



# Update on Phase 3 Ebola Vaccines Trials

Design and status

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World Health  
Organization

# Phase 3 trials

## GUINEA

### 1.FLW study

### 2.Ring vaccination RCT

Approx 190 rings.

Immediate vs 21 day.

rVSV vaccine

Started Mar 2015

MSF,  
WHO  
+ partners



## SIERRA LEONE

### Individual RCT

FLWs.

Immediate and deferred  
(6 months)

rVSV vaccine

Started April 2015



LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



NIH

## SIERRA LEONE

### Cluster RCT

800,000 vaccine courses.

Randomize by cluster

Ad26/MVA vaccine

Start May 2015.

## LIBERIA: "PREVAIL"

### Individual RCT

≥27,000 general public.

1:1:1 ChAd3:rVSV:placebo.

Started Jan 2015.

Slide courtesy of Conall Watson

# Ebola vaccines- Phase 3 trials (1)

Study	Study design	Location	Doses/ Vaccine(s)
Liberia PREVAIL	Double blinded RCT	Liberia (Redemption Hospital)	ONE DOSE rVSV ChAd3
Sierra Leone STRIVE	Individually randomized, (unblinded) to immediate or 3 months delayed arm	(Western, Port Loko, Bombali, Tonkolili)	ONE DOSE rVSV
Sierra Leone MOH/LSHTM/J&J EBOVAC	Cluster randomized (in 3 stages, and 2 arms. Half will be immediate and half delayed by 6 months)	Being finalized (Kambia and potentially other locations)	PRIME + BOOST Ad26 + MVA
Guinée <i>Ebola ça suffit-essai clinique</i>	Ring vaccination (cluster randomized in areas with EVD) Immediate vs delay (21 days) arms  Cohort study among FLWs	Basse-Guinée	ONE DOSE rVSV  (ChAd3)

# Ebola vaccines- Phase 3 trials (2)

Study	Study design	Sample size
Liberia PREVAIL	Double blinded RCT	Phase 2: 600 Phase 3: 27,570
Sierra Leone STRIVE	Individually randomized, unblinded	Phase 3: 800 Safety: 400
Sierra Leone MOH/LSHTM/J&J EBOVAC	Cluster randomised	Stage 1: 40 Stage 2: 400 Phase 3/Stage 3: 800,000 (Clusters of approx. 5,000 people)
Guinée <i>Ebola ça suffit- essai clinique</i>	Ring vaccination (cluster randomized in areas with EVD) Immediate vs delay (21 days) arms  Cohort study	190 rings Approximately 10,000 people  FLWs approx. 1,500

# Sierra Leone – Phase 3 STRIVE trial

**Locations:** Western Area, Port Loko, Bombali, Tonkolili

**Target:** 8,000 Front Line Workers

## Number of Cases, Past 7 Days



## Number of Cases, Past 21 Days



## Confirmed Case

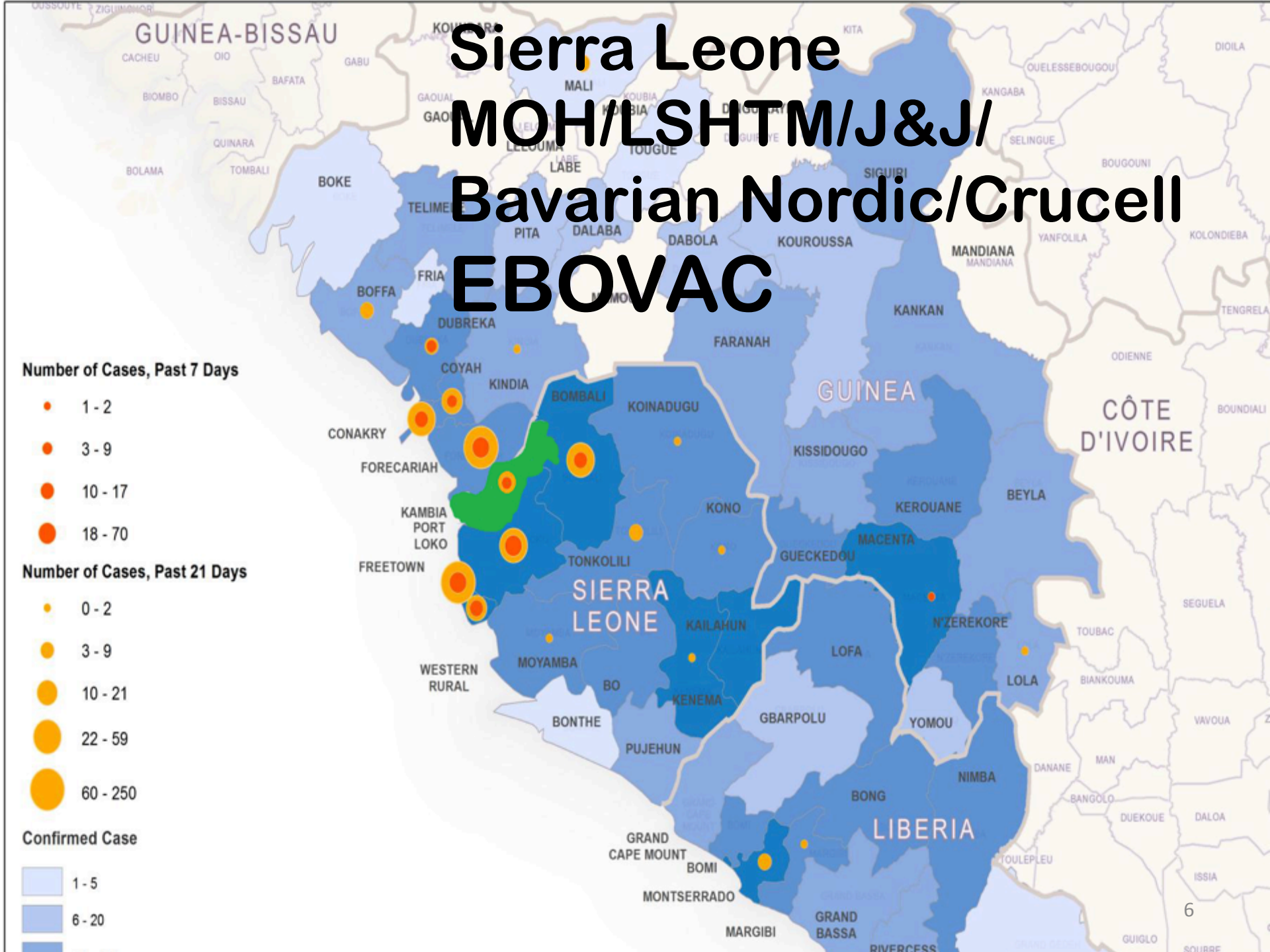


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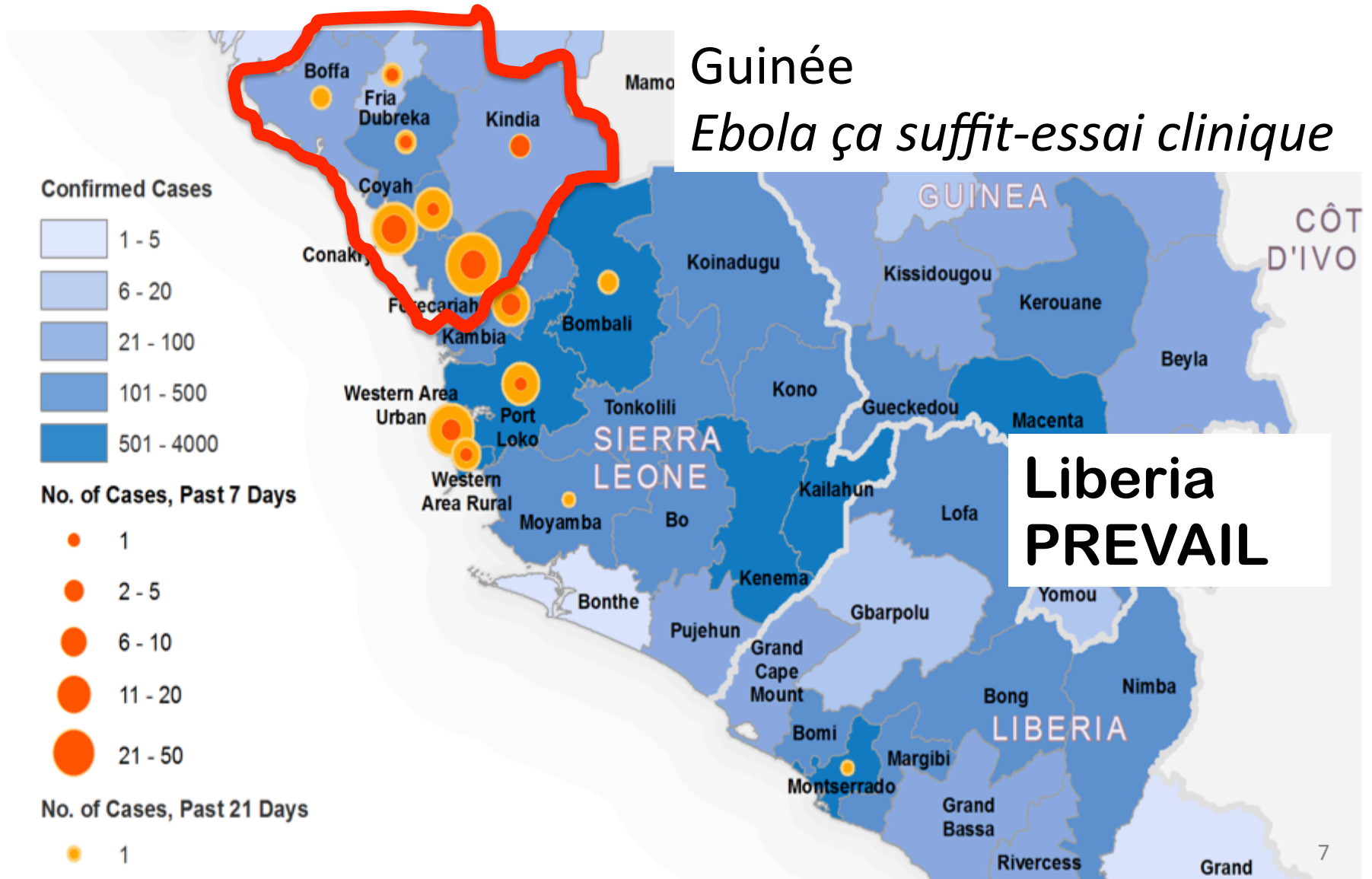
CDC



# EBOVAC



# Geographical distribution of new and total confirmed Ebola cases



# Ebola vaccines- Phase 3 trials (3)

Study	Target population	Inclusion criteria	Exclusion criteria
Liberia PREVAIL	Individuals at risk for EVD	≥ 18 years –	Fever (38.0 Celsius) History of EVD Pregnancy (negative urine pregnancy test required)
Sierra Leone STRIVE	Health Workers	≥ 18 years –	History of EVD or HIV Fever (algorithm for evaluation) <i>Pregnancy</i>
Sierra Leone MOH/LSHTM/J&J EBOVAC	General population	<u>Stage 1:</u> <u>18+</u> <u>Stage 2 &amp; 3:</u> <u>&gt;12months</u>	Pregnancy, individuals, medically unfit for vaccination through chronic illness
Guinée <i>Ebola ça suffit- essai clinique</i>	Eligible individuals who are contacts and contacts of contacts of lab confirmed EVD cases	≥ 18 years –	Fever Pregnancy History of EVD or HIV History of immunosuppression Disease requiring hospitalization at the time of vaccination



# Ebola vaccines- Phase 3 trials (4)

Study	Primary end points	Follow up period
Liberia PREVAIL	Ebola Virus Disease (EVD) lab confirmed	Monthly follow-up through event driven closing date
Sierra Leone STRIVE	EVD lab confirmed	One year
Sierra Leone MOH/LSHTM/J&J EBOVAC	EVD lab confirmed	Stage 1 & Stage 2: 1year Stage 3: 5months, with 1 year in sentinel groups
Guinée Arrêté Ebola	EVD lab confirmed	84 days after vaccination

# Ebola vaccines- Phase 3 trials (5)

Study	Number enrolled to date	Status
Liberia PREVAIL	Phase 2: Enrollment completed Phase 3: not initiated	Analysis ongoing  Searching new location
Sierra Leone STRIVE	Approx. 15 then 40 people/day vaccinated/site. (Unofficial estimate that approx. 100 should receive vaccine to date)	(Western Rural started last Thursday and Western Urban started on Monday)
Sierra Leone MOH/LSHTM/J&J EBOVAC	To start in May 2015	Not recruiting yet
Guinée Arrêté Ebola	Initiated ring vaccination on March 23, 2015: 8 rings (329 volunteers)  Initiated FLWs on March 7 FLWS: 222 volunteers	9 teams in the field: 30-40 rings per week

Deborah Malac, US ambassador to Liberia, speaks at a ceremony at Redemption hospital, formerly an Ebola holding centre



## Ebola vaccine trials begin on volunteers in Liberia

Two experimental vaccines are being tested on 600 volunteers in the first phase of trials that authorities hope will eventually include 27,000 people

**Associated Press in Monrovia**

Monday 2 February 2015 13.38 GMT

A large-scale human trial of two potential Ebola vaccines has started in Liberia's capital, part of a global effort to prevent a repeat of the epidemic that has now claimed nearly 9,000 lives in west Africa.

The trials in Liberia are taking place after smaller studies determined that the vaccines were safe for human use. By comparing them now with a placebo shot, scientists hope to learn whether they can prevent people from contracting the deadly virus that has killed 60% of those admitted to hospital with the disease.

# EBOLA VIRUS OUTBREAK

990  
STORIES

Continuing coverage of the ebola outbreak in Africa and its effects in the U.S. and around the world

## Guinea Ebola Vaccine Trial Uses Smallpox Strategy

COLLAPSE STORY

A new Ebola vaccine trial starts in Guinea this week, this one using the same "ring vaccination" strategy that eradicated smallpox in the 1970s.

Ebola vaccines are being tested in all three West African countries hit by the epidemic that's infected 24,000 people and killed 10,000 of them. Two different vaccines are being tested: one that uses an animal virus called vesicular stomatitis virus or VSV, and another using a chimpanzee cold virus called adenovirus.

Both vaccines carry a little piece of the Ebola virus into the body to jump-start an immune response.

"We have worked hard to reach this point," said World Health Organization Director-General Dr. Margaret Chan. "If a vaccine is found effective, it will be the first preventive tool against Ebola in history."

WHO, the Health Ministry of Guinea, Médecins Sans Frontières (MSF, or Doctors Without Borders), and Norwegian Institute of Public Health will start vaccinating volunteers March 7.

Mar 05



**AFRICA** | WORLD BRIEFING

## Sierra Leone: Ebola Trial Begins

By **SHERI FINK** APRIL 13, 2015

Researchers began vaccinating volunteers in Sierra Leone with an experimental Ebola vaccine in a study officially begun on Monday. The trial, the third to begin in the West African countries hardest hit by Ebola, is sponsored by the Centers for Disease Control and Prevention, Sierra Leone's Health Ministry and the University of Sierra Leone's College of Medicine and Allied Health Sciences. Scientists aim to enroll 6,000 health workers. The vaccine, rVSV-EBOV, licensed by Merck and NewLink Genetics, has also undergone testing in Liberia, Guinea, the United States and other countries. Earlier research showed that the vaccine is protective in nonhuman primates, but it has not yet been proved to prevent Ebola in humans. The epidemic is declining in Sierra Leone, which on Monday reported two new cases.

A version of this brief appears in print on April 14, 2015, on page A8 of the New York edition with the headline: Africa; Sierra Leone: Ebola Trial Begins.



# Ebola vaccines- Phase 3 trials (6)

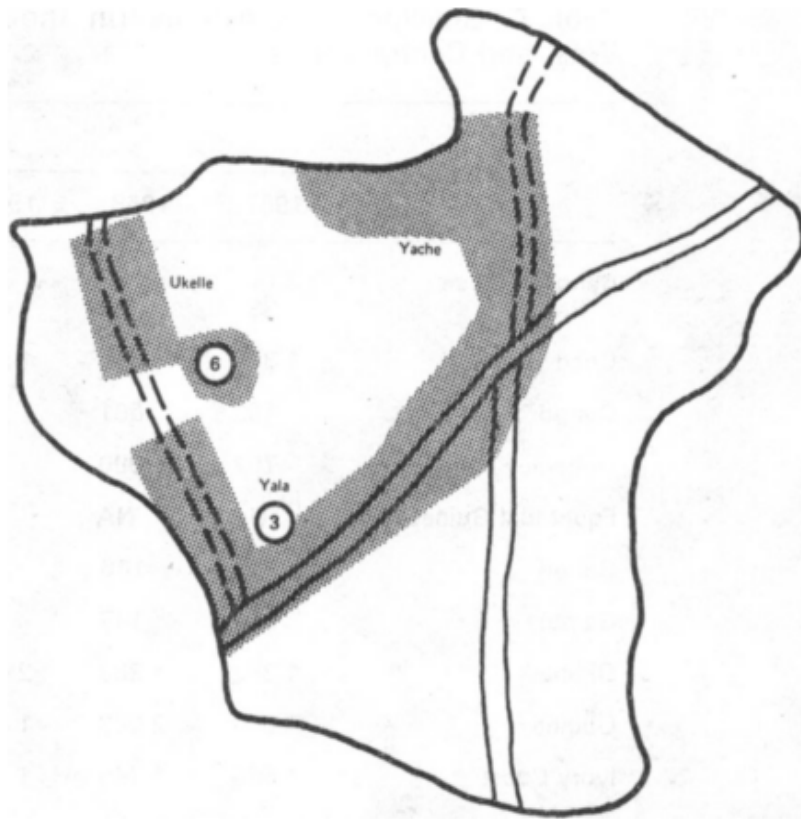
Study	Partners	Vaccine developers
Liberia PREVAIL	MOH Liberia, NIH-USA	GSK Merck
Sierra Leone STRIVE	MOH Sierra Leone, CDC	Merck
Sierra Leone MOH/LSHTM/J&J EBOVAC	MOH Sierra Leone, LSHTM	J&J Bavarian Nordic, Crucell
Guinée Arrêté Ebola	Designed by an international effort under the Guinea Working Group. Implemented by the Ministry of Health of Guinea, MSF, EPICENTRE and WHO. Funded by MSF; the Norwegian Research Council through Norway's Institute of Public Health ; Public Health Agency of Canada, Canadian Institutes of Health Research, International Development Research Center and Department of Foreign Affairs, Trade and Development; and WHO, with support from the Wellcome Trust, UK;sponsored by WHO	Merck (GSK)



# Smallpox eradication in West and Central Africa

WILLIAM H. FOEGE,<sup>1</sup> J. D. MILLAR,<sup>2</sup> & D. A. HENDERSON<sup>3</sup>

*BULL. WORLD HEALTH ORGAN.*, Vol. 52, 1975



	Smallpox	Ebola
Serial interval	17 days	15 to 19 days
$R_0$	5 to 7	1 to 2
Vaccine	Effective Works soon after administration	Unknown  Unknown

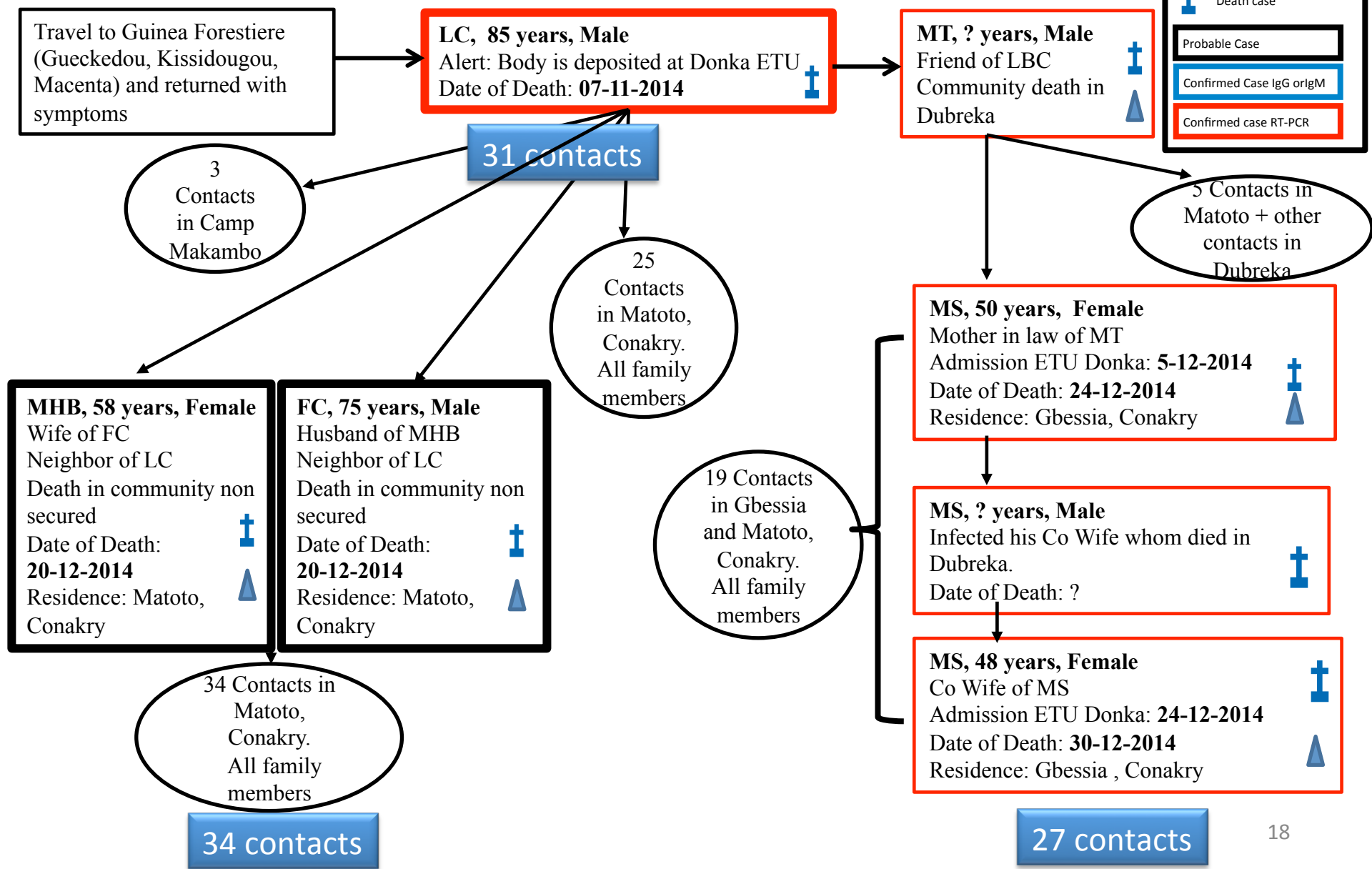
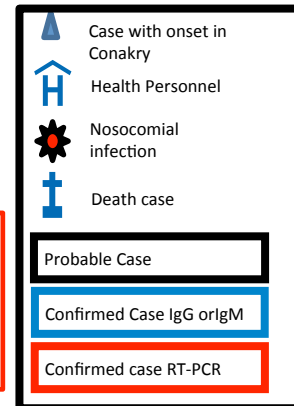
Fig. 7. Ogoja outbreak, 18-24 December.

# What is a vaccination ring?

A vaccination ring is not necessarily a single geographical site. It comprises of:

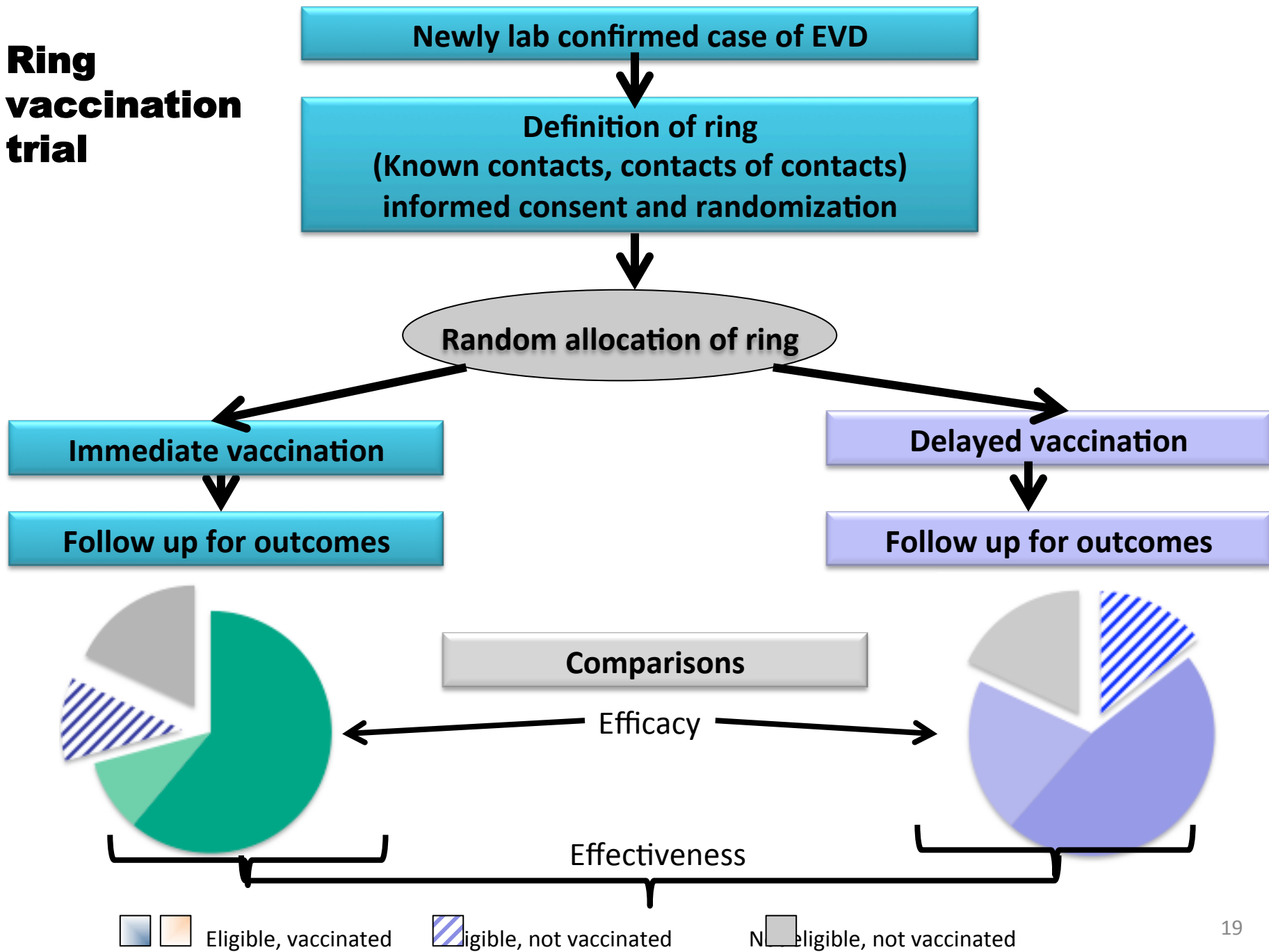
- **all the contacts of an index case of EVD, plus**
- **household members of any high-risk contact who do not live in the same locality as the case.**
- **the neighbours or extended family members to nearest geographic boundary in which the local contacts of the index case reside, plus**

# Example of Chain of Transmission in Guinea





# Ring vaccination trial



# Community sensitization and informed consent

- 1. Training of local social mobilizers



- 2. Initial visit to ring to explain study



- 3. Collective explanation of ICF



- 4. Individual ICF with witness



# Enrolment and vaccination

- 1. Eligibility assessment



- 2. Vaccination



- 3. 30 minutes observation



- 4. Individual card and info on next visit



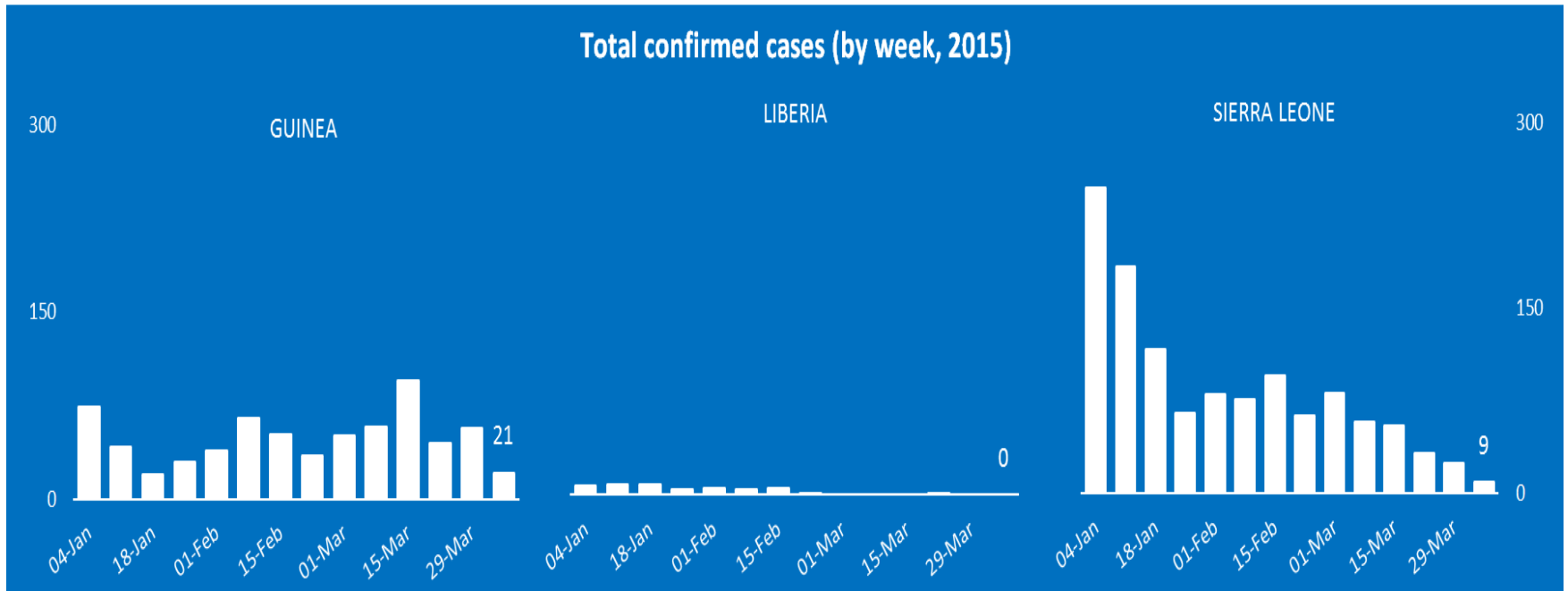


World Health  
Organization

# EBOLA SITUATION REPORT

8 APRIL 2015

Total confirmed cases (by week, 2015)







Many thanks