

Accelerating access to Ebola vaccines

How to launch a parallel or sequential pathways for experimental evaluation of Ebola candidate vaccines in Phase 3 Ebola vaccine clinical trials?

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**World Health
Organization**

How to launch a parallel or sequential pathways for experimental evaluation of Ebola candidate vaccines in Phase 3 Ebola vaccine clinical trials?

A challenge

Needs resources and coordination

Lots of diplomacy and political skills

A good plan with oversight mechanisms

A multilateral approach

Lots of hours of hard work

Guinea
MOH Guinea
Guinea Working Group

Guinea Working Group

Habib Béavogui, Centre National de Formation et de Recherche en Sante Rurale, Mafèrinyah centre, Conakry, Guinea

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Yves Lévy, CEO National Institute of Health and Medical Research, France

Thierry Damerval, Delegate General Manager of National Institute of Health and Medical Research, France

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Donald Heppner, US Army Medical Research and Materiel Command (MRMC), USA

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Wayne Summer, Department of Health, UK

James M. Wilson V, MD Chief of Station Ascel Bio National Infectious Disease Forecast Center

Marc Ouellette, Scientific Director, Research Centre, Laval, University, CIHR Institute of Infection and Immunity, Canada

Jennifer Raven, Assistant Director, Canadian Institutes of Health Research, Canada

WHO Secretariat

UNAIDS Joint United Nations Programme on HIV/AIDS

Smallpox eradication in West and Central Africa

WILLIAM H. FOEGE,¹ J. D. MILLAR,² & D. A. HENDERSON³

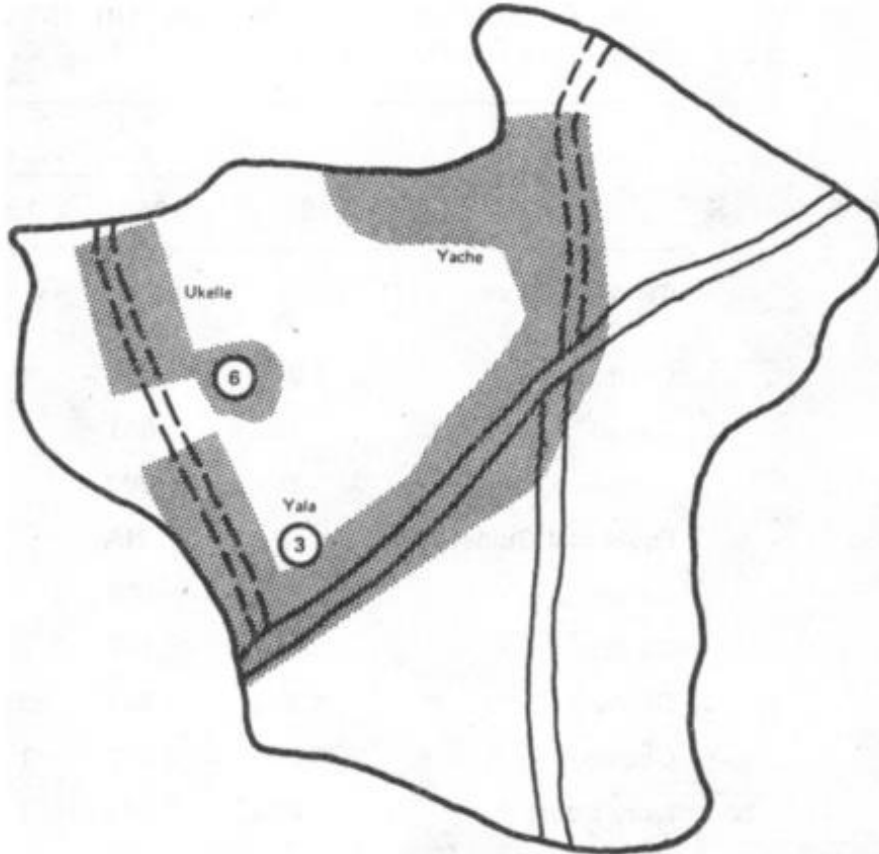


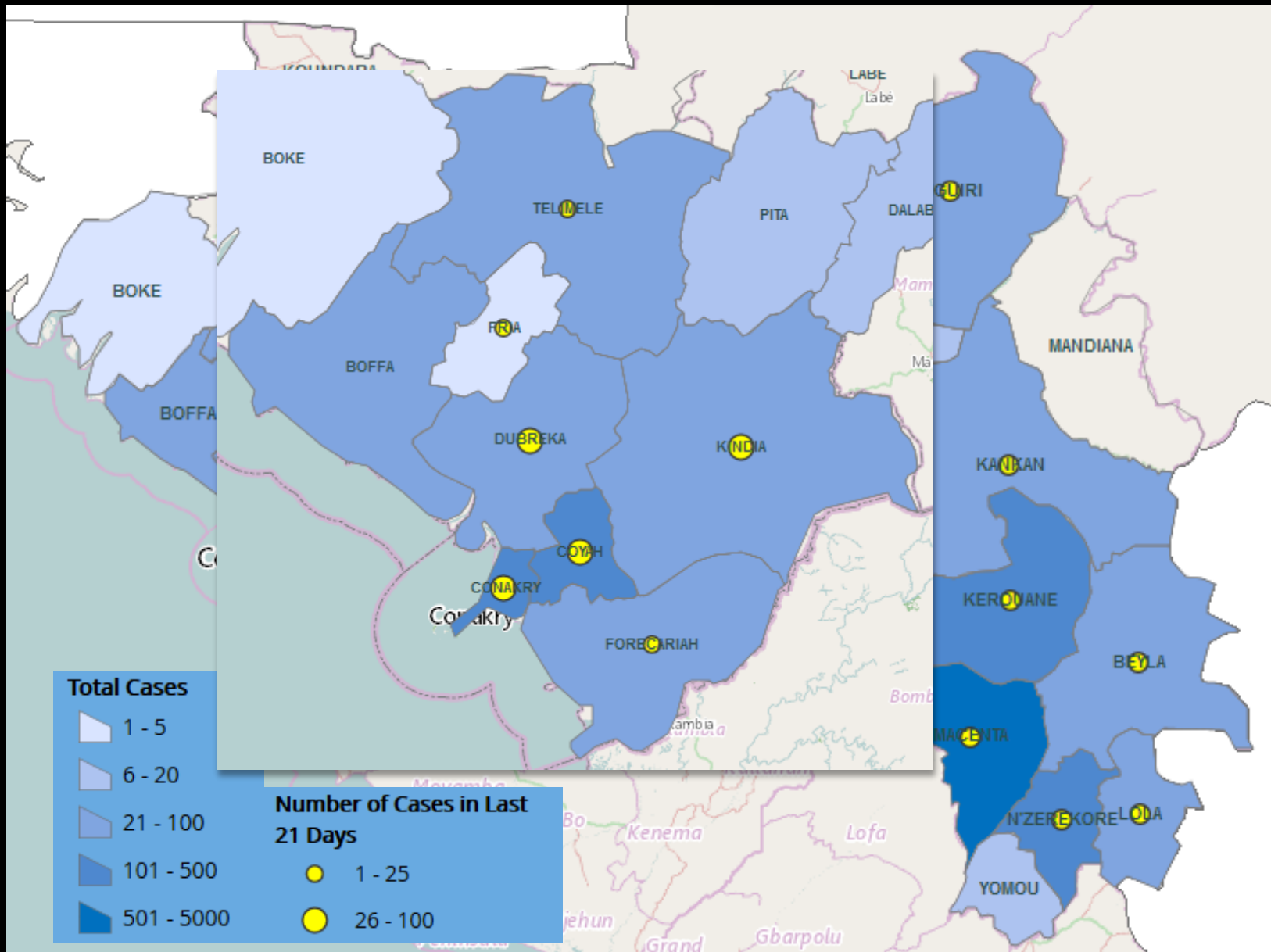
Fig. 7. Ogoja outbreak, 18-24 December.

The findings that only a fraction of villages were infected at any one time, that slow transmission allowed time for smallpox teams to react, and that surveillance-containment activities were effective in stopping individual outbreaks led to a growing awareness that surveillance and containment should be given a much higher priority.

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

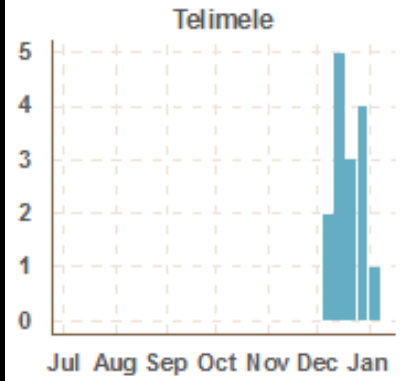
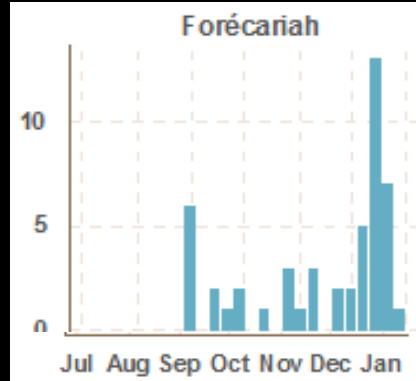
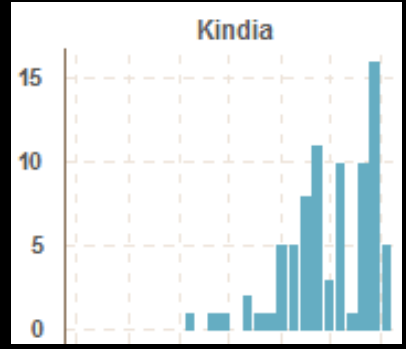
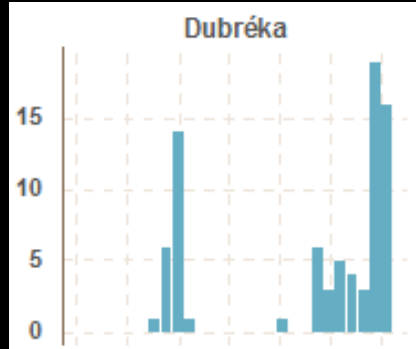
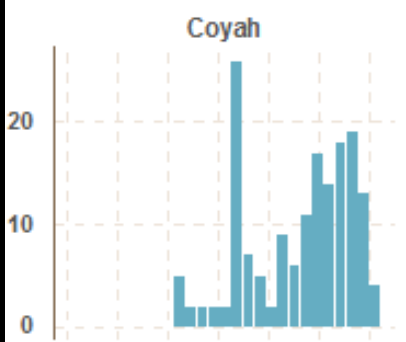
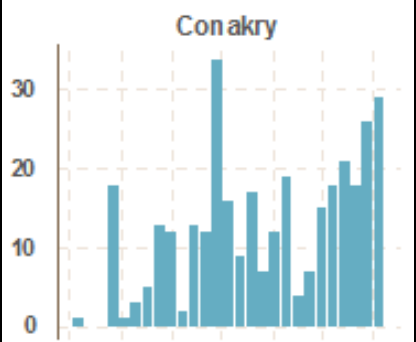
	Smallpox	Ebola
<i>Serial interval</i>	17 days	15 to 19 days
R_0	5 to 7	1 to 2

Current situation



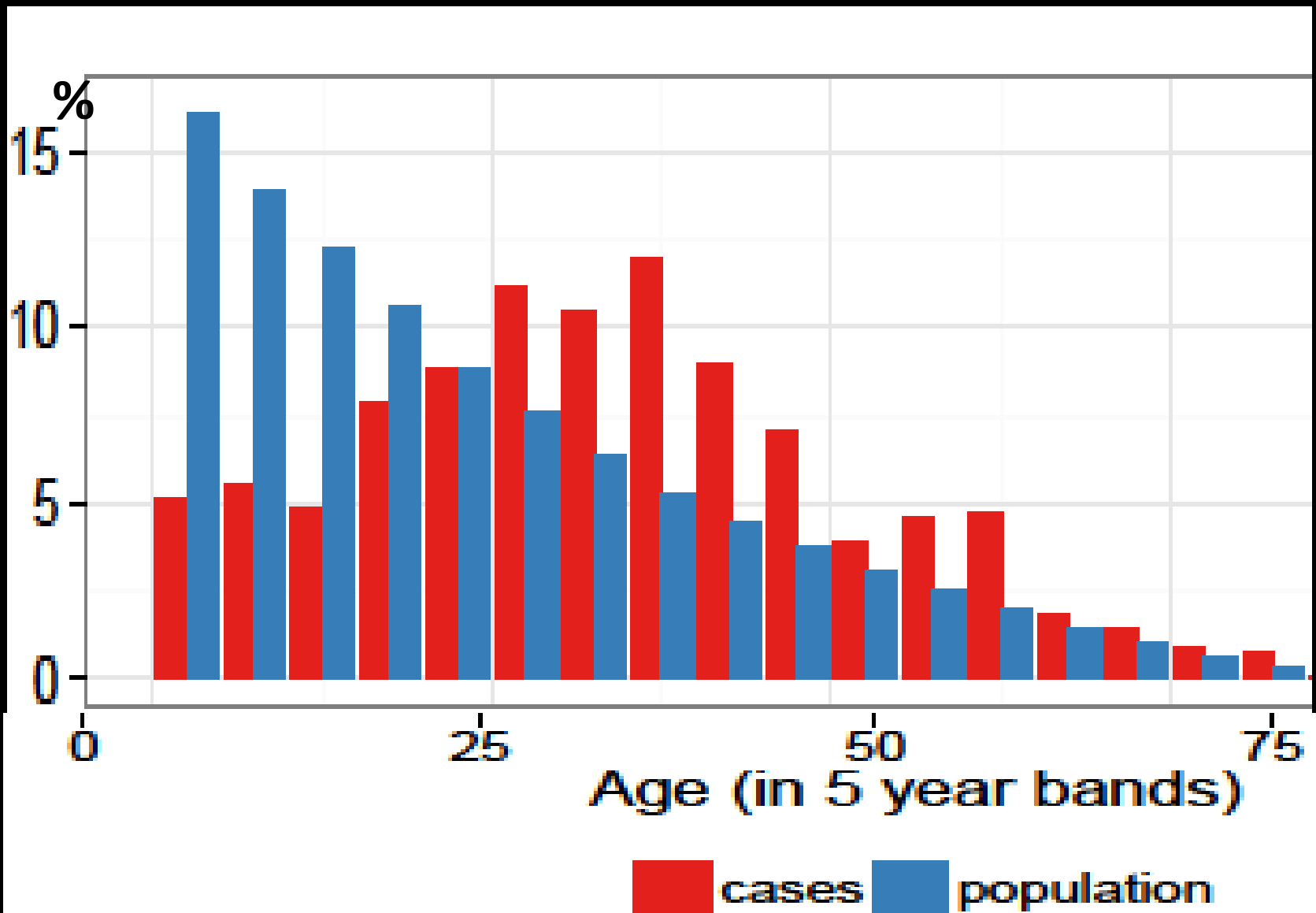
Ebola trend in préfectures of Basse Guinée with >5 confirmed cases in last 21 days

Préfecture	Cases
Conakry	72
Coyah	36
Dubrêka	36
Kindia	31
Forécariah	10
Télémélé	8



Source: MOH sitreps to 4 Jan 2015

EVD cases and population age distribution, Guinea



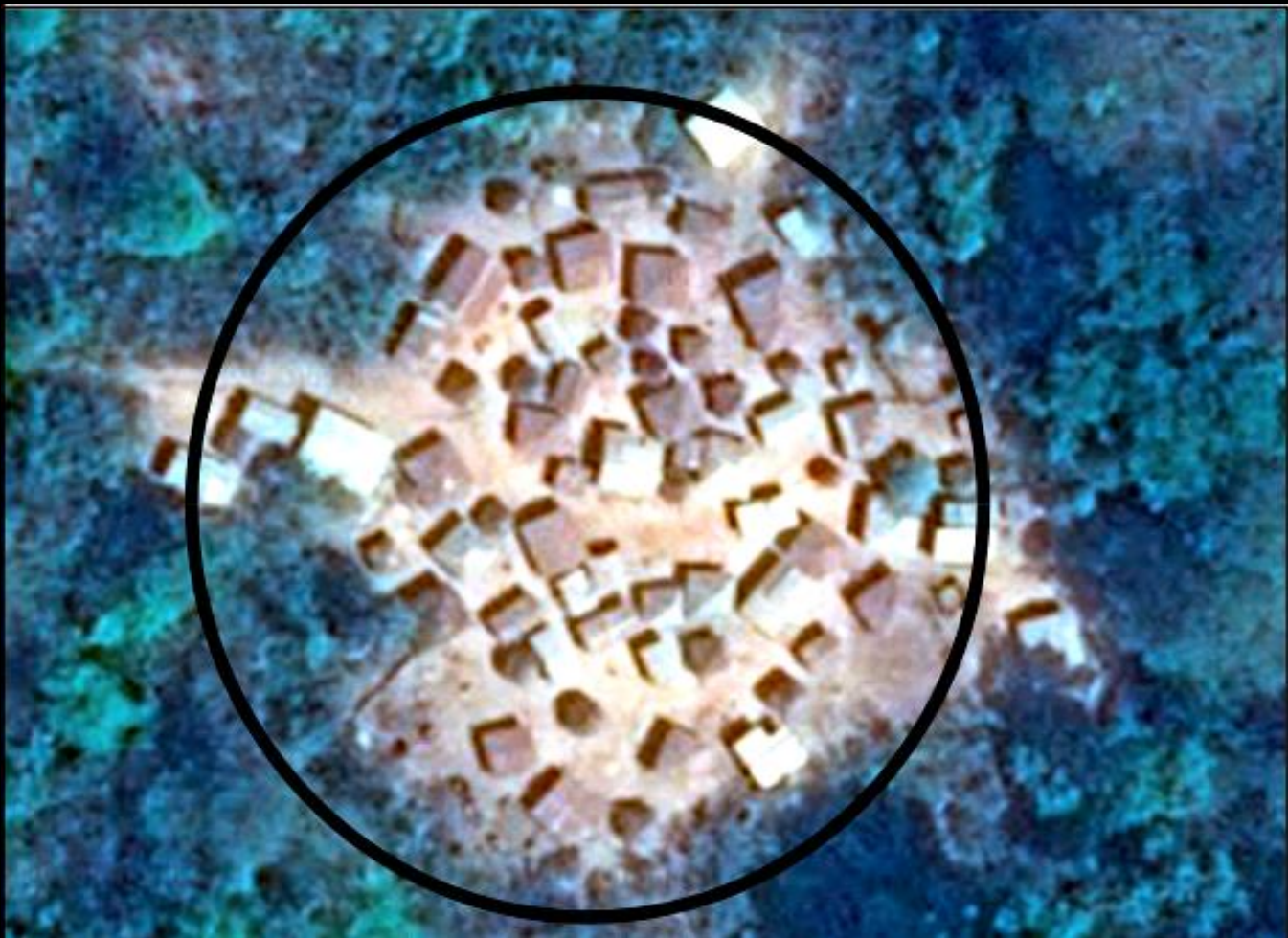


All epidemiology is local

Field epidemiology suggest that:

- **Transmission in funerals, close household contacts**
- **Transmission between places is usually adult-to-adult**
- **Children are usually infected from adults within the household or village.**

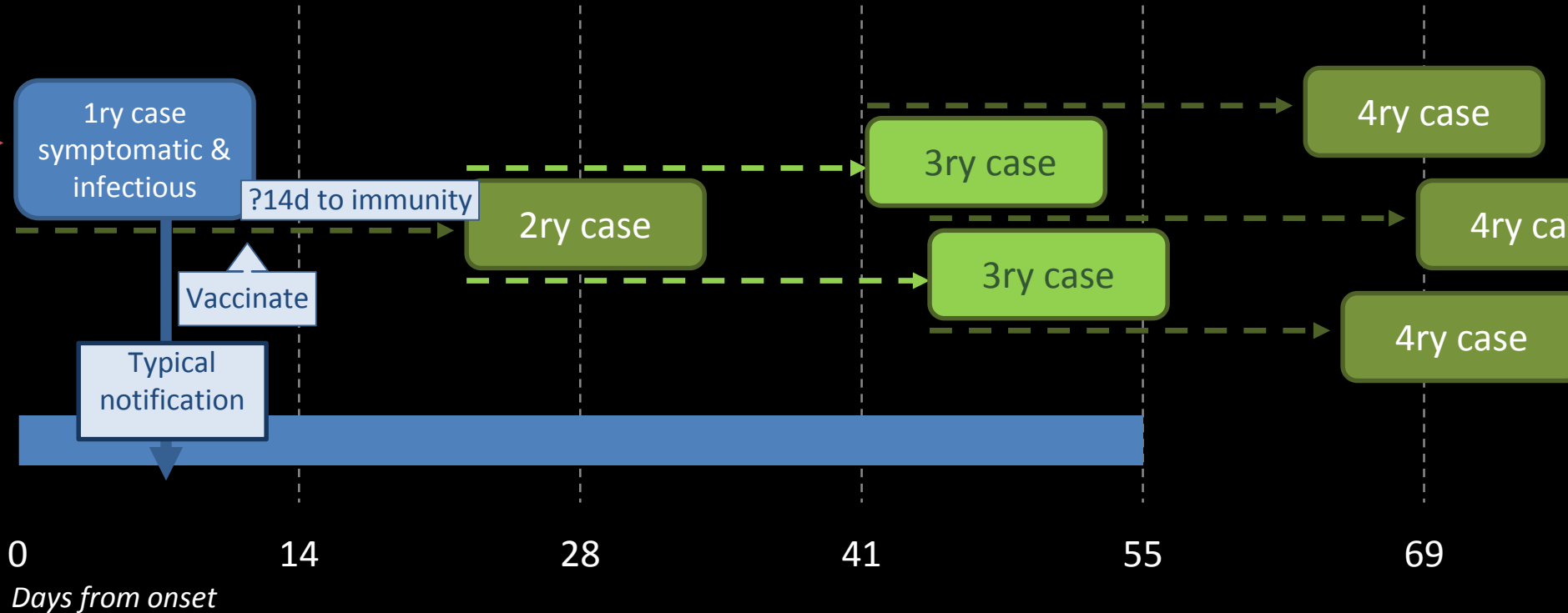
Photo: A home in Guekedou town. Idrissa Soumaré, Mail & Guardian Africa.



Ring vaccination study design

Ring vaccination against Ebola

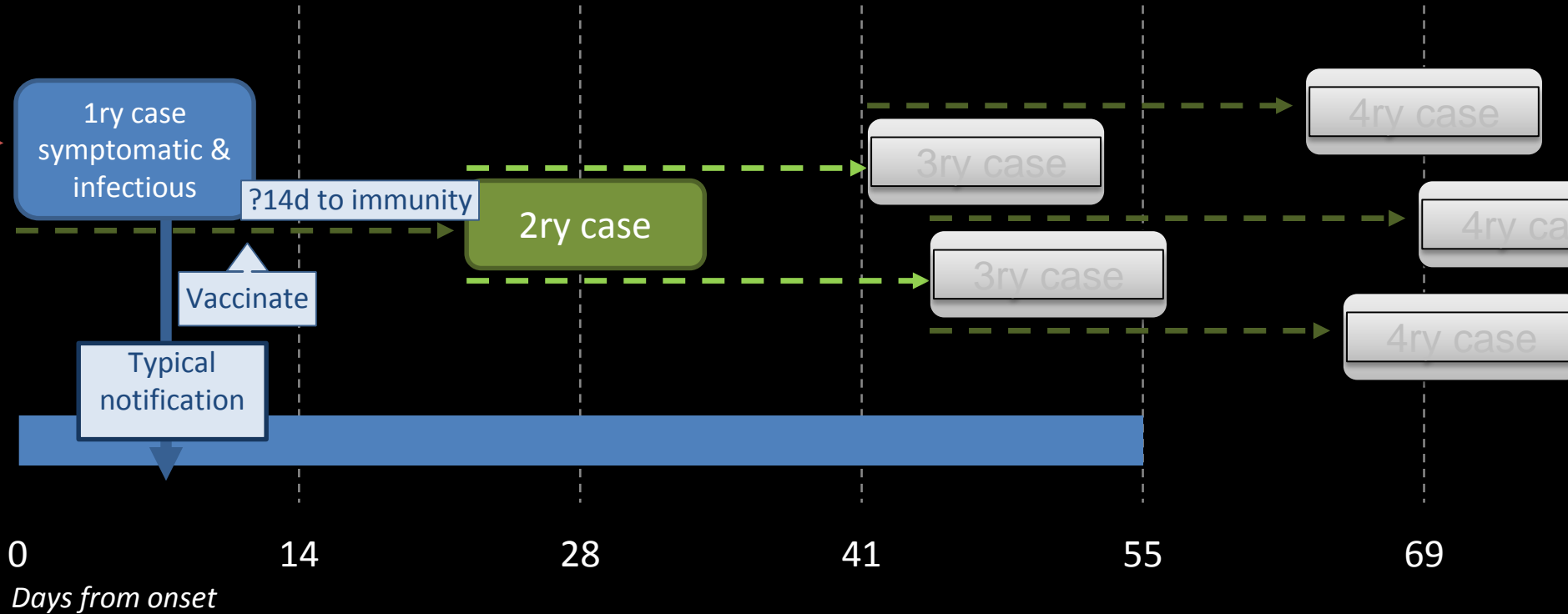
Hypothetical scenario of a Guinean village with $R_0=1.5$.
Serial intervals and notification time from NEJM 2014,
EVD in West Africa – The First 9 Months



Immediate ring vaccination most probably will not prevent 2ry cases.
The anticipated effect of ring vaccination will be preventing 3rd, 4th,
5th and later generation cases.

Ring vaccination against Ebola

Hypothetical scenario of a Guinean village with $R_0=1.5$.
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Ring vaccination study objectives

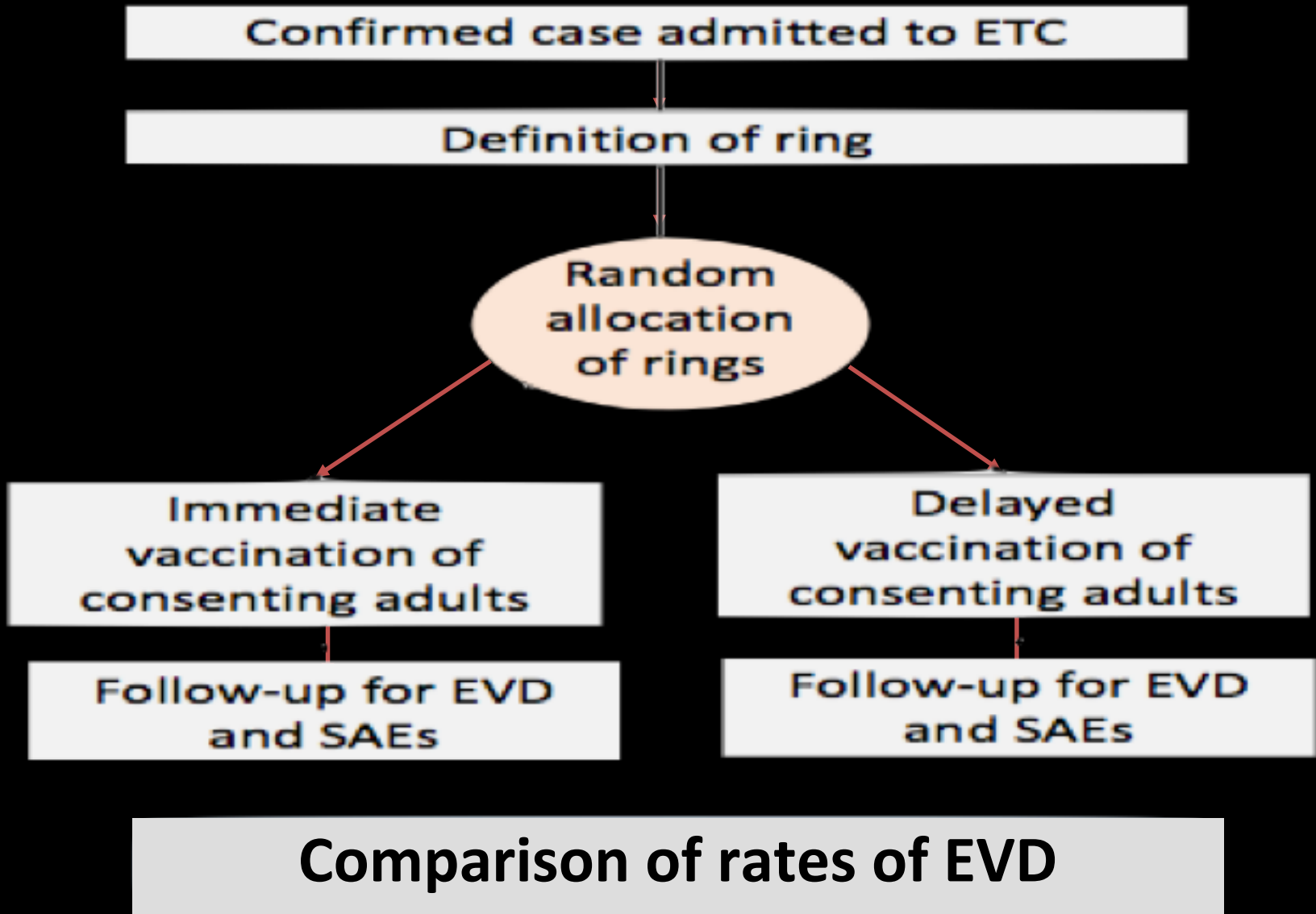
Primary endpoint

- Laboratory-confirmed Ebola disease (EVD)

Secondary end points

- For vaccine efficacy
 - Laboratory-confirmed death from EVD
 - Probable and suspected EVD cases
- For safety
 - Frequency, nature and incidence of SAE
- For vaccine effectiveness
 - Laboratory-confirmed EVD at the level of the ring

Ring vaccination



What is a vaccination ring?

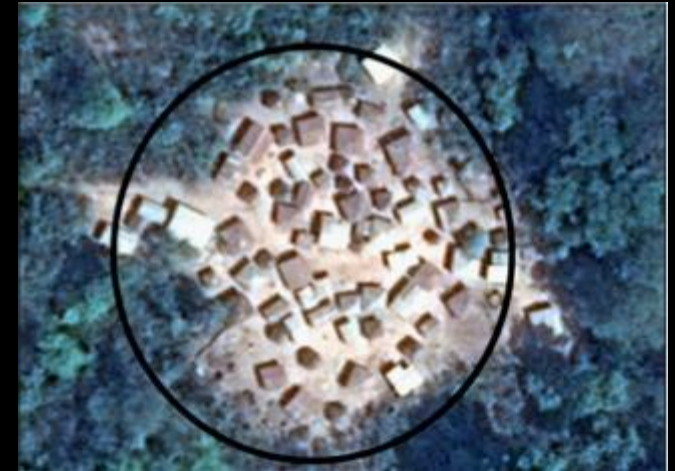
Ring vaccination refers to targeted vaccination of a defined geographical area (a ring)

where a newly diagnosed **case of EVD** resides

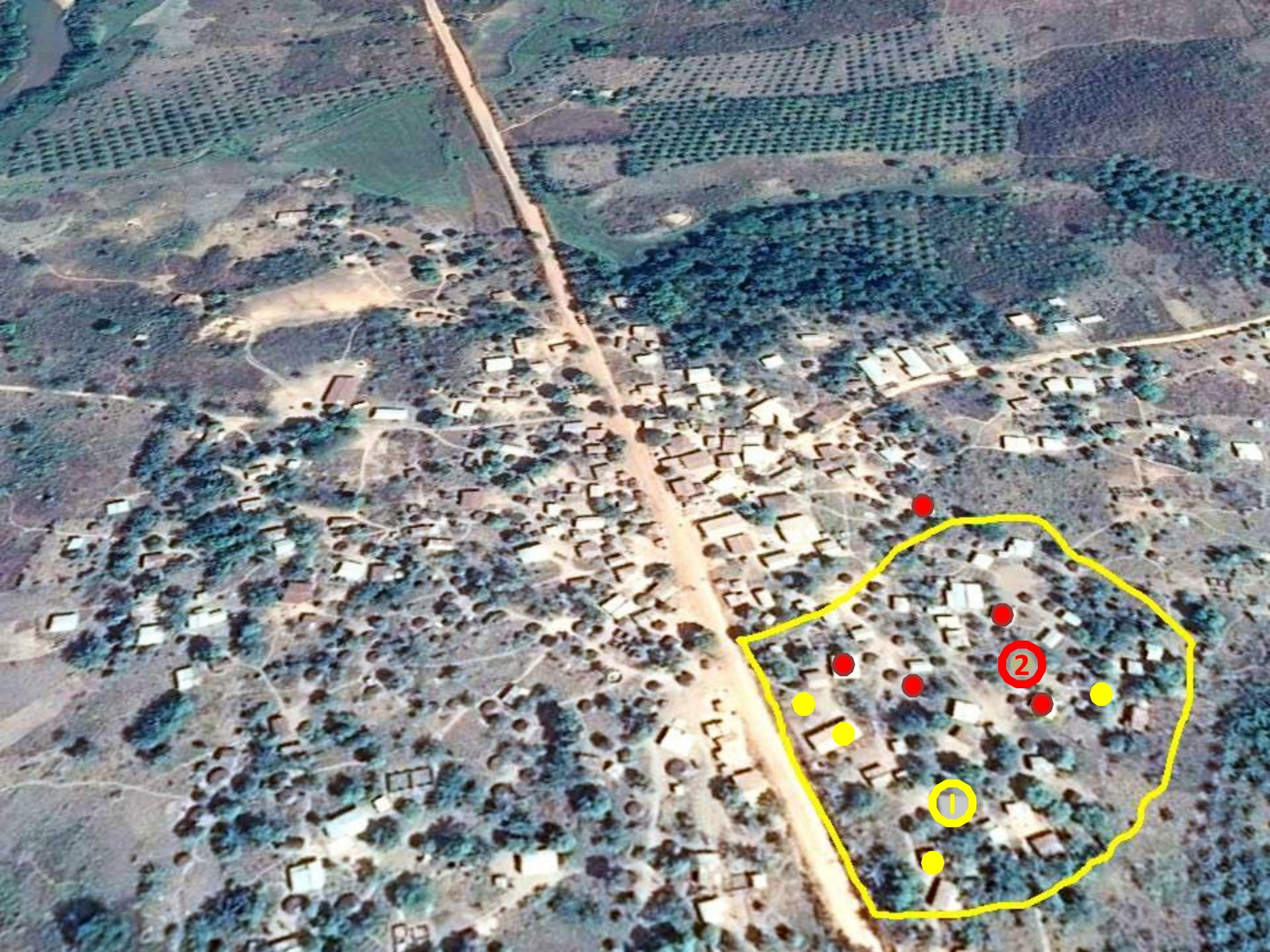
AND

where it is expected most of its **contacts** reside

3 examples of vaccination rings







Estimated number of rings needed in each group

Vaccine efficacy	% developing EVD during 1 month				
	1%	2%	3%	4%	5%
50%	432	215	142	106	84
70%	191	95	63	47	38
90%	98	49	33	24	20



Front line workers vaccination
study design

Front line workers study objectives

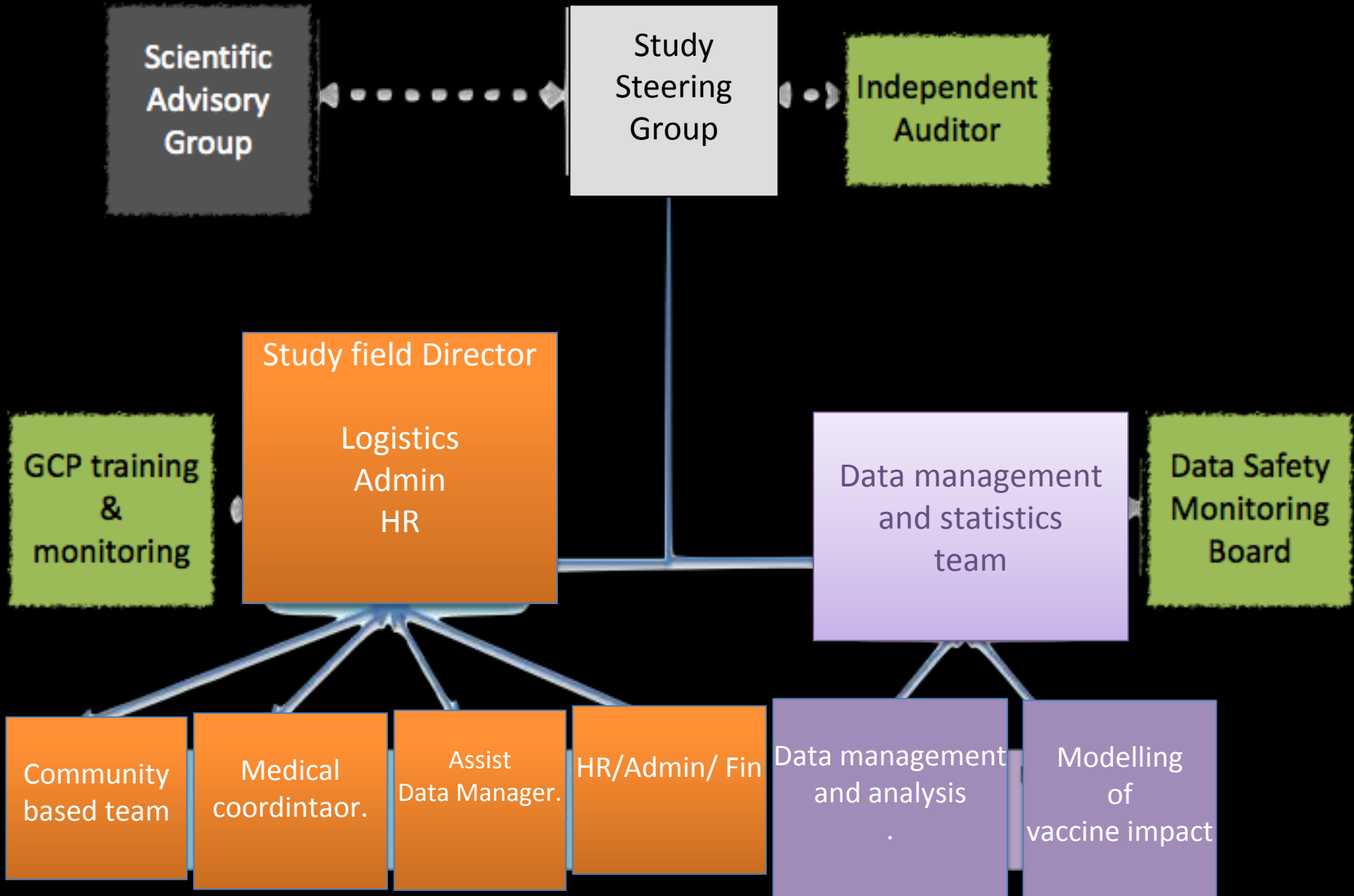
Primary objective - assessing vaccine safety

–Frequency, incidence and nature of SAE

{Samples and data on EVD will be collected and frozen for future analysis as and when a correlate of protection is known or to contribute to the scientific development of a correlate}

Approximately 1200 FLWs work in a Prefecture

Trial study team, Guinea



Community engagement

COMMUNITY ENGAGEMENT

- Become knowledgeable about the community's culture, structures, norms, values.
- Identify influential and credible actors (e.g. *"Comite Vielle Villagoise"*)
- Listening to the community and promote community ownership
- Establish relationship and build trust - transparency

APPROPRIATE INFORMED CONSENT



Photo: Guinea, MSF/Epicentre

Addressing ethics and regulatory requirements

Guinea

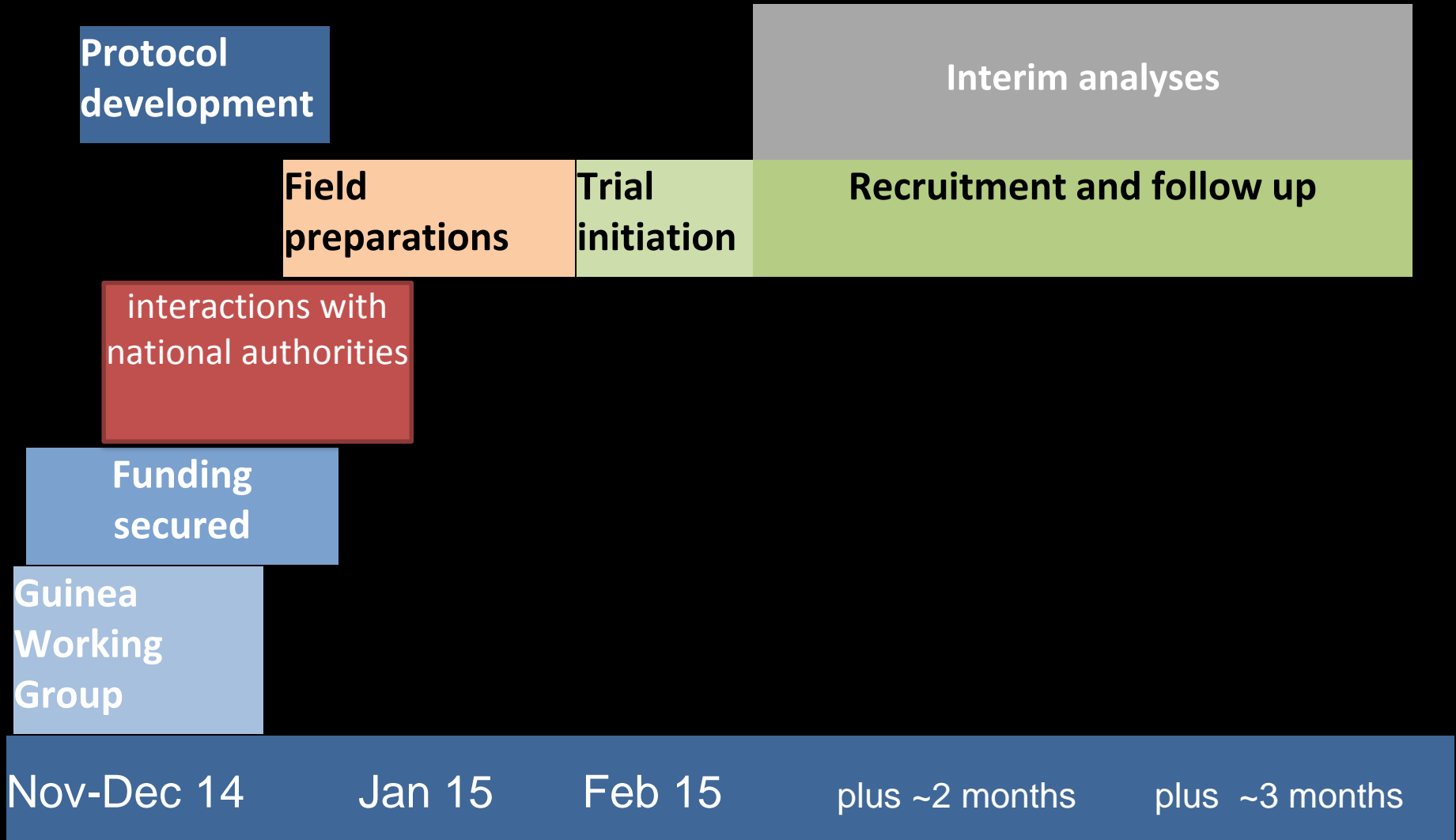
Ministère de Santé Publique
National Regulatory Authority
National Ethics Committee

Elsewhere

AVAREF
Ethic Review Committees of
Partner Institutions

GCP Compliance

Trial timeline

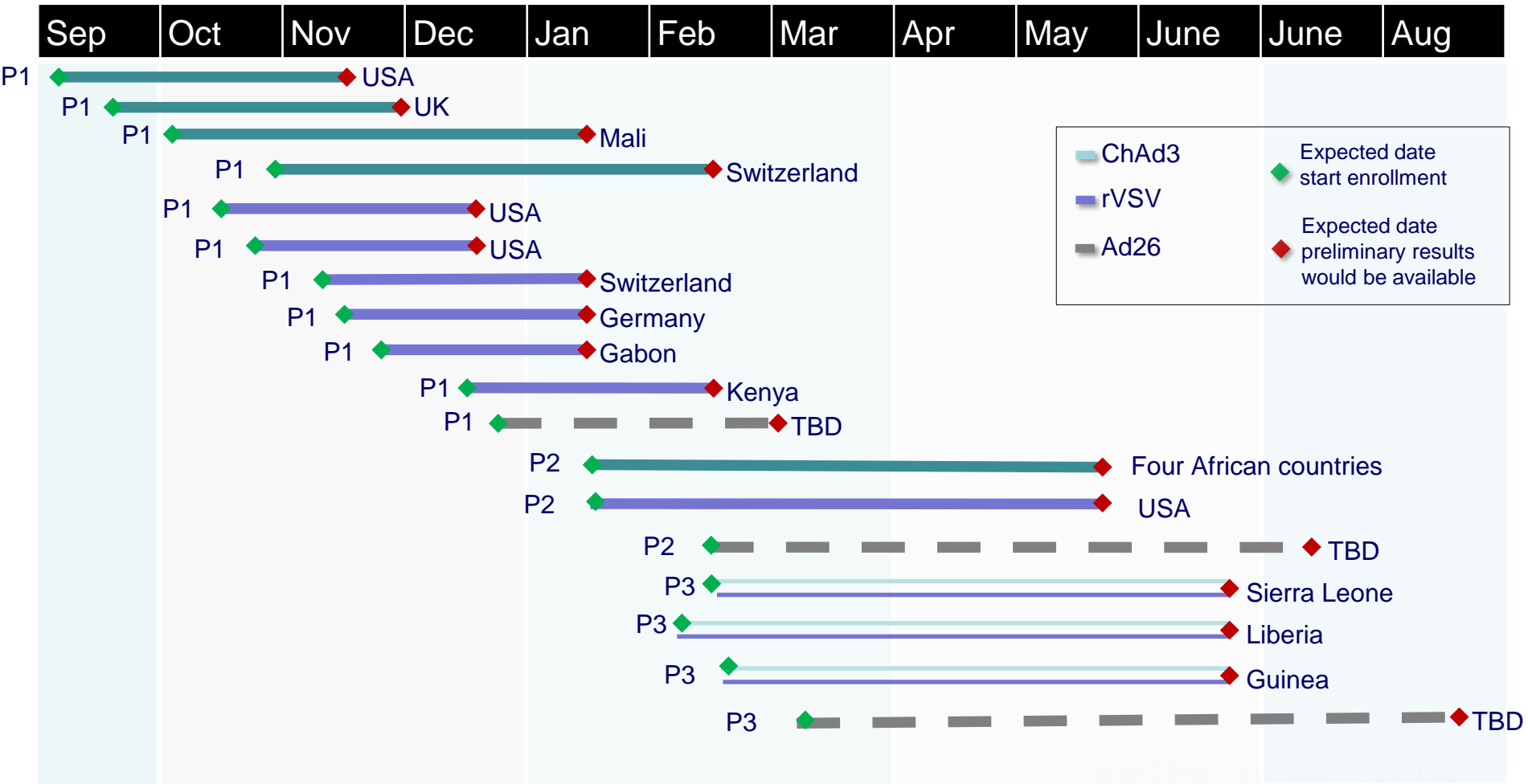


Three messages

- 1** Ring vaccination trial is likely to provide information on efficacy of vaccine and on the delivery strategy for stopping the outbreak
- 2** Ring vaccination trial is feasible and efficient:
 - targets areas with high to moderate disease incidence
 - anticipated faster recruitment time
- 3** Good community engagement is anticipated as populations in all communities with cases will be vaccinated

Ebola vaccine research and anticipated development timelines

(information available to WHO as of Jan 11, 2015)



Important elements to accelerate access to Ebola vaccines

1

Trials to generate the required evidence are conducted in an accelerated fashion and in compliance with ethical and regulatory standards.

2

Functional independent oversight bodies are in place to review evidence, provide oversight and formulate policy recommendations and; to inform funding decisions.

3

National plans and microplans for the vaccine roll out are developed including detailed logistics and vaccination strategies.

4

Vaccine supply is available (or a vaccine management system is in place) to allow the efficient use and implementation of the desirable vaccination strategies.

5

Vaccine can be successfully introduced with community support and impact of vaccination strategies be accomplished.

Ebola vaccines: WHO Oversight

RESEARCH AND DEVELOPMENT PATHWAY

Strategic and Technical Advisory Committee on Experimental Ebola Therapeutics and Vaccines (STAC-EE): Review of development plan, expert opinion on protocol design, and interpretation of data emerging from trials

REGULATORY MATTERS

African Vaccine Regulators Forum (AVAREF): Review of IND application: Protocols, IB, Ethics and informant consent

WHO Advisory Committee on Regulatory Emergency Authorization of unlicensed Ebola Vaccines: Review of GMP, evidence on safety and efficacy, programmatic suitability. Time limited authorization for use

SAFETY AND RISK ASSESSMENT

WHO Ebola Vaccines Risk Assessment Group and WHO Global Advisory Committee on Vaccine Safety: Evaluation of safety data and opinion on potential risks and benefits.

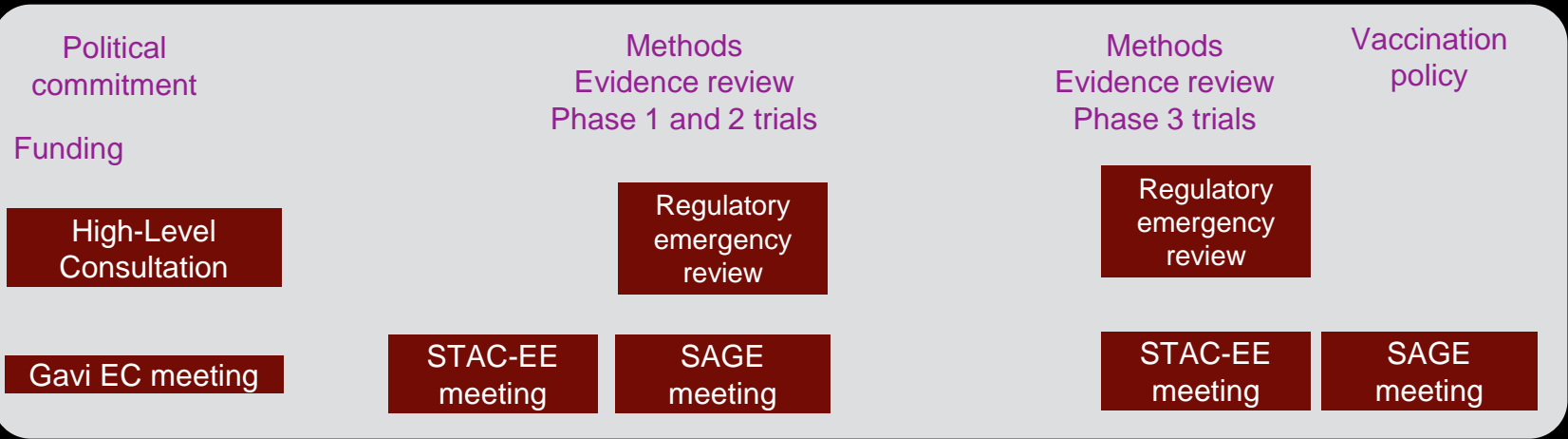
POLICY AND IMPLEMENTATION

Strategic Advisory Group of Experts (SAGE) : Review of evidence to inform policy considerations for large scale use, if appropriate

Task Force on Immunization (TFI): Operational implementation and monitoring in Africa



1



2



3



4



5

Jan Feb -Mar April May June July Aug

"The vaccine is not the magic bullet.

But when ready, they may be a good part of the effort to turn the tide of this epidemic."



Thank you

