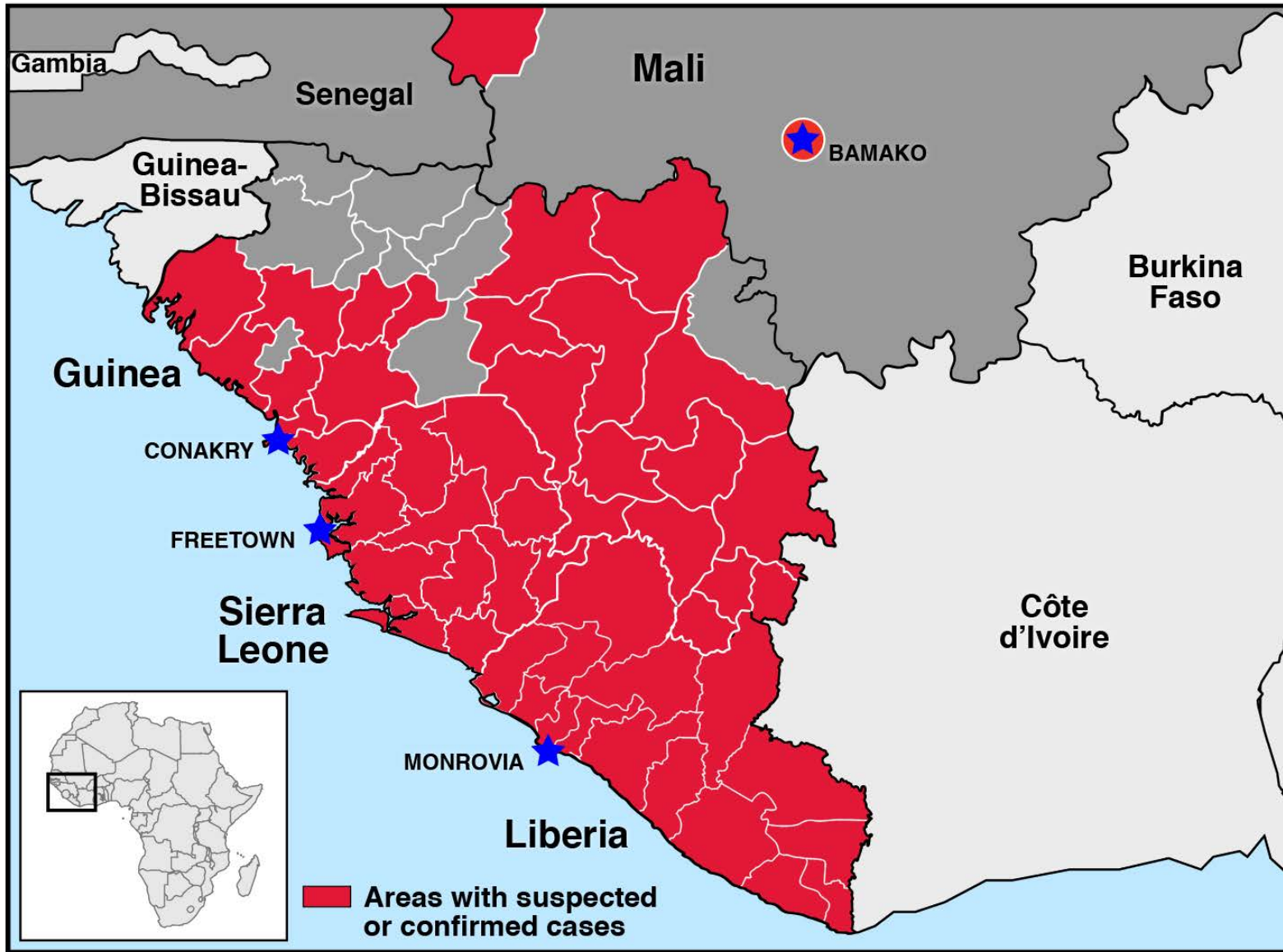


State of the Outbreak: Oct. 2014

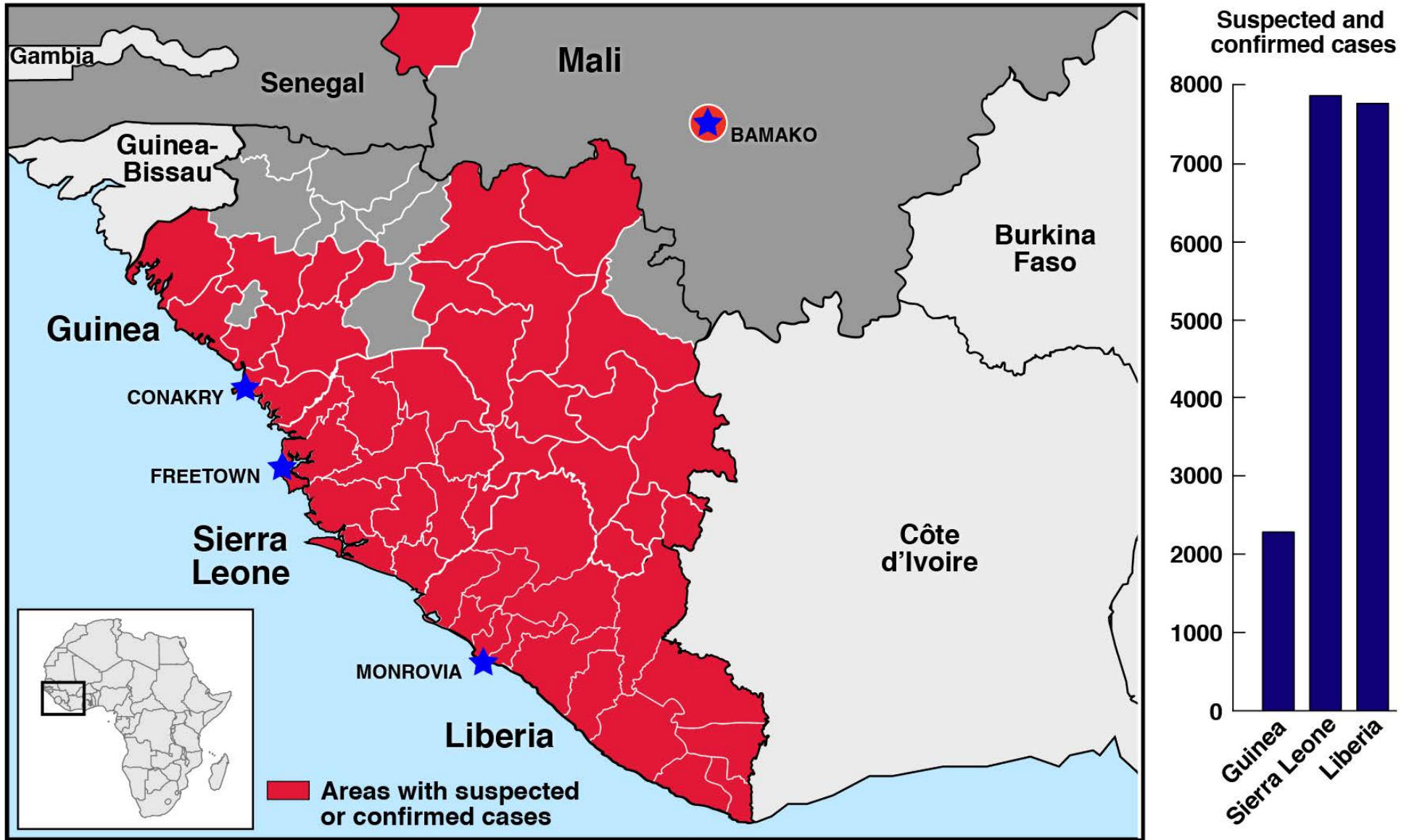


Source: E Ervin, CDC, WHO

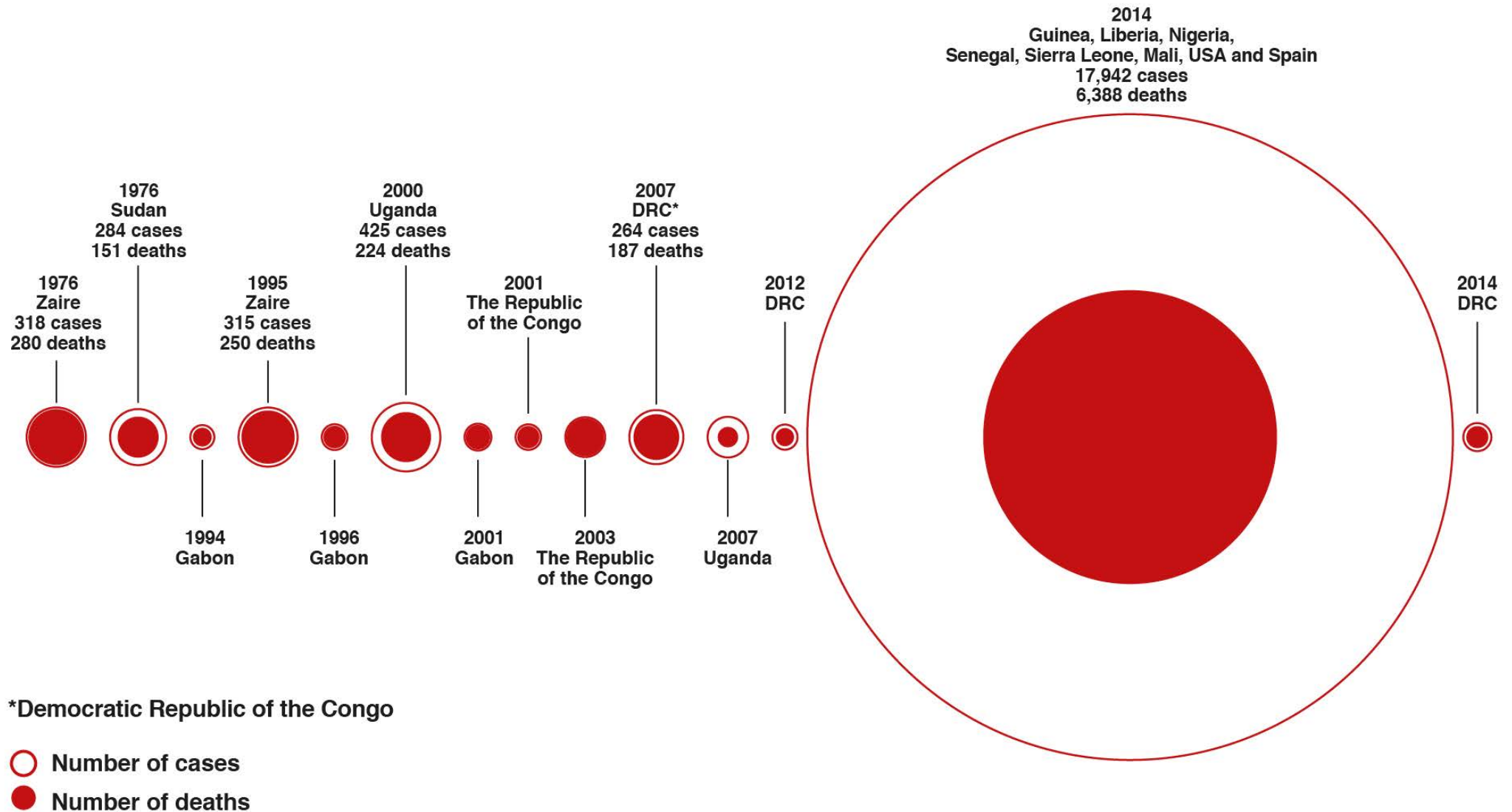
State of the Outbreak: Nov. 2014



State of the Outbreak: Dec. 2014

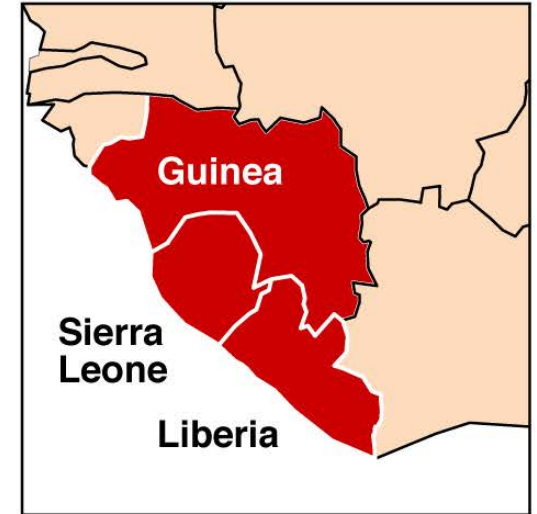


Ebola Outbreaks 1976 to Present Day



Factors Facilitating Spread

- 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

- 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



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

- 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



“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**

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USA TODAY

October 14, 2014

Fear Spreads Faster than Ebola: Our View

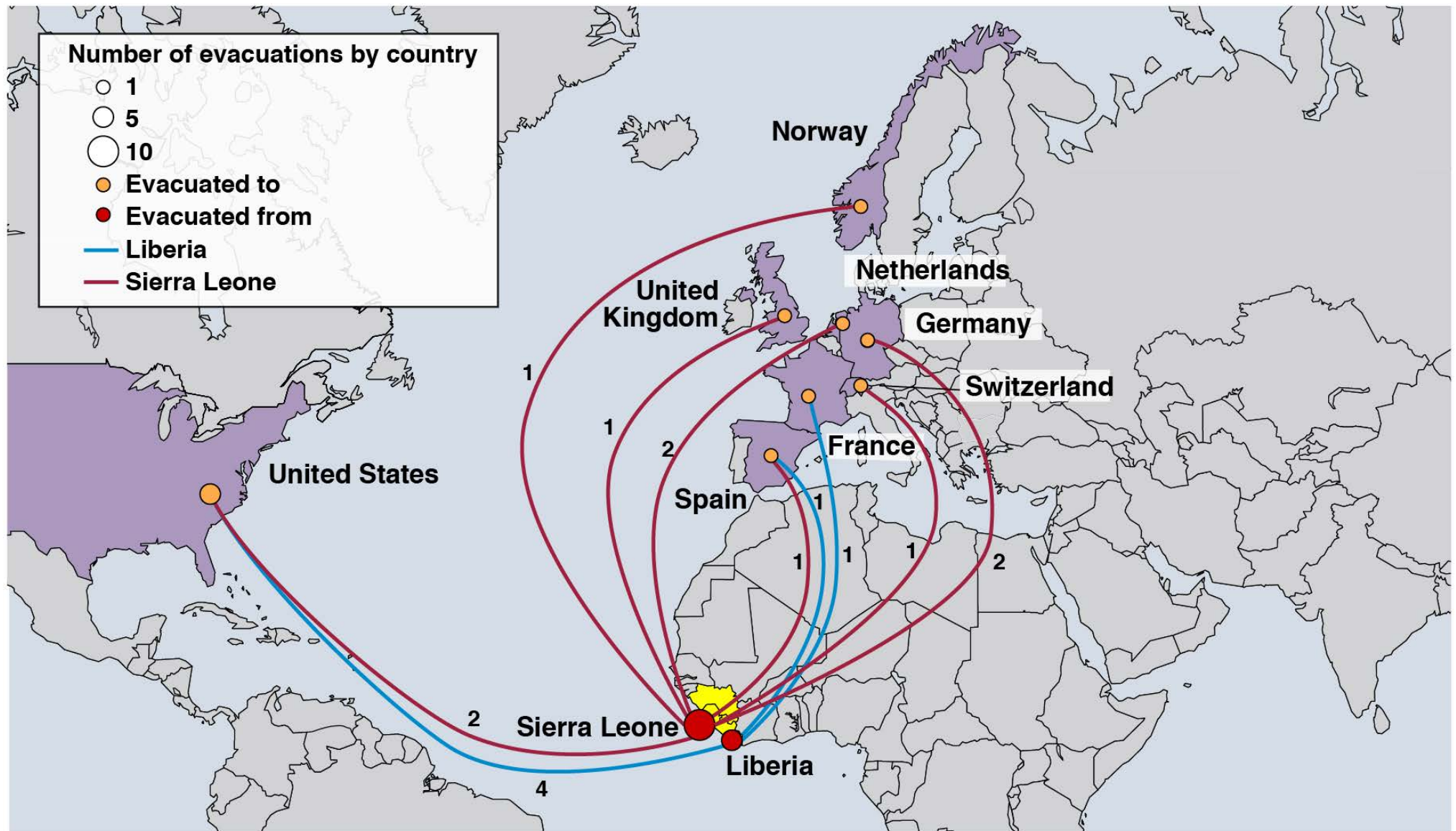
By USA Today Editorial Board



Ebola in the USA

- **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

The Washington Post

August 1, 2014

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

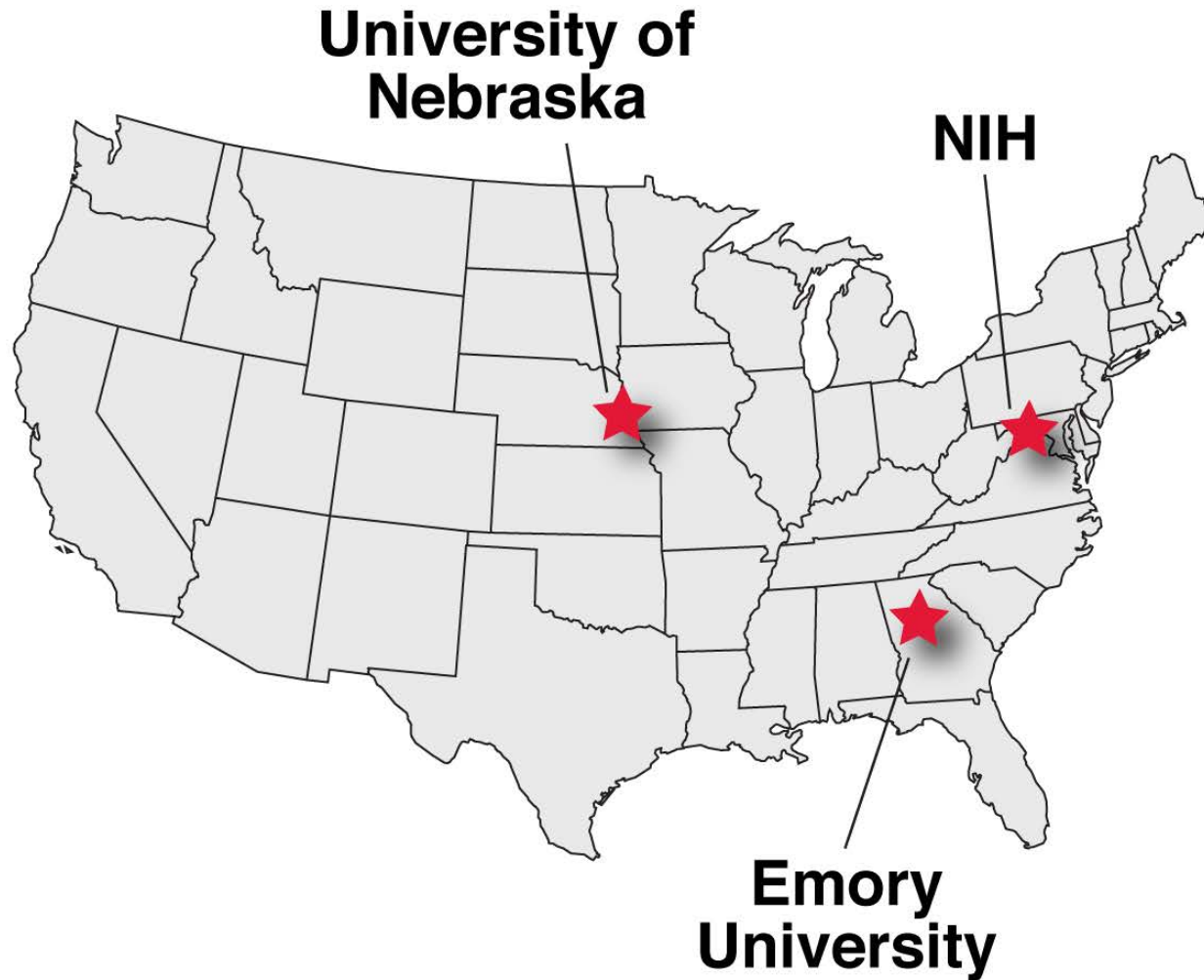


Kent Brantly, MD



Nancy Writebol

Additional Medevac Cases



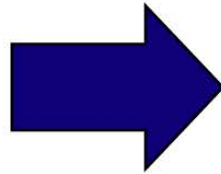
- Richard Sacra, MD
- Ashoka Mukpo
- Lewis Robinson, MD (Ebola exposure)
- Ian Crozier, MD
- Martin Salia, MD
- Unnamed patient monitored for Ebola exposure

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

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

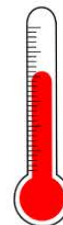


Sept 20
Arrives
and
departs
Brussels,
Belgium

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.

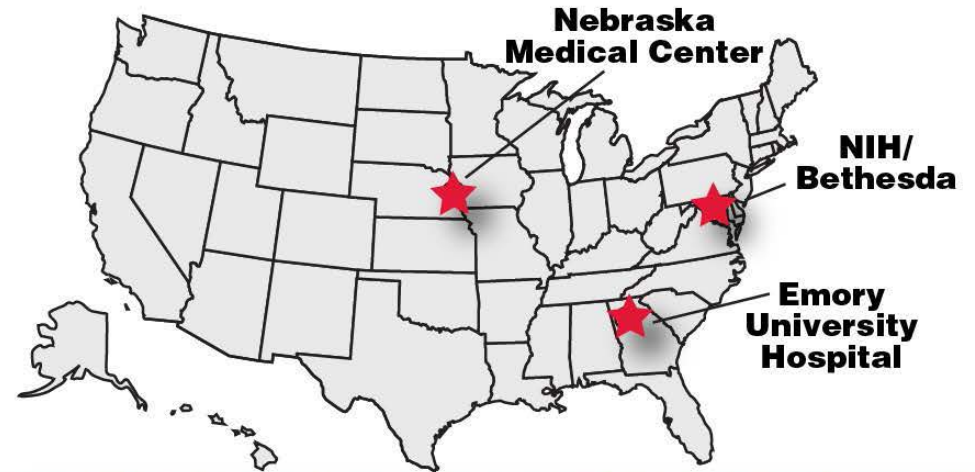
The New York Times

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



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



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

Dr. David B. Samadi

Airport Screening for Ebola Virus Infection



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

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

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**



October 23, 2014

Doctor Who Treated Ebola Patients Rushed to NYC Hospital



The New York Times

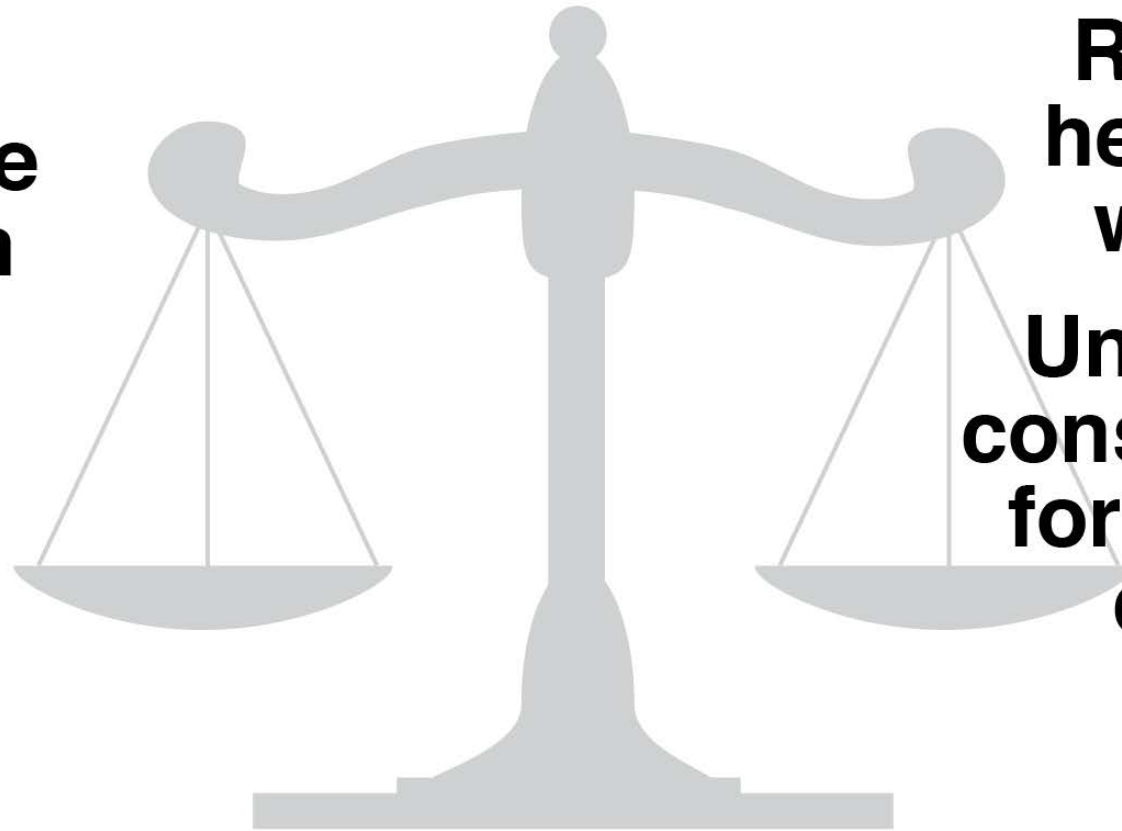
October 24, 2014

New York and New Jersey Will Quarantine Medical Workers

Isolation vs. Quarantine

- **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

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

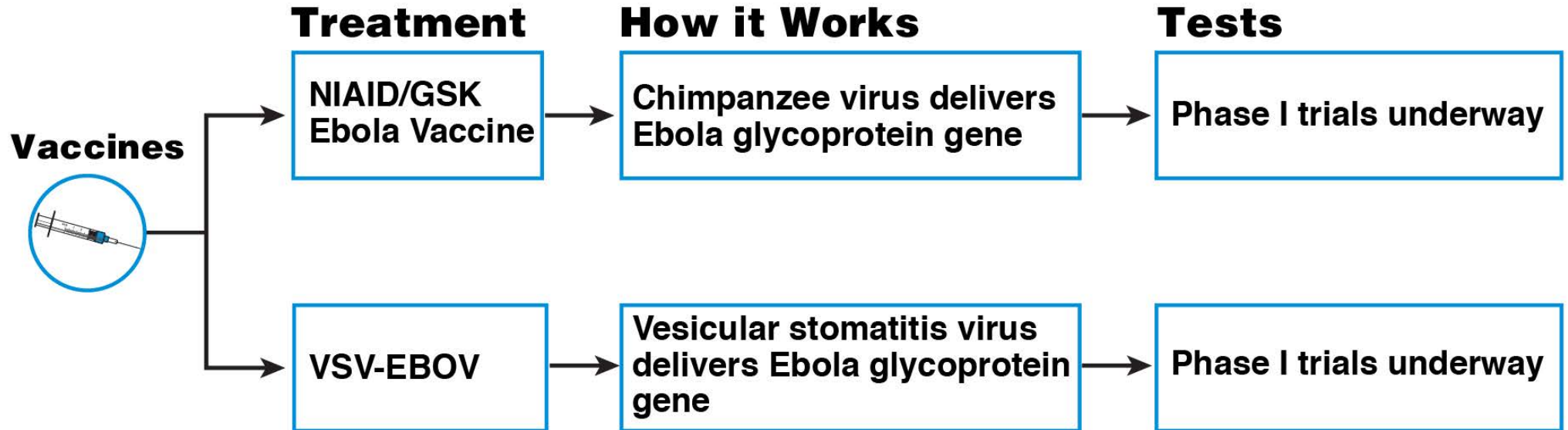
* Direct Active for healthcare workers who have worked in ETUs in Sierra Leone, Liberia and Guinea with *no known exposure*

Source: CDC

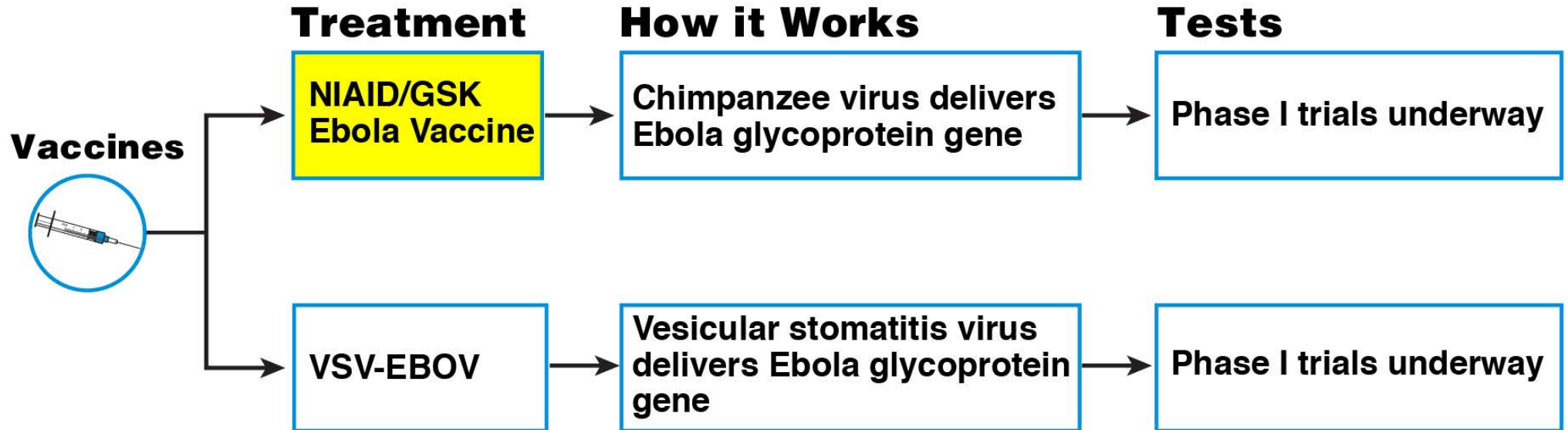
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Pipeline of Vaccines



Pipeline of Vaccines





Chimpanzee Adenovirus Vaccine Generates Acute and Durable Protective Immunity Against Ebola Virus 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

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

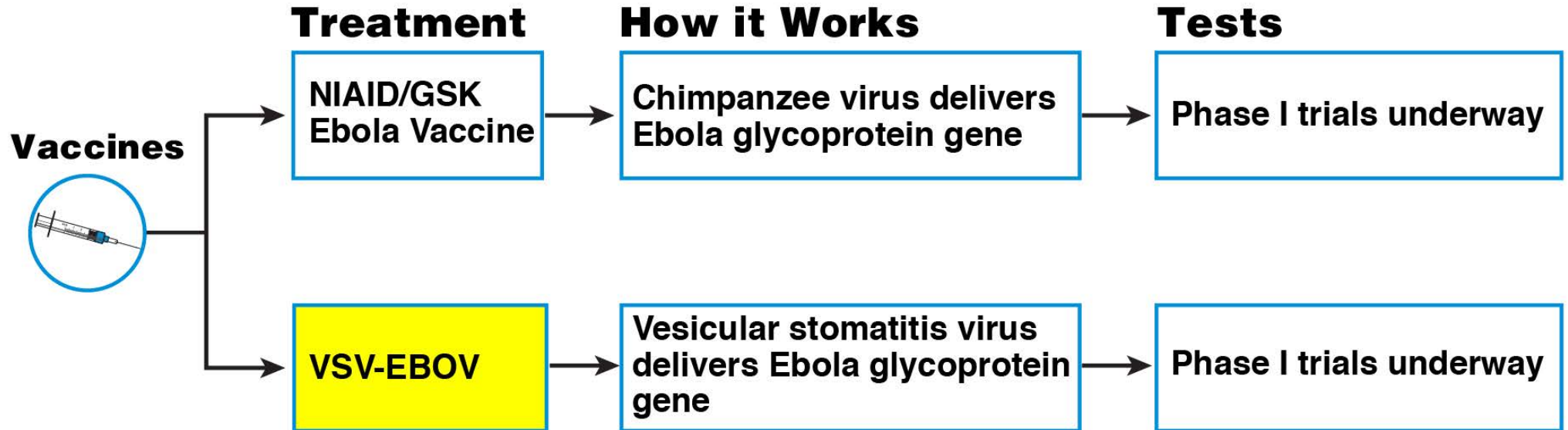
EPub ahead of print November 26, 2014

Chimpanzee Adenovirus Vector Ebola Vaccine – Preliminary Report

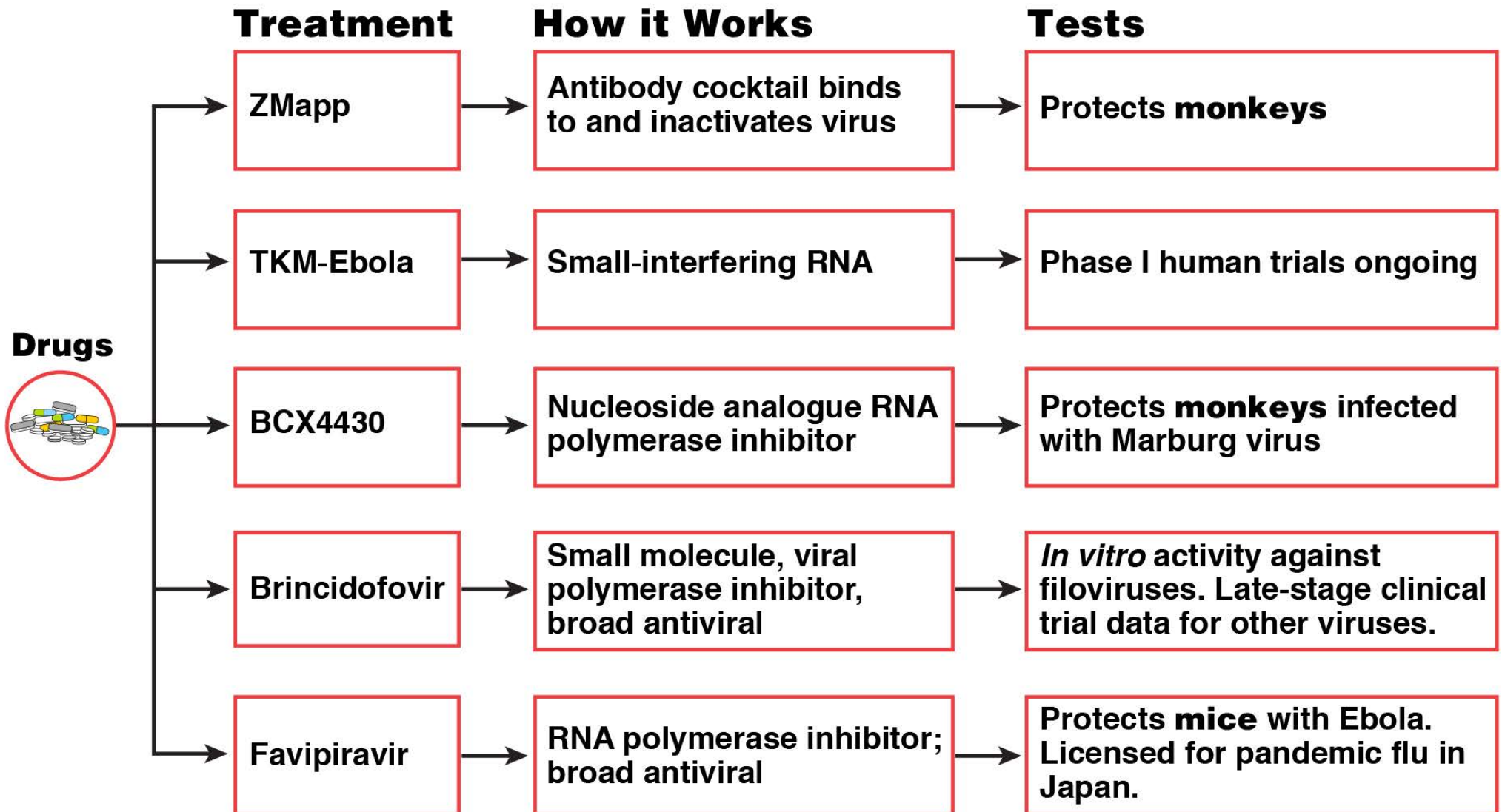
JE Ledgerwood, BS Graham, the VRC 207 Study Team, et al.

- **Phase I clinical trial of 20 healthy volunteers aged 18-50 yrs, two dose groups (2×10^{10} and 2×10^{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



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

Is the Blood of Ebola Survivors an Effective Treatment?

Looking Ahead

- **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**