

# Ebola vaccine – and now?

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NECTM7 Stockholm, 3 May 2018



# Conflict of interest

Nothing to declare





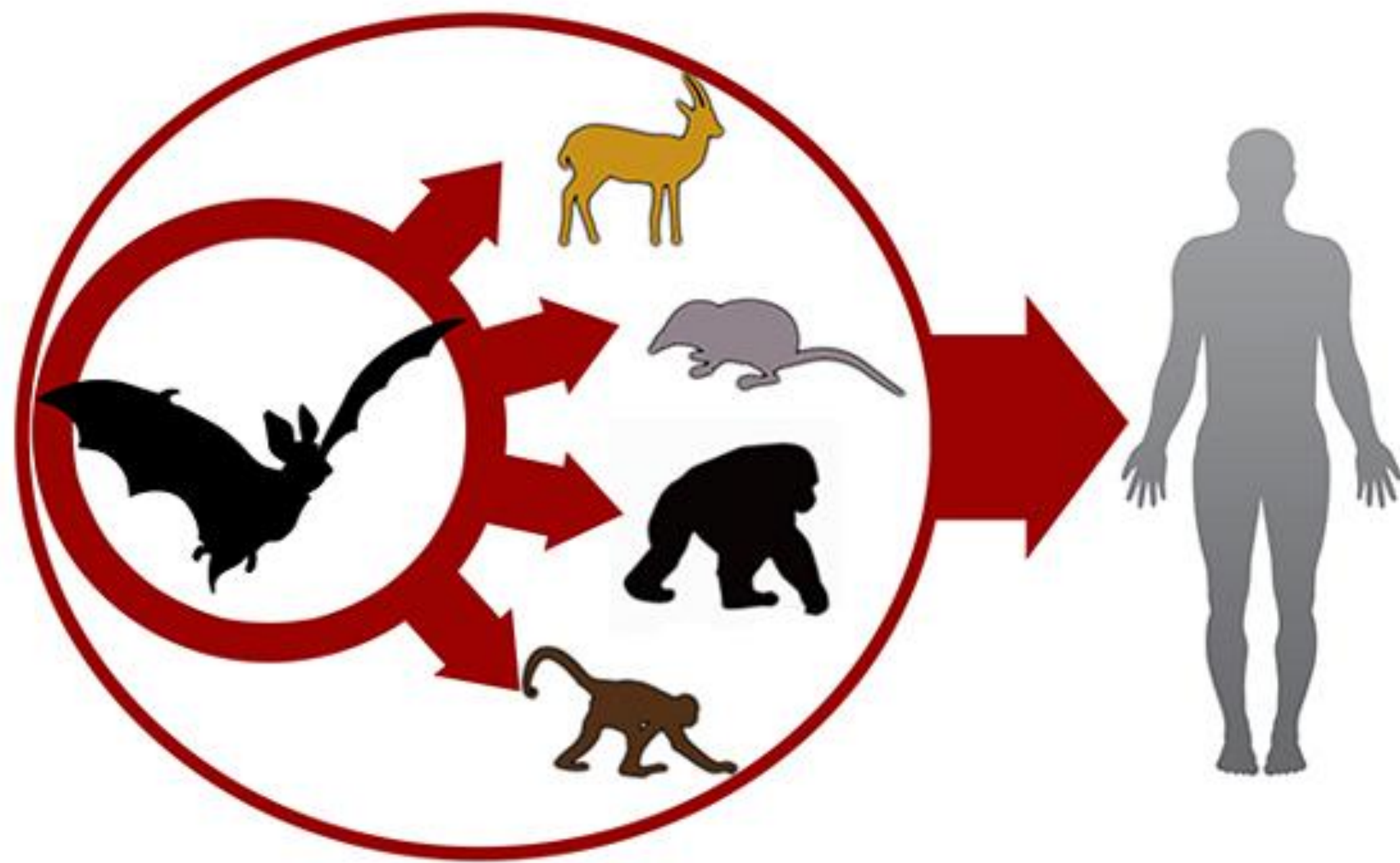
**The Ebola epidemic 2014-2016**

**28 646 cases**

**11 323 deaths**

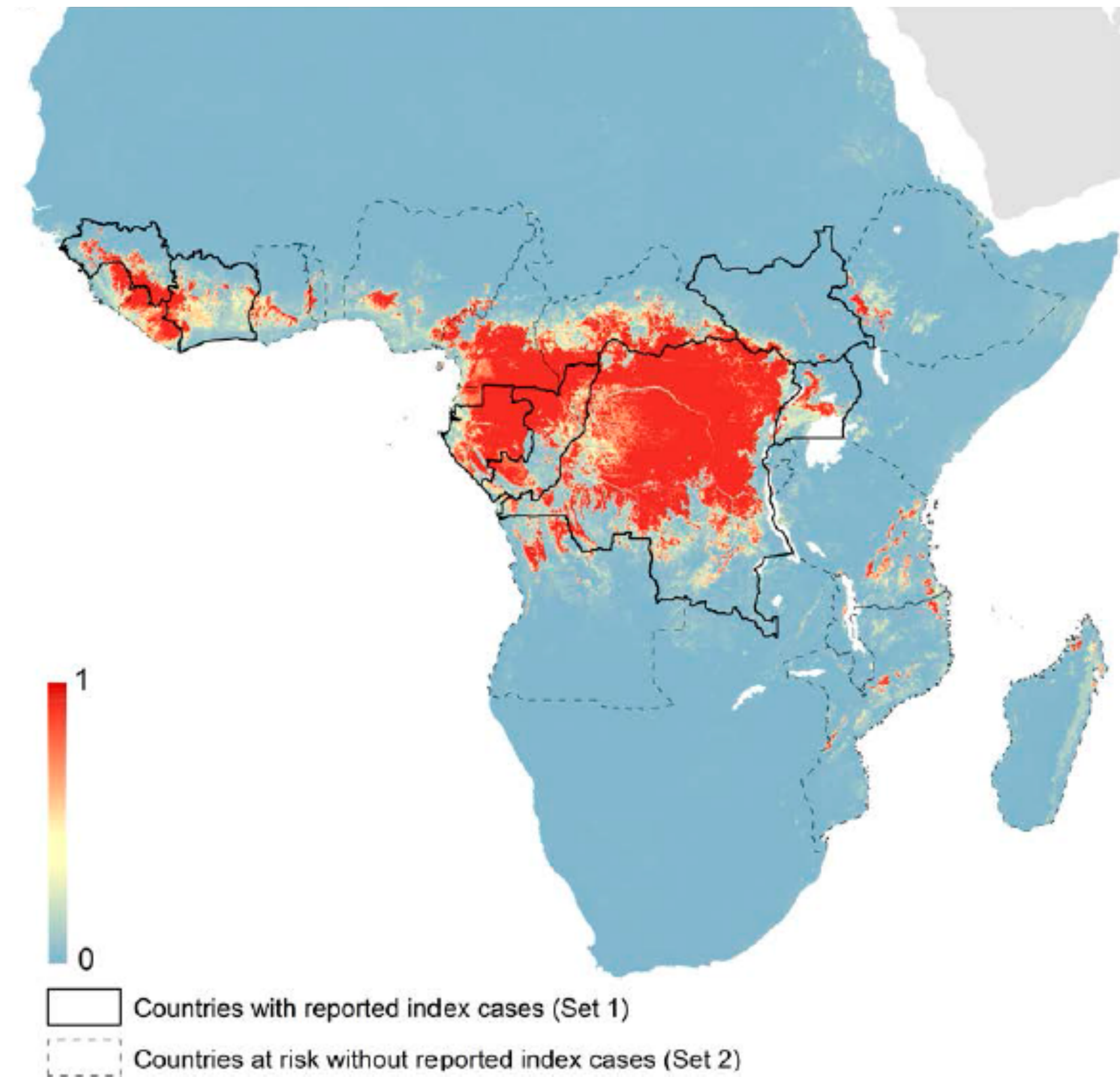


# The fruitbat is probably the viral reservoir





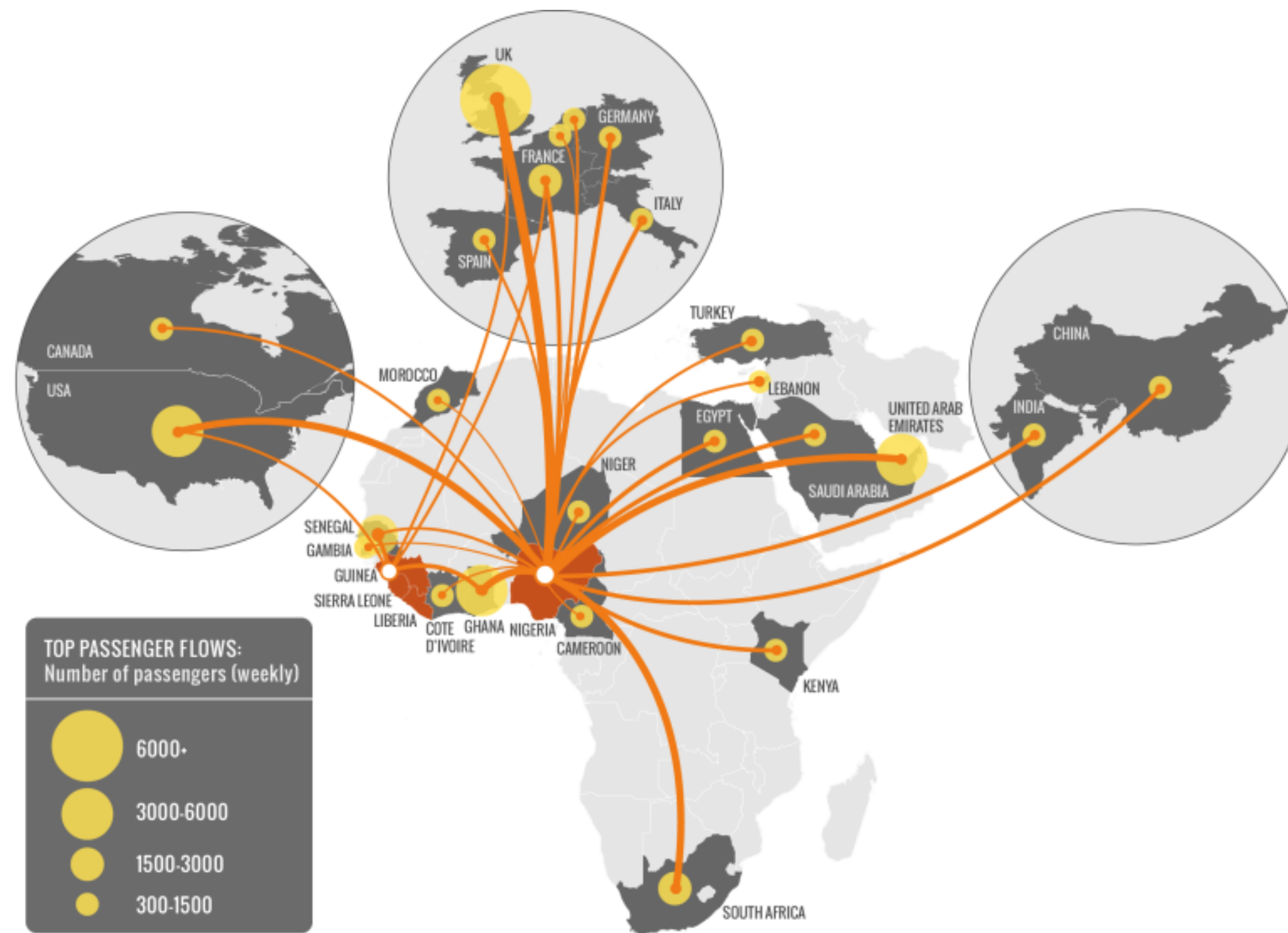
# Zoonotic niche of Ebola virus disease in Africa



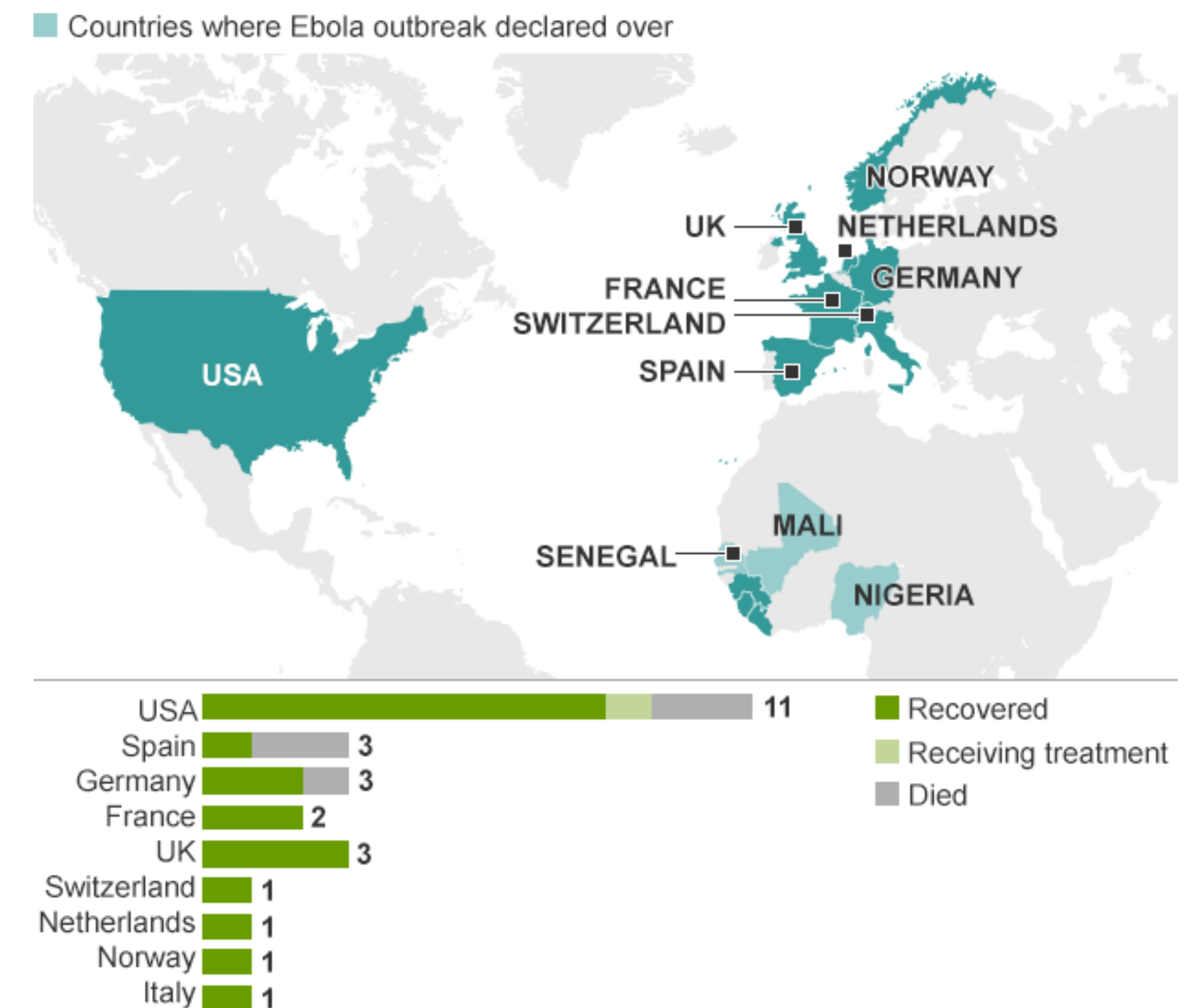


# Ebola can rapidly spread to other continents

Prediction September 2014

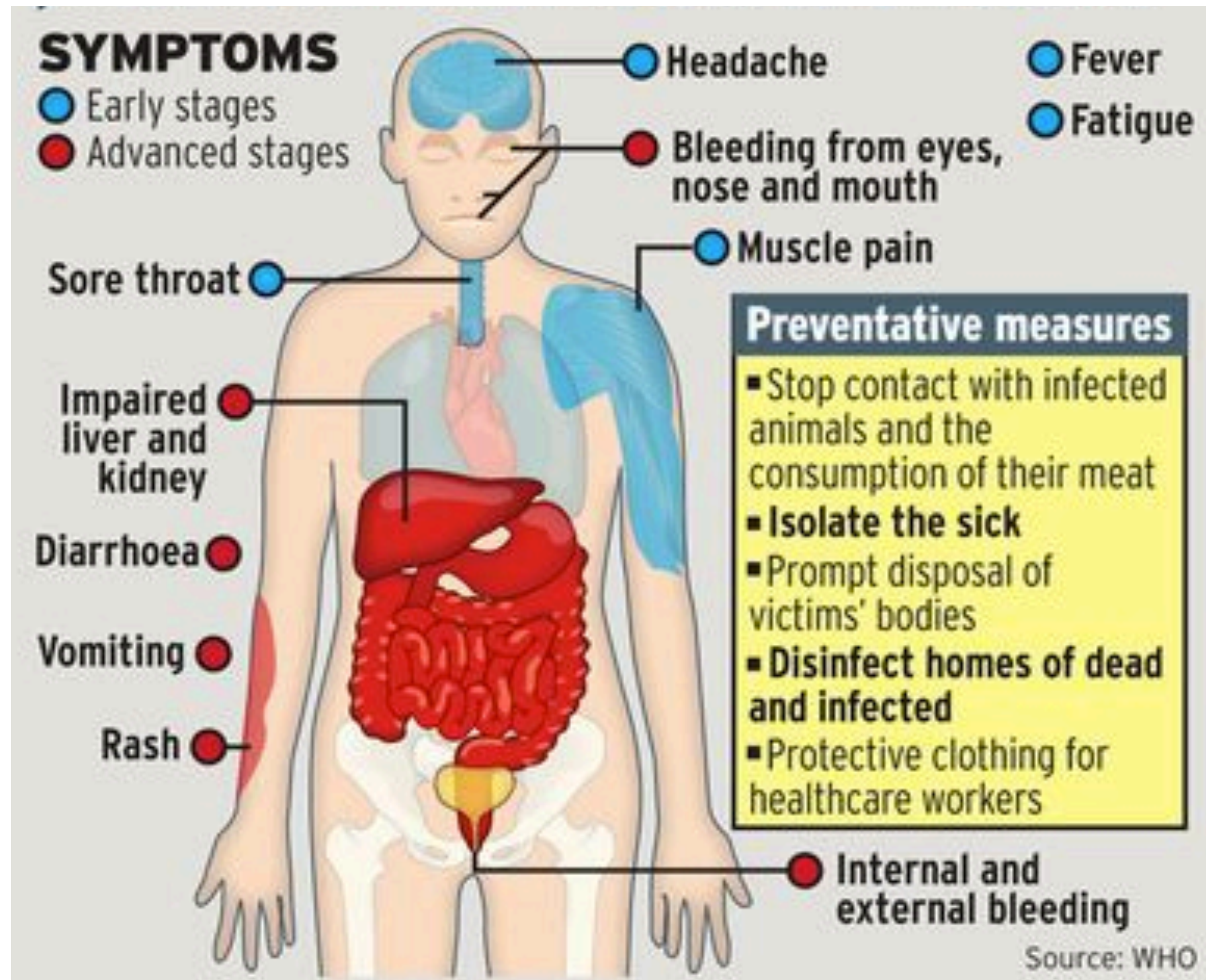


Status June 2015





# Vague initial symptoms can delay diagnosis



Hepatitis?

Influenza?

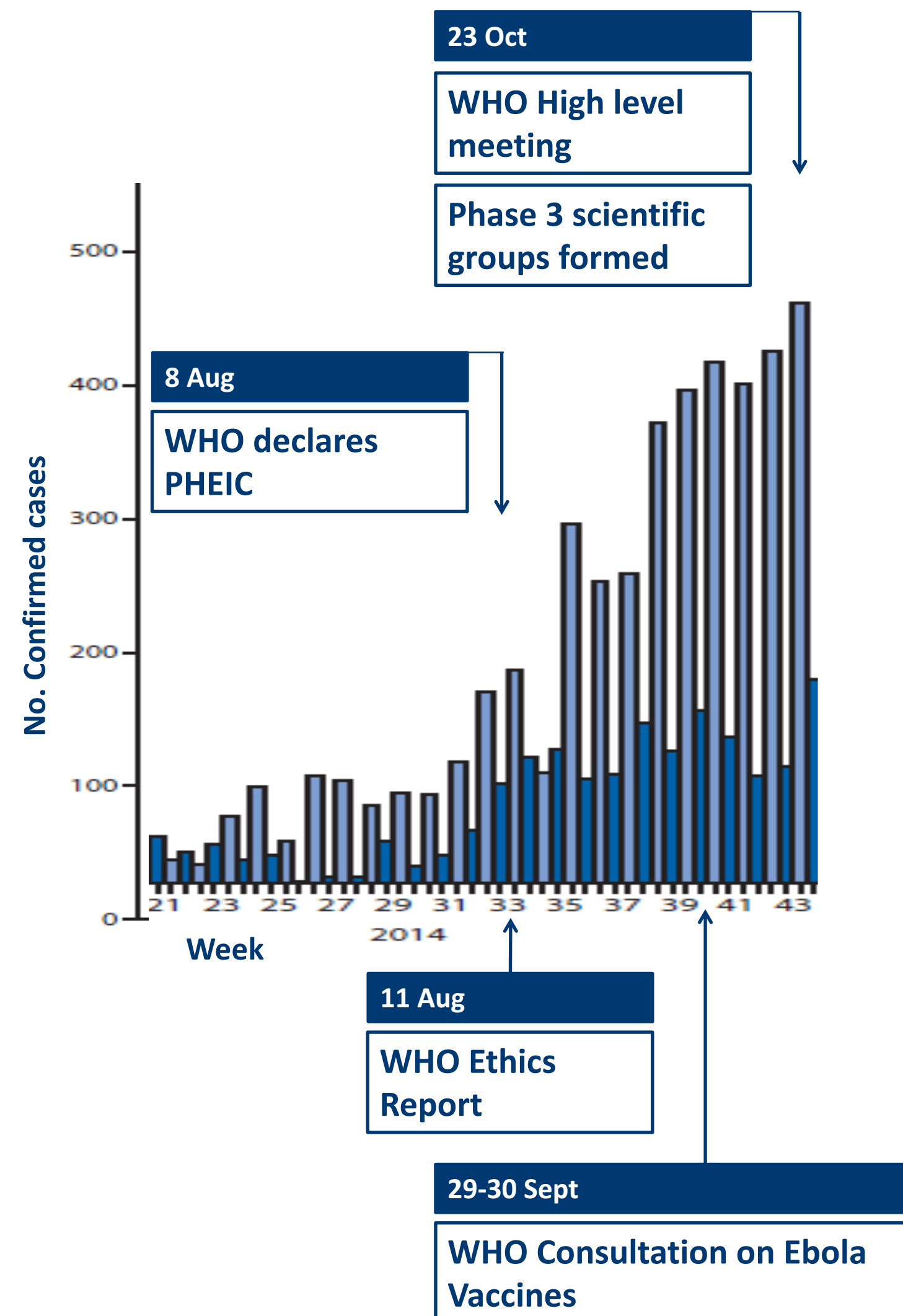
Dengue fever?

Malaria?

Typhoid fever?



# Vaccines could play a role in ending the epidemic



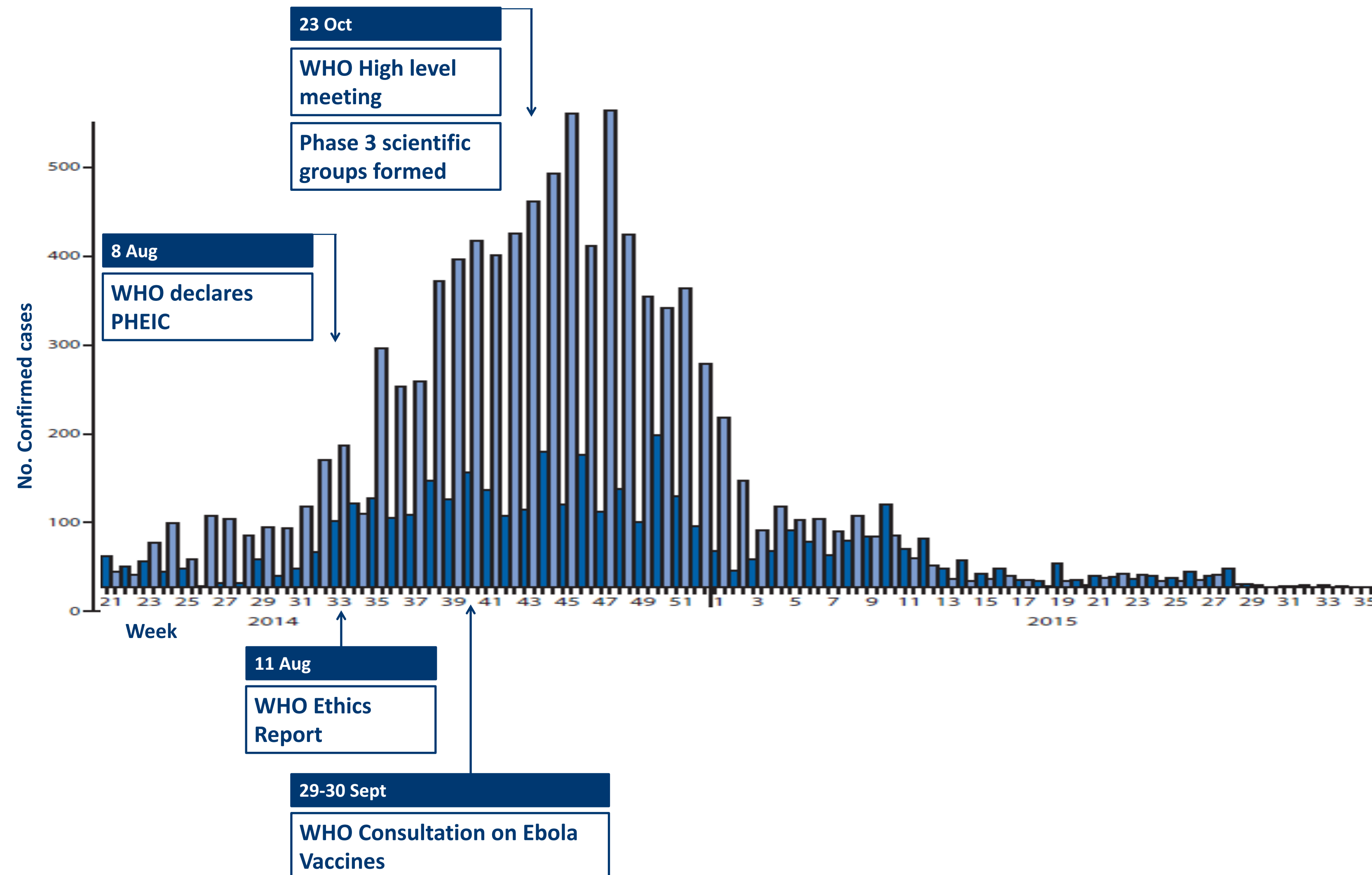
## Predictions

WHO: **20 000** before November 2014

CDC : 500'-**1.4 mill** before January 2015

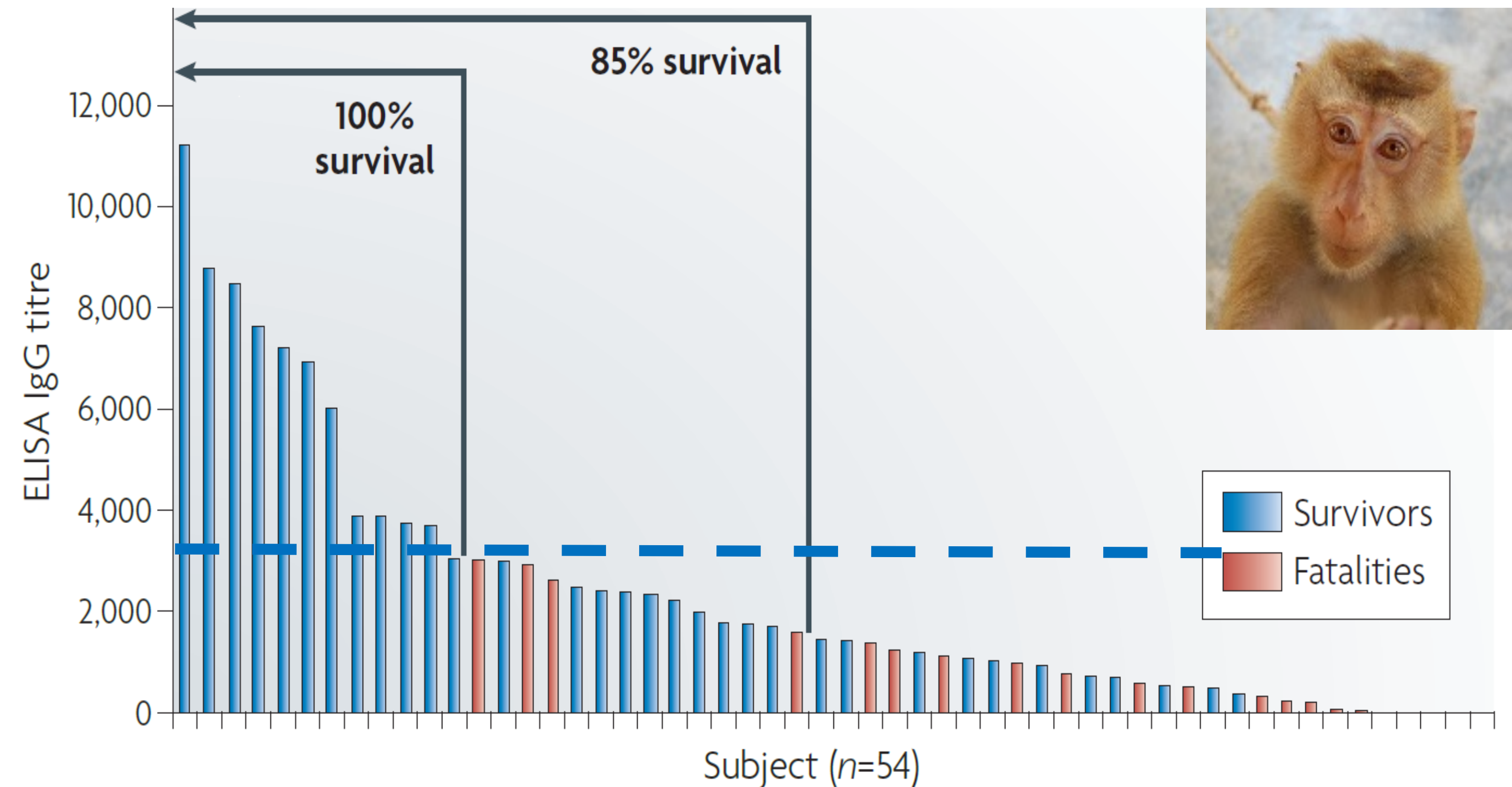
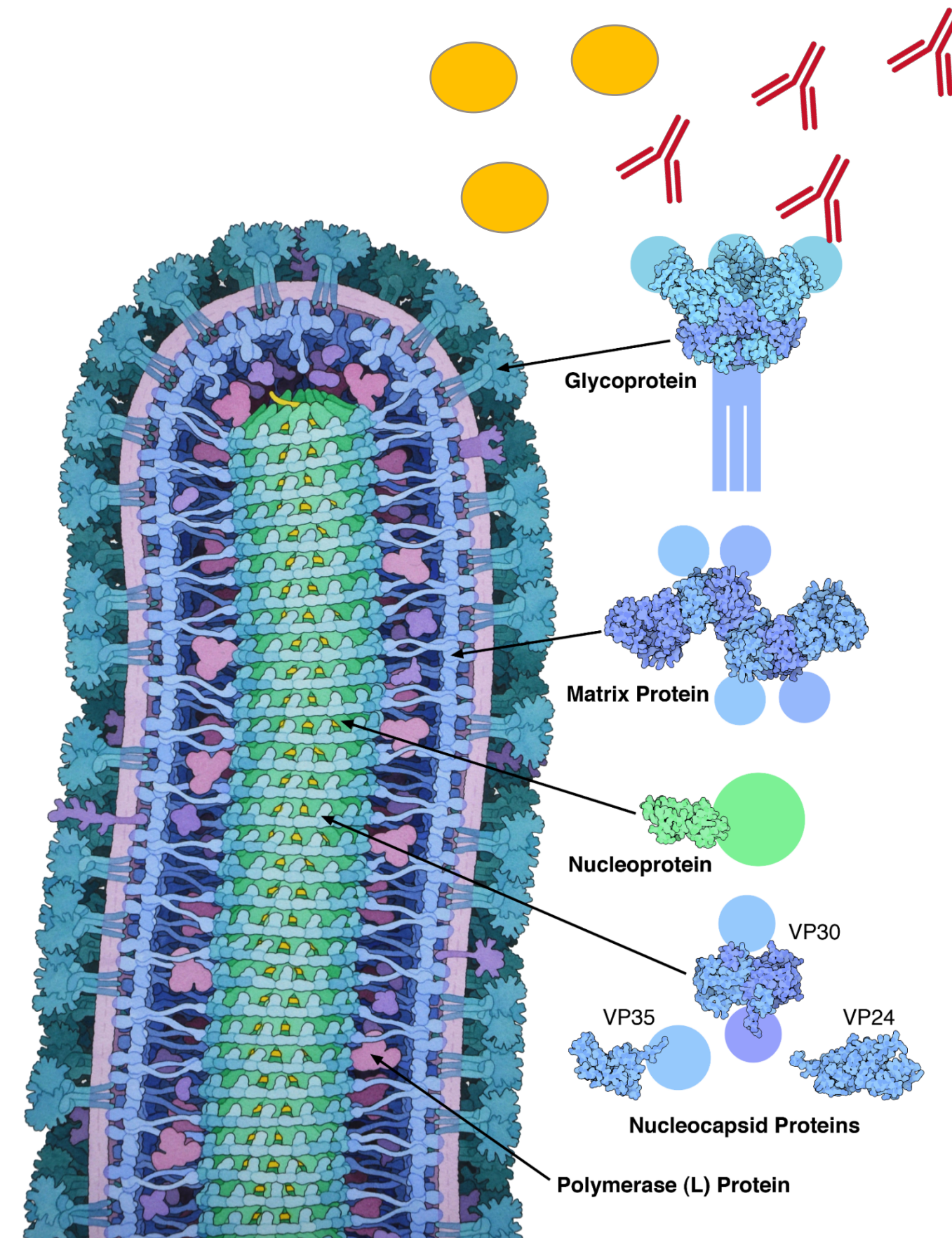


# Vaccines could play a role in ending the epidemic



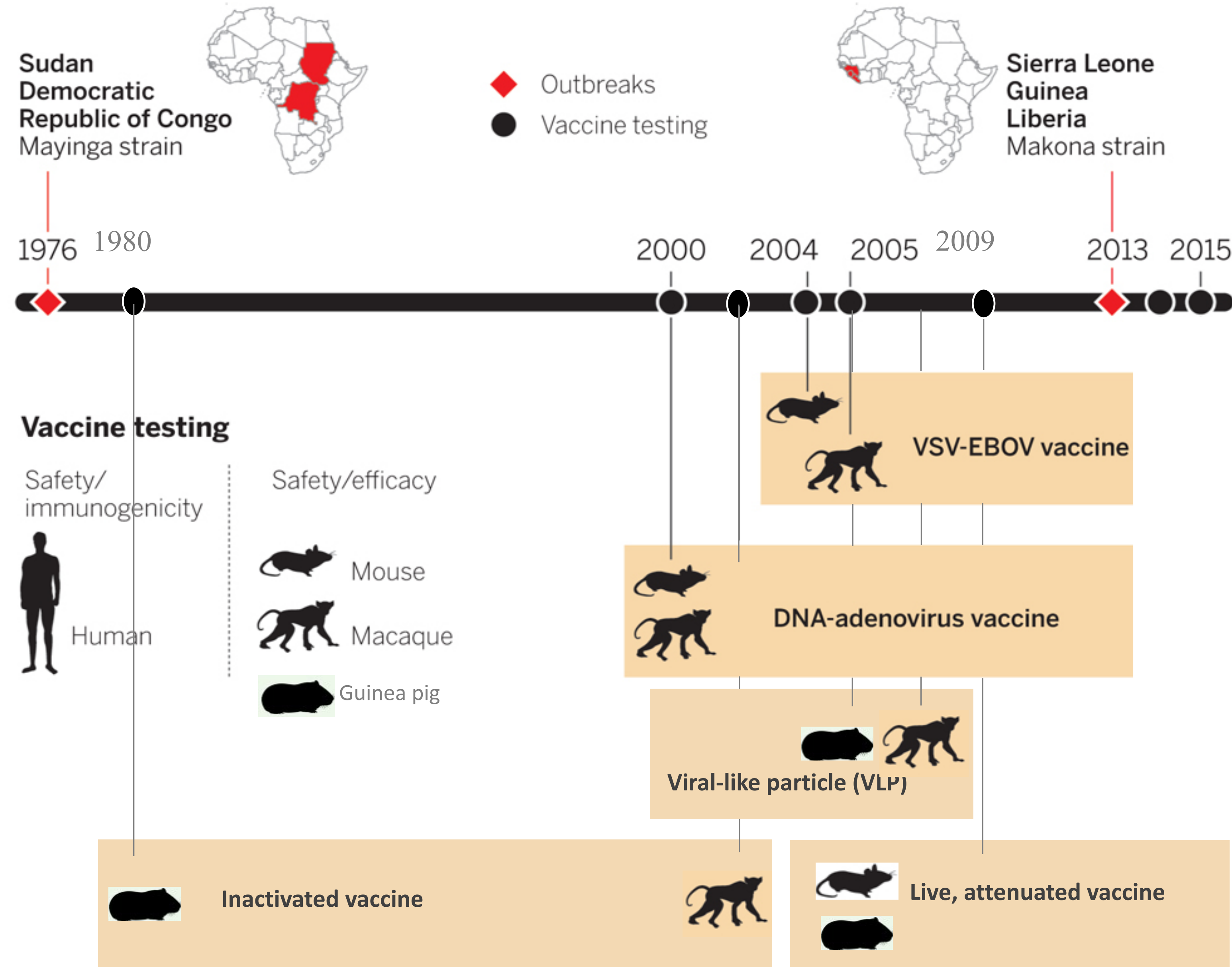


# Ebola surface glycoprotein (GP) is the target antigen used in most vaccines



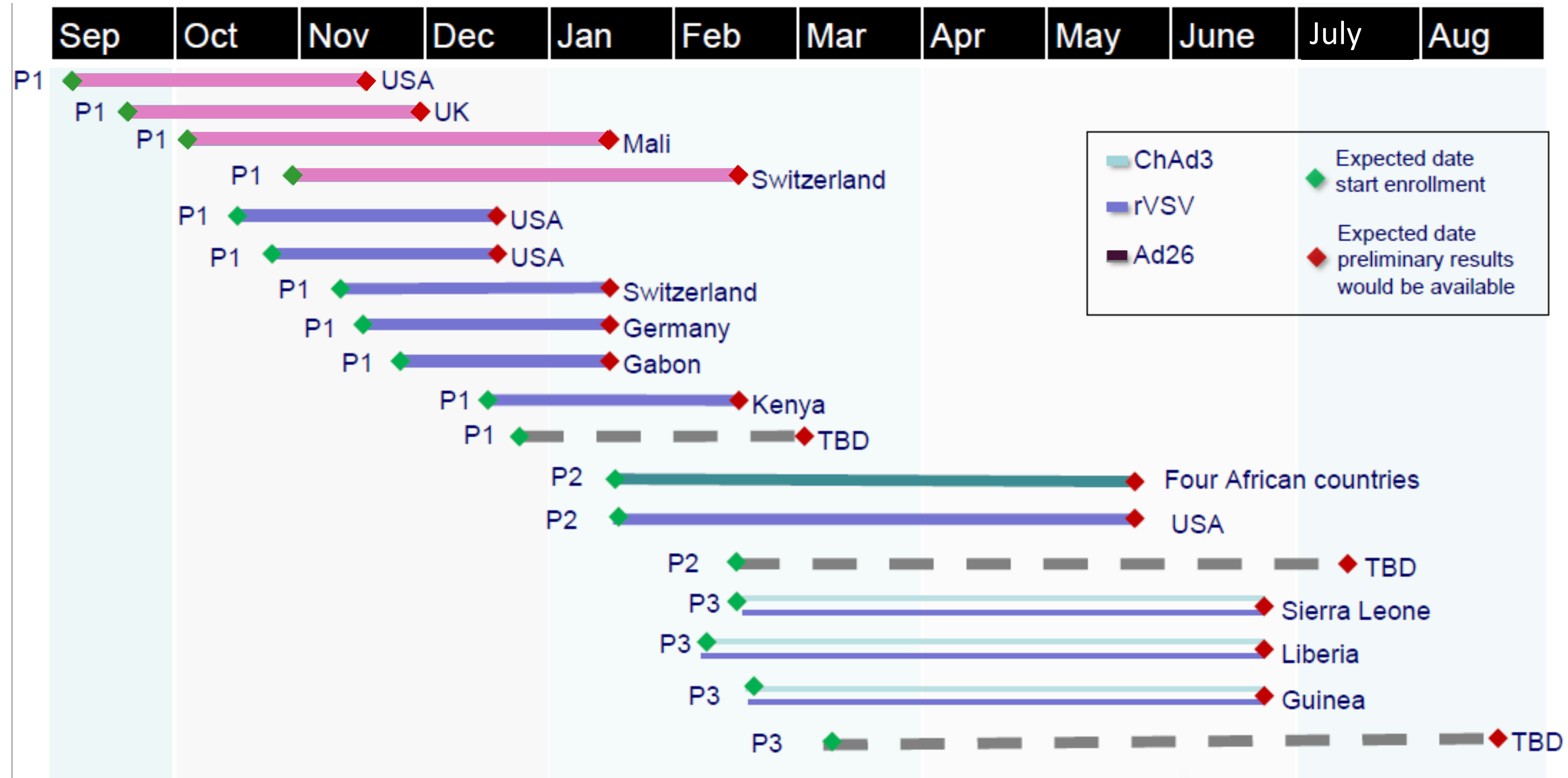


# Vaccine candidates prior to clinical trials





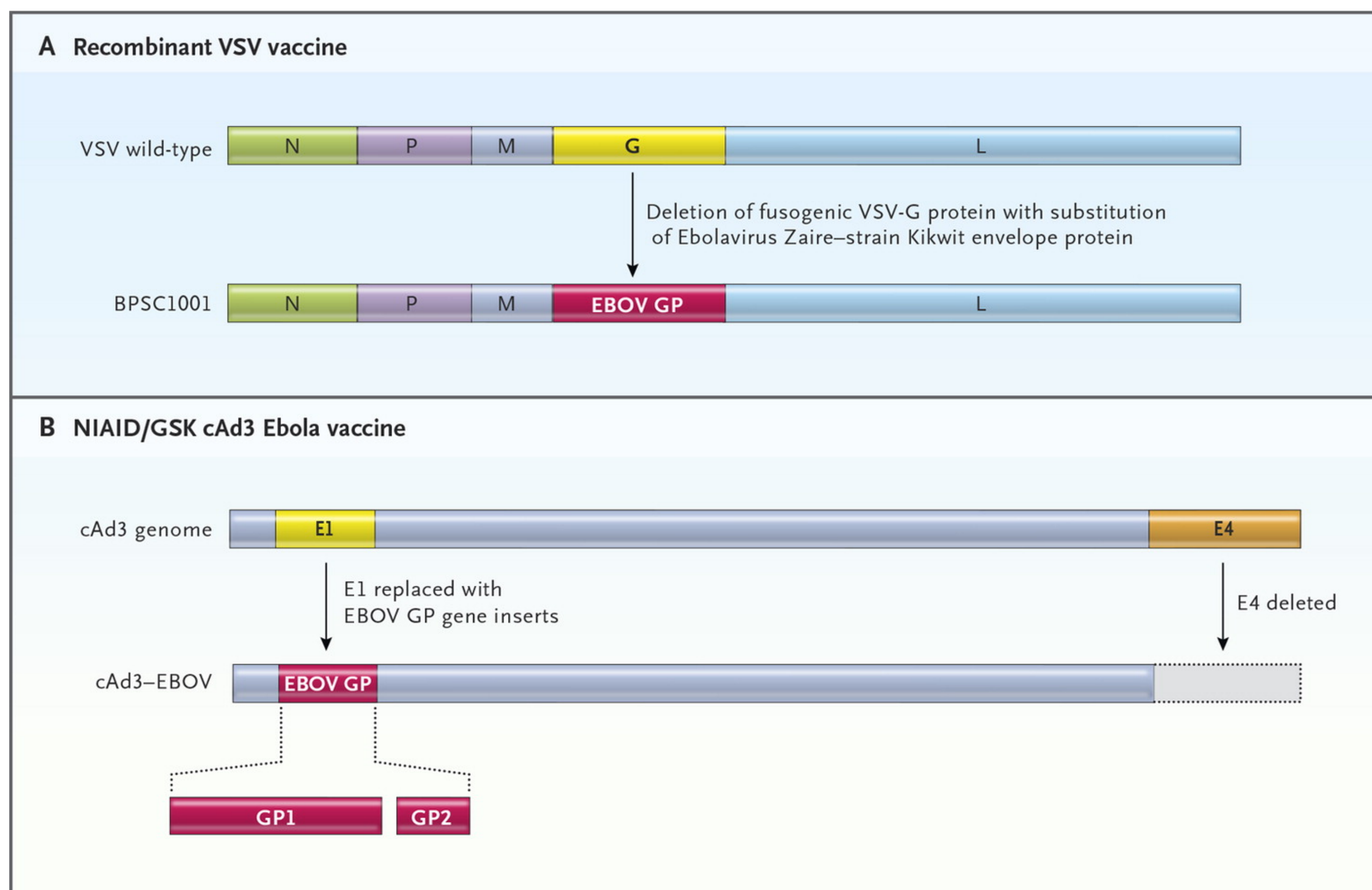
# Phase I, II and III trials were planned to be conducted in parallel





# WHO fast-tracked development of two vaccine candidates

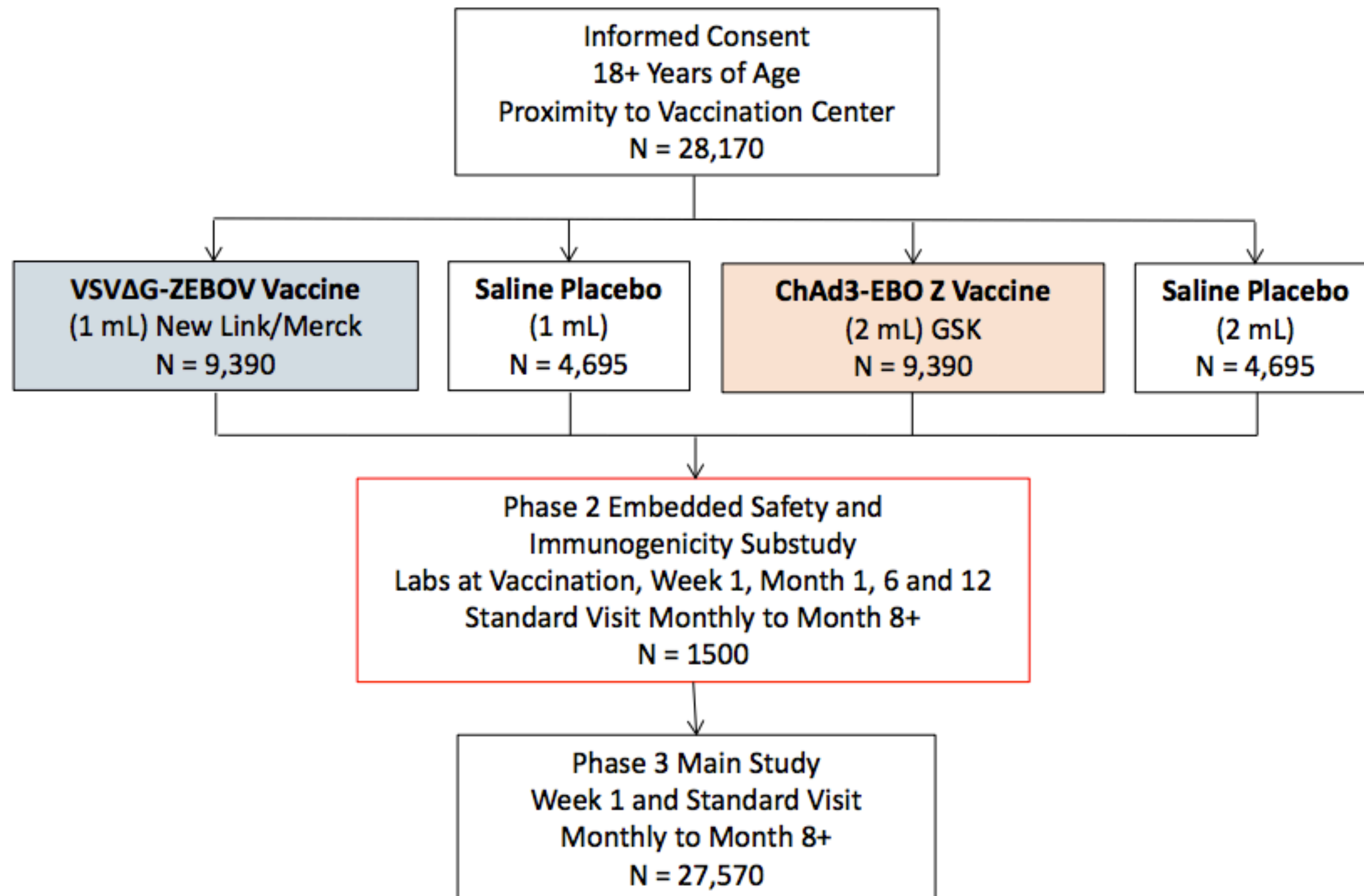
1. 100% protection in non-human primates (NHP)
2. GMP product available for use in clinical trials





# PREVAIL I study in Liberia

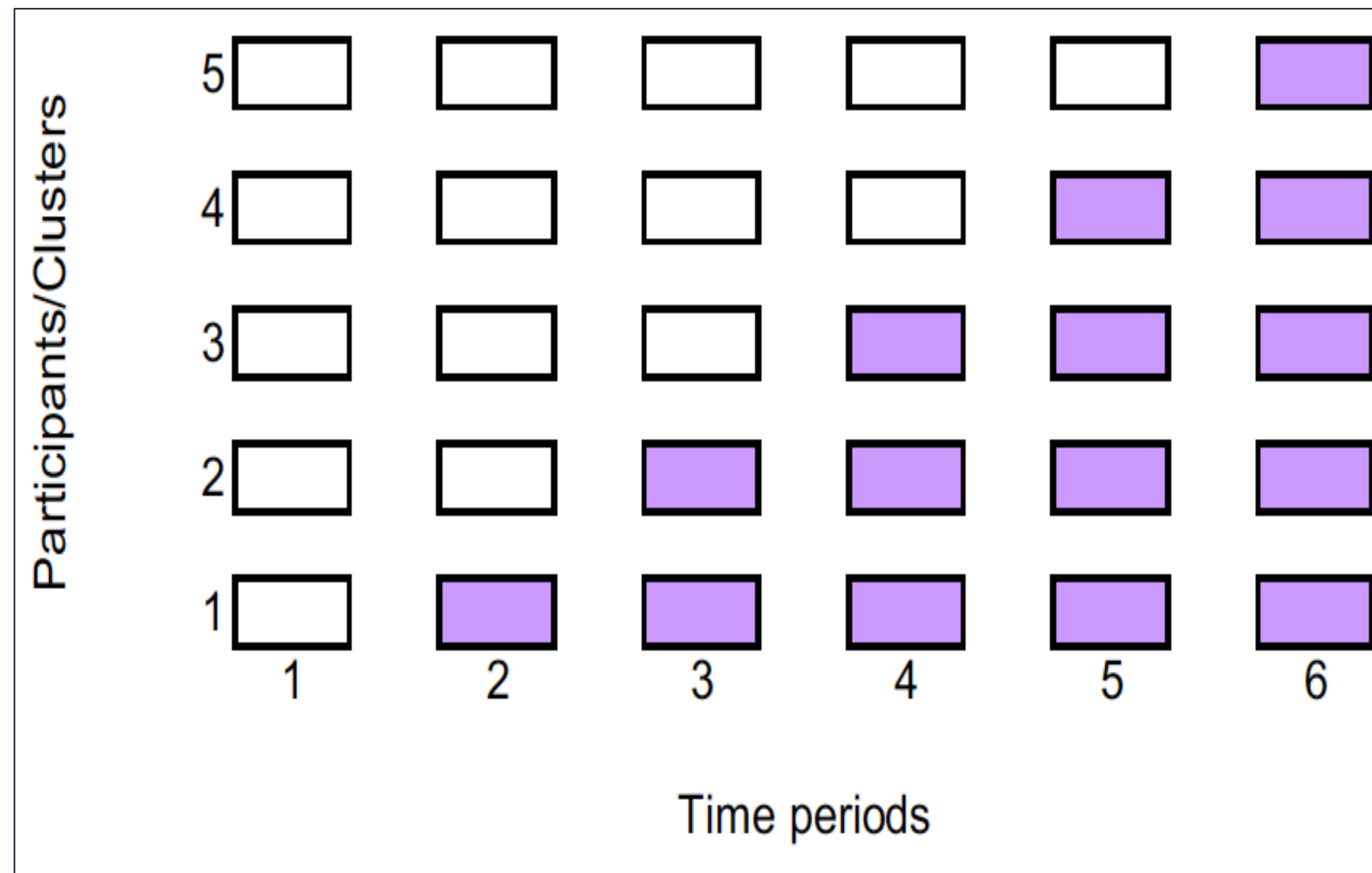
Gold standard double-blind, randomized controlled trial (RCT)





# STRIVE study in Sierra Leone

Unblinded, cluster randomized stepped wedge trial

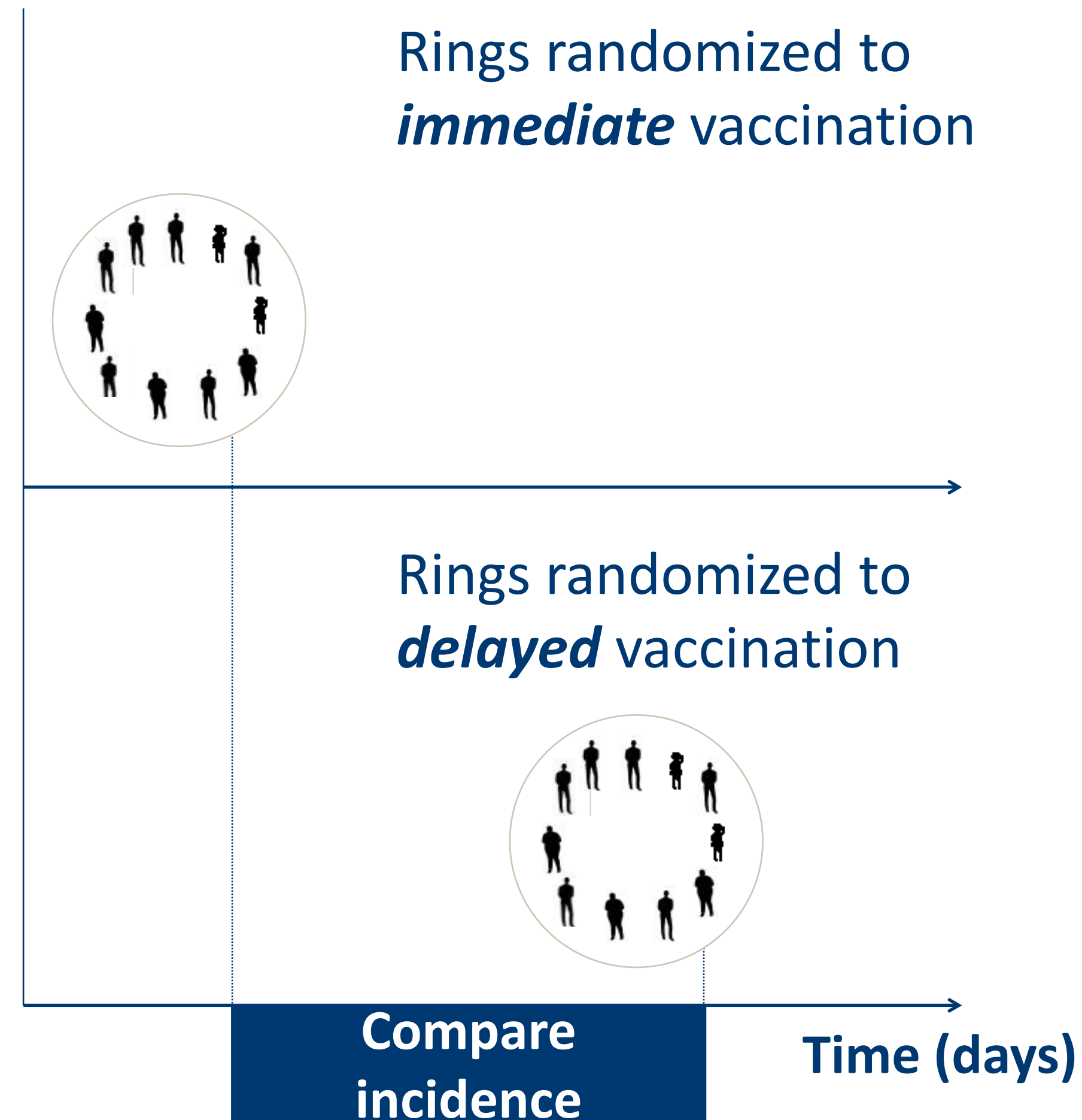
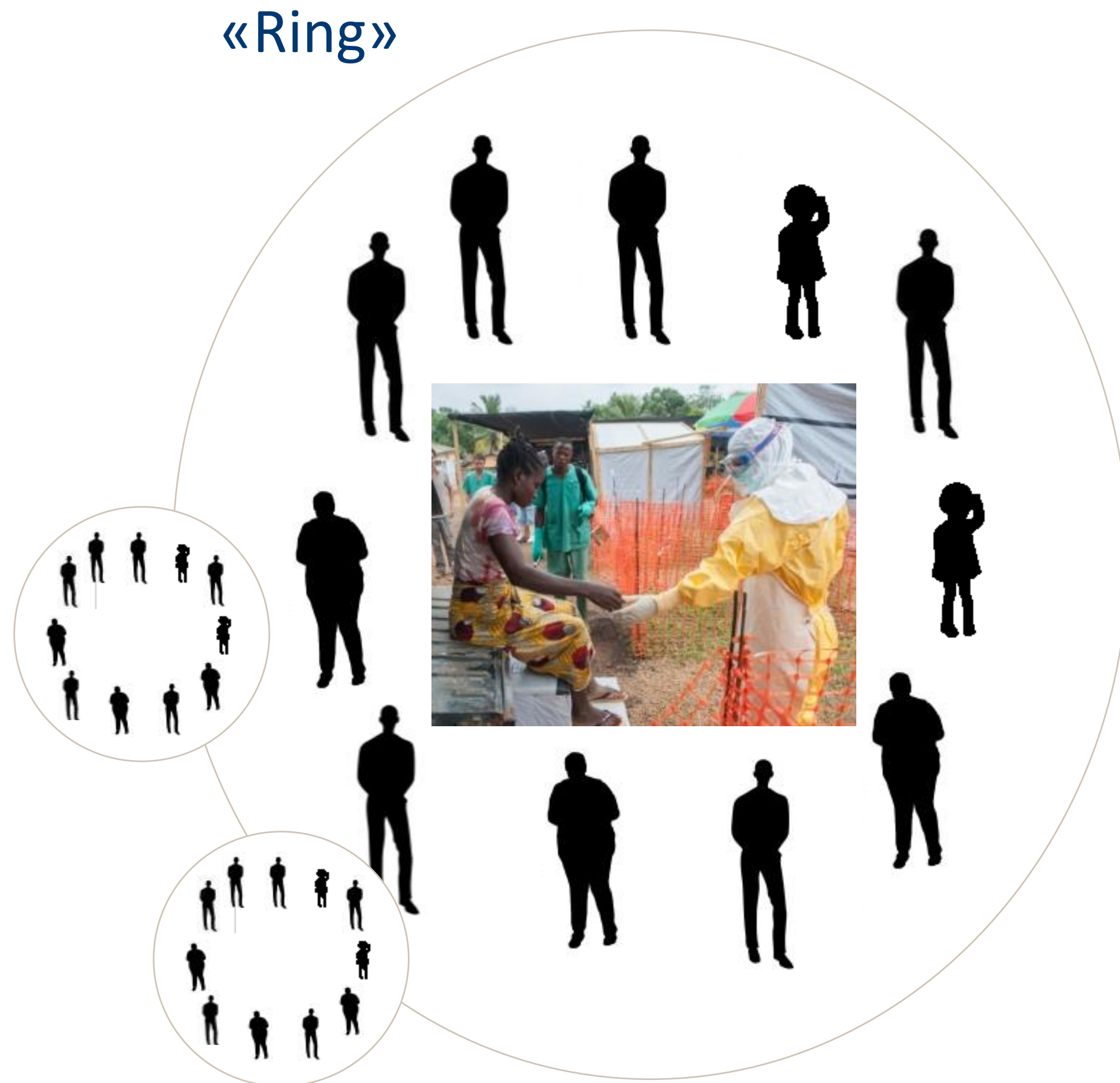


Converted to individually randomized trial in healthcare personell with participants vaccinated immediately or after 6 months.



# *Ebola ça suffit! (Ebola that's enough)* study in Guinea

## Ring vaccination





# THE LANCET

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## Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!)

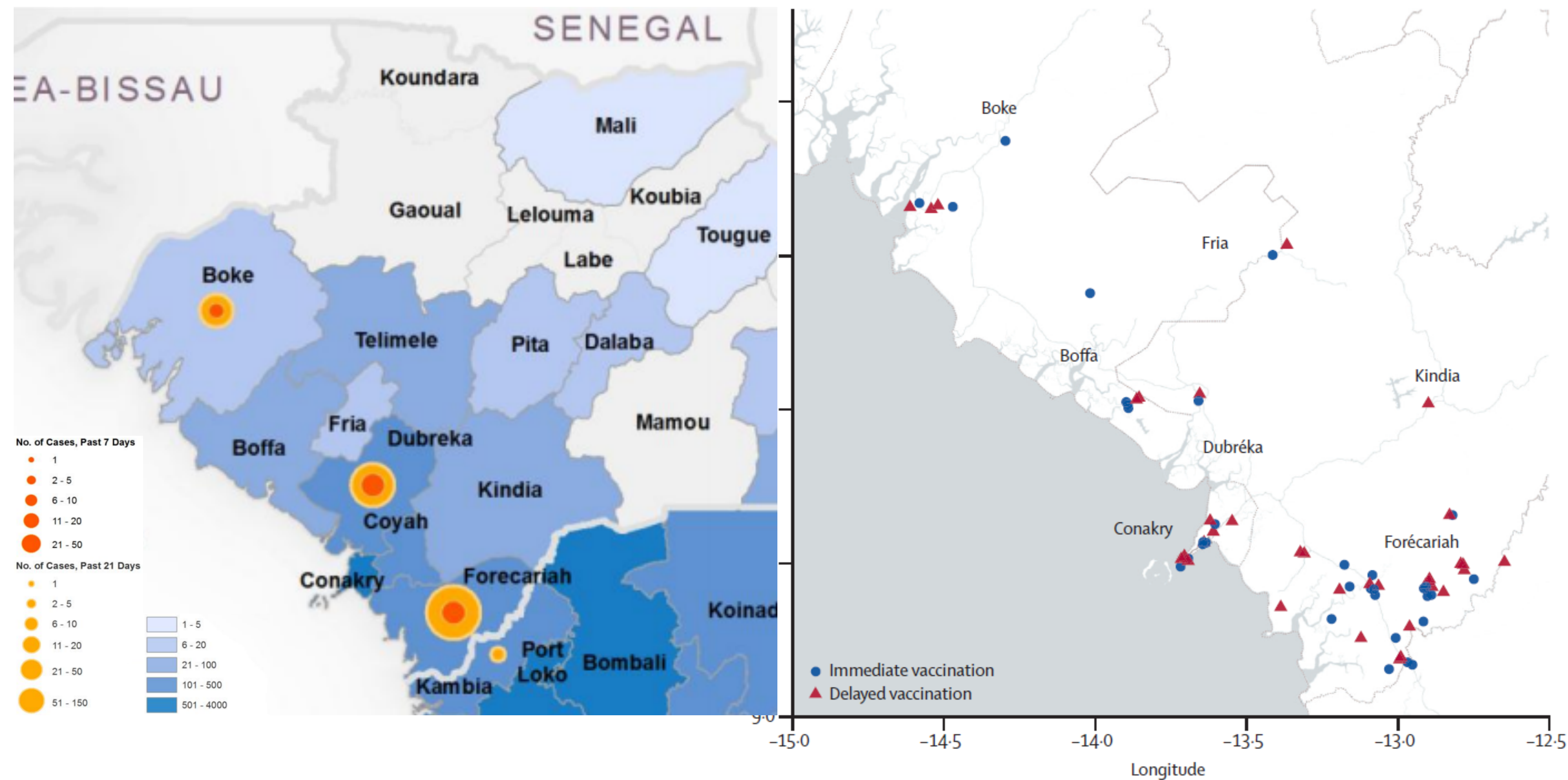


Ana Maria Henao-Restrepo, Anton Camacho, Ira M Longini, Conall H Watson, W John Edmunds, Matthias Egger, Miles W Carroll, Natalie E Dean, Ibrahima Diatta, Moussa Doumbia, Bertrand Draguez, Sophie Duraffour, Godwin Enwere, Rebecca Grais, Stephan Gunther, Pierre-Stéphane Gsell, Stefanie Hossmann, Sara Viksmoen Watle, Mandy Kader Kondé, Sakoba Kéïta, Souleymane Kone, Eewa Kuisma, Myron M Levine, Sema Mandal, Thomas Mauget, Gunnstein Norheim, Ximena Riveros, Aboubacar Soumah, Sven Trelle, Andrea S Vicari, John-Arne Røttingen\*, Marie-Paule Kieny\*





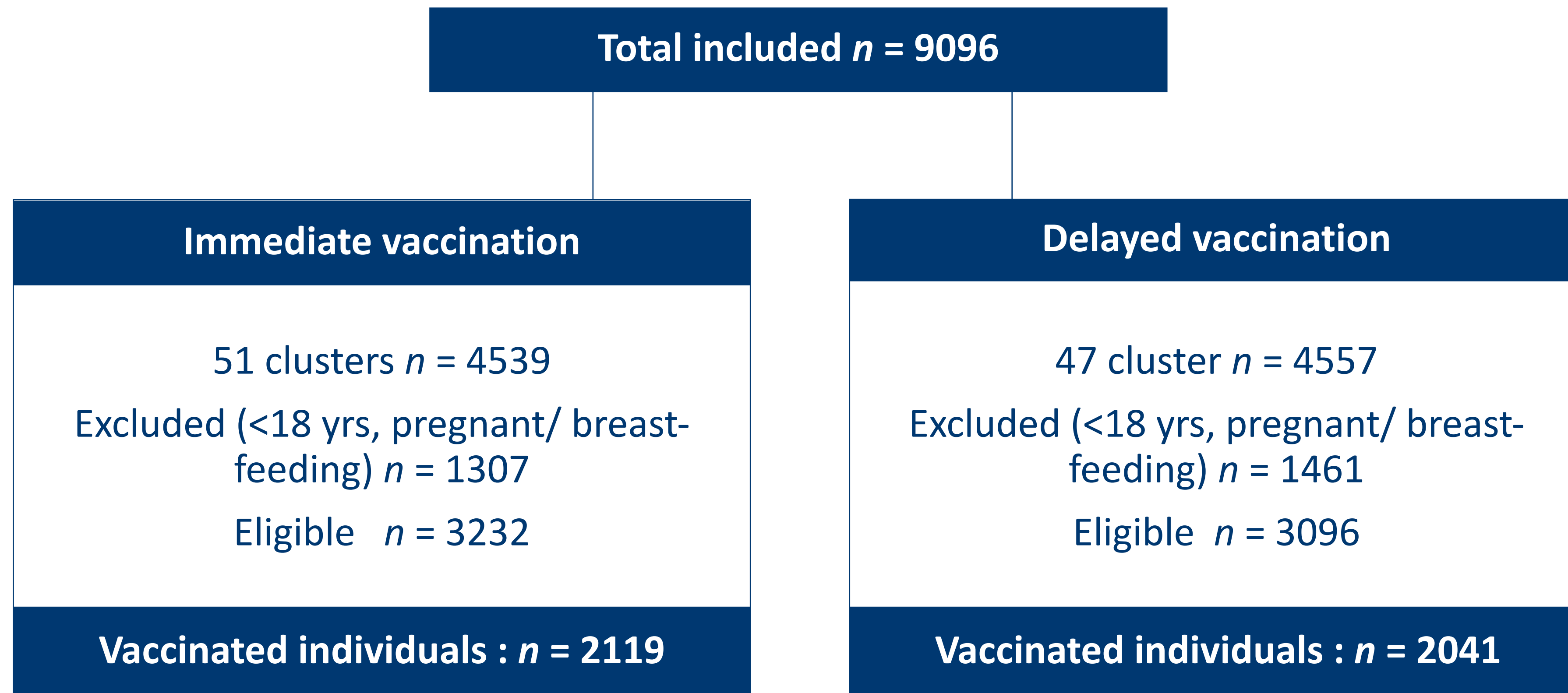
# Trial design was able to follow the outbreak geographically





# Final results

## Inclusion of study subjects

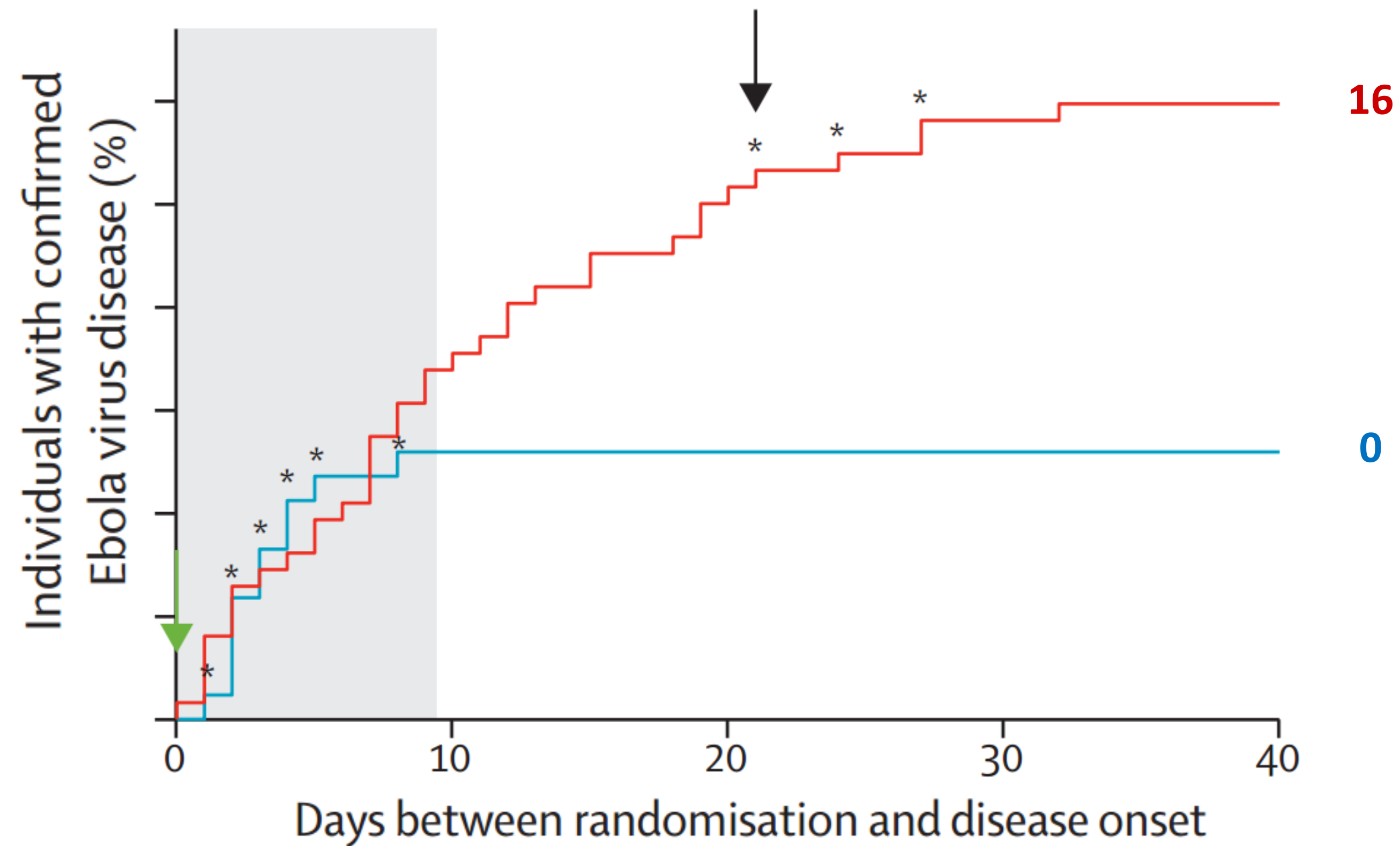




# Final results

## Vaccine efficacy

All vaccinated in immediate (**A**) vs all eligible in delayed (**B**)



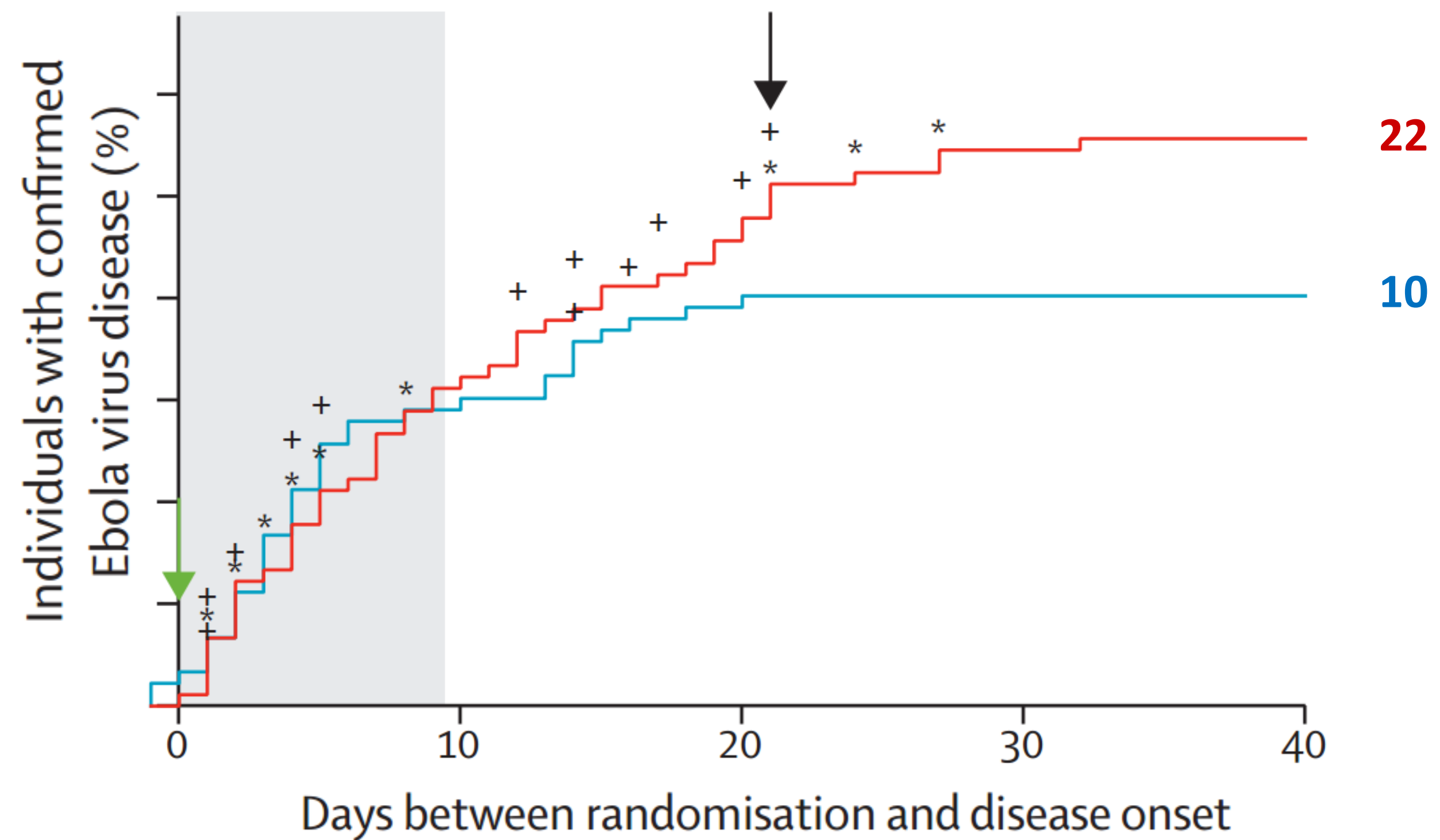
**Vaccine efficacy: 100 % (68.9 – 100)**



# Final results

## Vaccine effectiveness

All contacts and contacts of contacts in immediate (A) vs delayed (B)



**Vaccine effectiveness: 64 % (-44.2 – 91.3)**



# Final results

## Vaccine safety

### Most common adverse events

- Headache 25 %
- Fatigue 19 %
- Arthralgia 19 %
- Muscle pain 13 %

### 80 serious adverse events

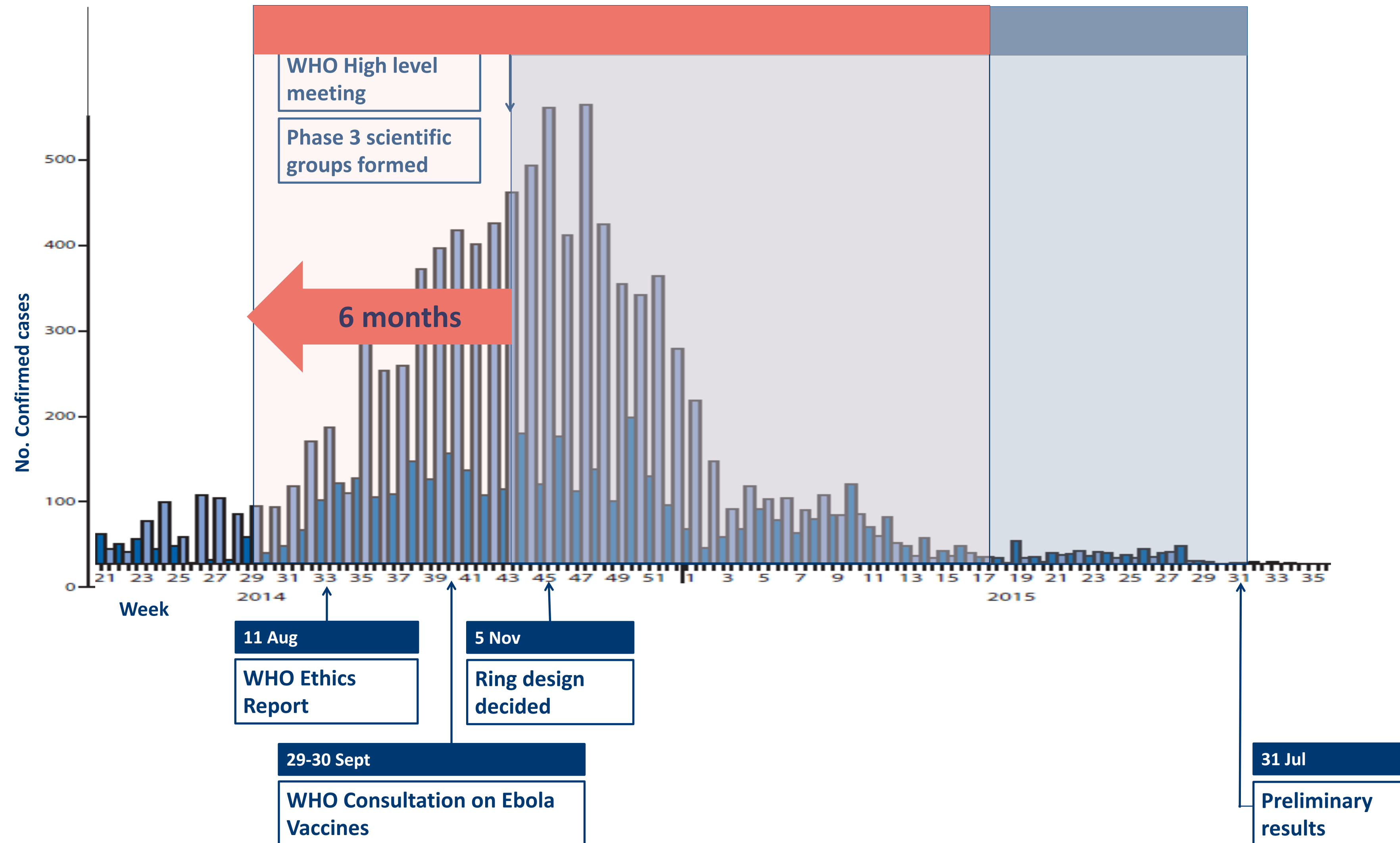
- Anaphylaxis
- Fever
- 39 confirmed EVD cases
- 9 cases of malaria
- 4 cases of road traffic accidents
- Other (infections, appendicitis etc)



Henao-Restrepo et al. Lancet February 2017



# Fast, but not fast enough?





# The WHO R&D Blueprint

## 2018 annual review of the Blueprint list of priority diseases

The second annual review of the Blueprint priority diseases was held in February 2018. WHO has developed a special tool for determining which diseases and pathogens to prioritize for research and development in public health emergency contexts. This tool seeks to identify those diseases that pose a public health risk because of their epidemic potential and for which there are no, or insufficient, countermeasures. Experts consider that given their potential to cause a public health emergency and the absence of efficacious drugs and/or vaccines, there is an urgent need for accelerated research and development for nine diseases.

List of Blueprint priority diseases



### A

## Improving coordination

1. Global coordination
2. Funding
3. Communication

### B

## Accelerating R&D

1. Disease prioritization
2. Roadmap & Target product profile
3. Regulatory & Ethical pathways

### C

## Developing norms & standards

1. Clinical trial designs
2. Data & sample sharing

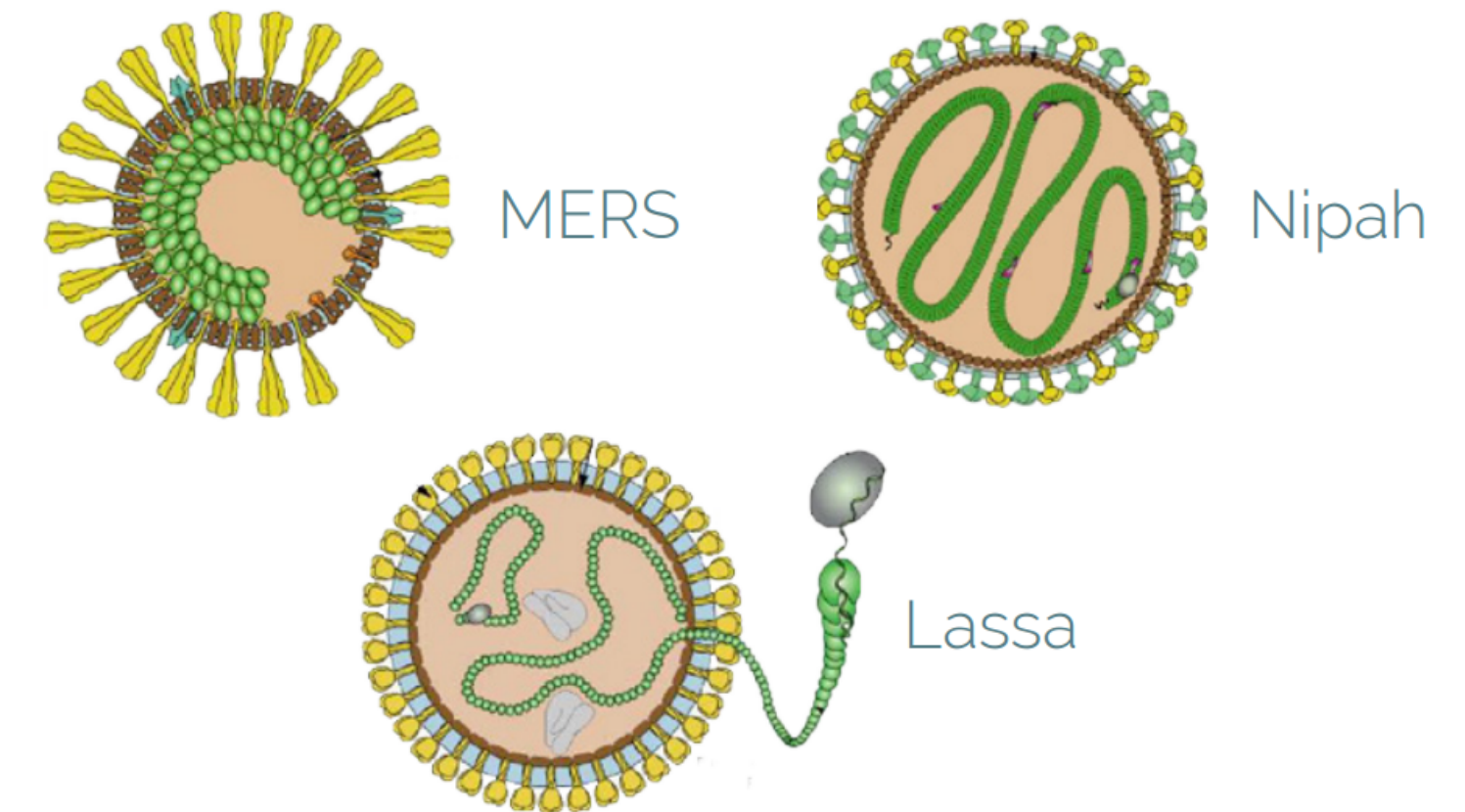
## Response plan



# CEPI – Coalition for Epidemic Preparedness Innovation

Partnership of public, private, philanthropic and civil society organisations

- Stimulate, finance and coordinate vaccine development against priority threats
- Targeted vaccine candidates from late preclinical studies to proof of concept and safety in humans
- Build technical platforms that can be rapidly deployed against new and unknown pathogens



# When will a vaccine against Ebola be available and to whom?

## Licensed vaccines

- Russia Dec 2016

GamEvacCombi (rVSV + Ad5)

HUMAN VACCINES & IMMUNOTHERAPEUTICS  
2017, VOL. 13, NO. 3, 613–620  
<http://dx.doi.org/10.1080/21645515.2016.1238535>



RESEARCH PAPER

OPEN ACCESS

### Safety and immunogenicity of GamEvac-Combi, a heterologous VSV- and Ad5-vectored Ebola vaccine: An open phase I/II trial in healthy adults in Russia

I. V. Dolzhikova<sup>a</sup>, O. V. Zubkova<sup>a</sup>, A. I. Tikhvatulin<sup>a</sup>, A. S. Dzharullaeva<sup>a</sup>, N. M. Tikhvatulina<sup>a</sup>, D. V. Shcheblyakov<sup>a</sup>, M. M. Shmarov<sup>a</sup>, E. A. Tokarskaya<sup>a</sup>, Y. V. Simakova<sup>a</sup>, D. A. Egorova<sup>a</sup>, D. N. Scherbinin<sup>a</sup>, I. L. Tutykhina<sup>a</sup>, A. A. Lysenko<sup>a</sup>, A. V. Kostarnoy<sup>a</sup>, P. G. Gancheva<sup>a</sup>, T. A. Ozharovskaya<sup>a</sup>, B. V. Belugin<sup>a</sup>, L. V. Kolobukhina<sup>a</sup>, V. B. Pantyukhov<sup>c</sup>, S. I. Syromyatnikova<sup>c</sup>, I. V. Shatokhina<sup>c</sup>, T. V. Sizikova<sup>c</sup>, I. G. Rummyantseva<sup>c</sup>, A. F. Andrus<sup>c</sup>, N. V. Boyarskaya<sup>c</sup>, A. N. Voytyuk<sup>c†</sup>, V. F. Babira<sup>d</sup>, S. V. Volchikhina<sup>d</sup>, D. A. Kutaev<sup>c</sup>, A. N. Bel'skih<sup>b</sup>, K. V. Zhdanov<sup>b</sup>, S. M. Zakharenko<sup>b</sup>, S. V. Borisevich<sup>c</sup>, D. Y. Logunov<sup>a</sup>, B. S. Naroditsky<sup>a</sup>, and A. L. Gintsburg<sup>a</sup>

- China Oct 2017

Ad5-EBOV (Makona)

Human Vaccines & Immunotherapeutics >  
Volume 13, 2017 - Issue 9

Research Papers

### Open-label phase I clinical trial of Ad5-EBOV in Africans in China

Lihua Wu, Zhe Zhang, Hainv Gao, Yuhua Li, Lihua Hou, Hangping Yao, ...show all

Pages 2078-2085 | Received 04 Apr 2017, Accepted 08 Jun 2017, Accepted author version posted online: 14 Jul 2017, Published online: 03 Aug 2017

➤ Neither submitted to WHO for prequalification



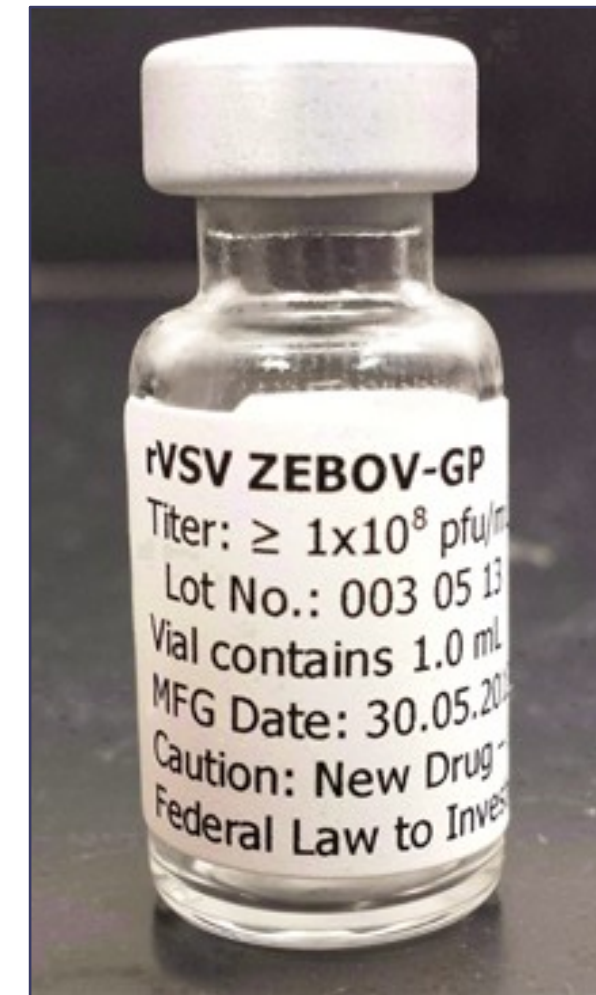
# When will a vaccine against Ebola be available and to whom? (cont.)

**PRIME** status (EMA) and **Breakthrough Therapy designation** (FDA)

- rVSVΔG-ZEBOV-GP

## **GAVI, the Vaccine Alliance**

- Advance purchase commitment to manufacturer
- Ensurance of 300,000 doses of rVSVΔG-ZEBOV-GP for stockpiling



**BARDA** Biomedical Advanced Research and Development Authority

- Commitment to fund remaining R&D needed to obtain licensure of rVSVΔG-ZEBOV-GP and Ad26.ZEBOV/MVA-BN-Filo and to stockpile for emergency use

# When will a vaccine against Ebola be available and to whom? (cont.)

## **SAGE** recommendations

- Individual protection of target groups (HCW/FLW and other risk groups)
- Interruption of transmission (ring vaccination, geographically targeted vaccination)



## **EUAL** WHO Emergency Use and Assessment Listing application

## **Expanded Access Framework** using a study protocol

- rVSVΔG-ZEBOV-GP
- Ad26.ZEBOV/MVA-BN-Filo





# Emergency use of experimental Ebola vaccine is challenging





# Emergency use of experimental Ebola vaccine is challenging

TheGuardian

## WHO may deploy Ebola vaccine for first test in DRC

By Chukwuma Muanya  
(Assistant Editor),  
Terhemba Daka (Abuja)  
and Charles Ogugbuaja  
(Owerri)

18 May 2017 | 5:20 am



- Coordination team
- Vaccination strategy
- Local regulatory and ethical approval
- Training according to Good Clinical Practice
- Cold chain equipment and transport capacity
- Community engagement

... and several other requirements ...



# Further needs for Ebola vaccine development

- Licensed vaccine
- Plans for use in affected countries with little resources
- Vaccine for vulnerable populations (pregnant, immunocompromized)
- Longterm protection
- Vaccine covering other Ebola species







Cecilia, Age 6, Liberia  
Photo: Alphonso Appleton



Norwegian Institute of Public Health



### Funding *Ebola ça suffit!*

- Wellcome Trust
- Research Council of Norway
- International Development Research Centre, Canada
- WHO
- Medecins Sans Frontieres