Development and implementation of a protocol to evaluate the safety immunogenicity and efficacy of SUDV candidate vaccines during the 2022 SUDV outbreak-SOLIDARITY TRIAL -- Solidarity against Ebola / 'Tokemeza Ebola'

Working together to find a vaccine against Ebola in Uganda

Bruce J Kirenga MBchB, Mmed, PhD, FRCP; On behalf of the trial team

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Solidarity Against Ebola

Introduction

- Yesterday, the 11th of January 2023, Uganda was declared ebola outbreak free at an event I oversaw in Mubende—the epicentre of the sudan ebolavirus (SUDV) outbreak
- Announced on the 20th of Sept, the outbreak spread to affect 9 districts including Kampala, the capital city
- 142 cases were recorded with 55 deaths and 87 survivors
- Yesterday represented a record, under 120 days for the control of an EVD outbreak in history
- Research on candidates pharmacological interventions for epidemic control was embedded early into the outbreak control.
- Work on evaluation of candidate SUDV vaccines was undertaken by a consortium of national and global partners coordinated by WHO
- We developed two protocols
    1. Solidarity against Ebola/Tokomeza Ebola Trial
    2. TokomezaPlus

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What is the Solidarity against Ebola trial?

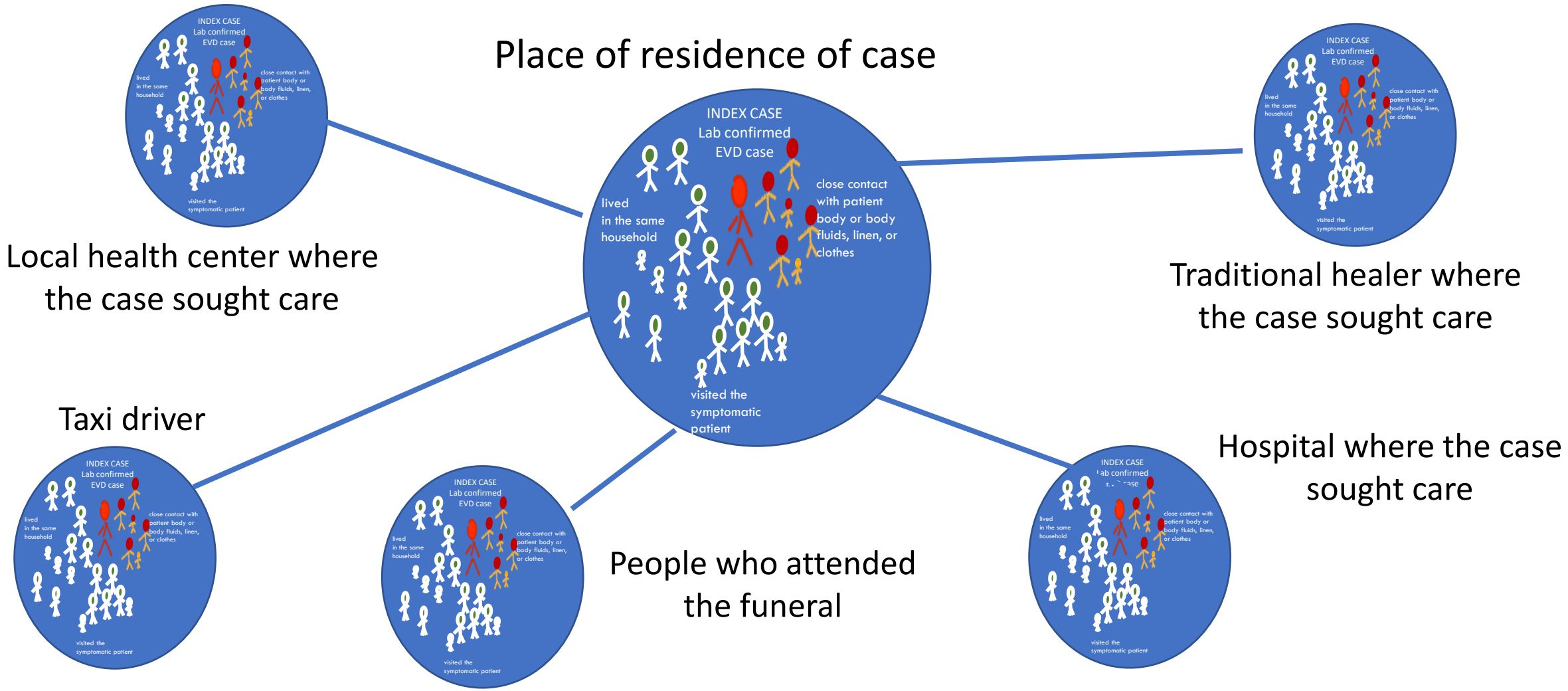
Solidarity against Ebola is a "ring vaccination" cluster-randomized trial to assess the effect of one single promptly given dose of a candidate Sudan Virus Disease (SUVD) vaccine in protecting recent contacts of a newly confirmed case of SUVD against lab-confirmed SUVD in Uganda.

A "ring vaccination" trial strategy means all people who have come into contact with a confirmed case of SUVD (they are known as the 'ring') are offered the chance to participate in a trial to assess an untested vaccine.

- If the vaccine is found to be efficacious it may protect the individual vaccinated or help create a small buffer zone of immunized people that could limit spread of the infection.
- Simulation and field studies have shown that ring vaccination around new cases can in some circumstances be effective and help contain outbreaks of infectious diseases with relatively low reproductive rates.
- This was true for smallpox and for Zaire Ebola virus disease.

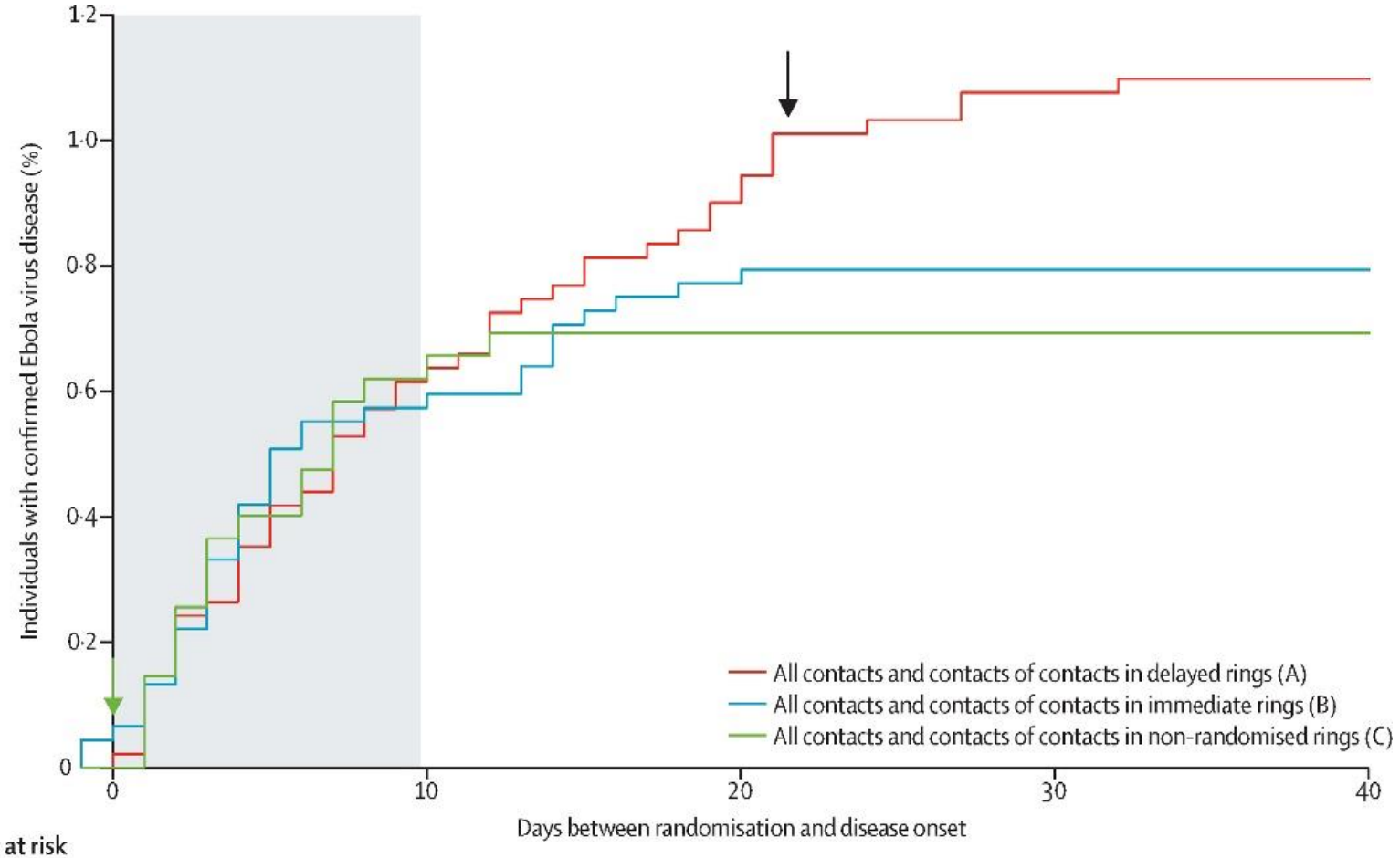
A ring is not a geographic site

A ring includes **all recent contacts** of the cases in the place of residence of the case and in each and every location visited by the SUVD case since the onset of symptoms



Findings

- 0 cases of Ebola virus disease occurred 10 days or more after randomization among randomly assigned contacts and contacts of contacts vaccinated in immediate clusters versus 16 cases individuals in delayed clusters.
- Vaccine efficacy was 100% (95% CI 68·9–100·0, p=0·0045)



Number at risk					
All contacts and contacts of contacts in delayed rings	4556	4528	4514	4508	4507
All contacts and contacts of contacts in immediate rings	4536	4512	4503	4503	4503
All contacts and contacts of contacts in non-randomised rings	2745	2727	2726	2726	2726

Aim and objectives

Aim

The aim of this cluster-randomized trial is to assess the effect of candidate vaccines in protecting against laboratory-confirmed SUDV.

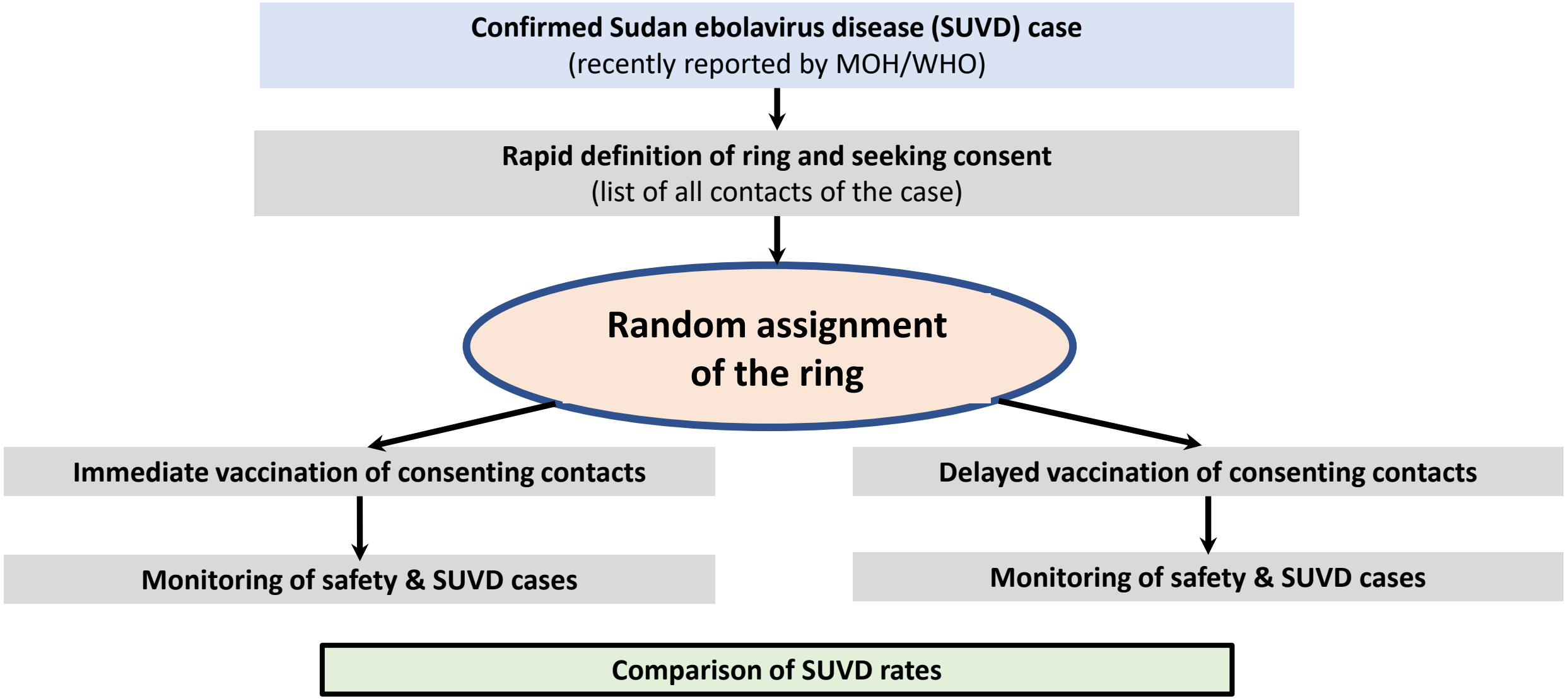
Primary objective

The primary objective is to assess the effect of one single promptly given dose of a candidate Sudan Virus Disease (SUVD) vaccine in protecting recent contacts of a newly confirmed case of SUVD against lab-confirmed SUVD in Uganda (from samples taken either while the person is living, or within 48 hours of their death).

Secondary objectives

- The main secondary objective is to assess the safety of the vaccines by monitoring weekly for 21 days for any adverse reactions to the vaccination and any other serious adverse events.
- Other secondary objectives include:
  - monitoring cases of suspected SUVD that were not confirmed and did not cause death
  - Probable SUVD and death from confirmed SUVD
  - studying how the risk of developing SUVD depends on factors such as time since vaccination, time from index case onset until vaccination, age, sex, and pregnancy
  - seeing whether the outcomes of any pregnancies are affected.
- *Although efforts will be made to determine whether ring vaccination helps control disease spread beyond the vaccinated contacts, there may be too few cases to answer this directly*.

Solidarity against ebola



Inclusion / exclusion criteria

The inclusion criteria are:

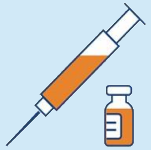
- male or female contact of a newly confirmed SUVD index case
- at least 6 years of age or older at the time of randomization
- capable of giving signed informed consent/assent/have parent(s)/legal guardian capable of giving signed informed consent

The exclusion criteria are:

- history of SUVD (self-reported or laboratory confirmed)
- history of administration of other experimental treatments in the last 28 days.
- history of anaphylaxis from a vaccine or component of a vaccine
- serious bed-confining illness requiring hospitalization at the time of vaccination

3 candidate vaccines are being considered.

There is substantial uncertainty about the clinical efficacy of these candidate vaccines, and this informs the rationale for the need to generate randomized evidence

Type of vaccine	Vaccine developer	Viruses targeted	No. of doses	Immunogenicity + safety in humans?	Efficacy against SUVD in animals?[1]
cAd3	Sabin Vaccine Institute + US NIH	Sudan ebolavirus	Single 	Yes 	Yes 
cAdOx1	University of Oxford	Sudan + Zaire ebolaviruses	Single 	Yes 	Yes 
rVSV SUVD	Merck/IAVI	Sudan ebolavirus	Single 	No	Yes 

[1] *Each vaccine incorporates the ebolavirus surface protein into a harmless adenovirus (Ad). Both vaccines can protect animals against a potentially lethal dose of the Sudan ebolavirus.*

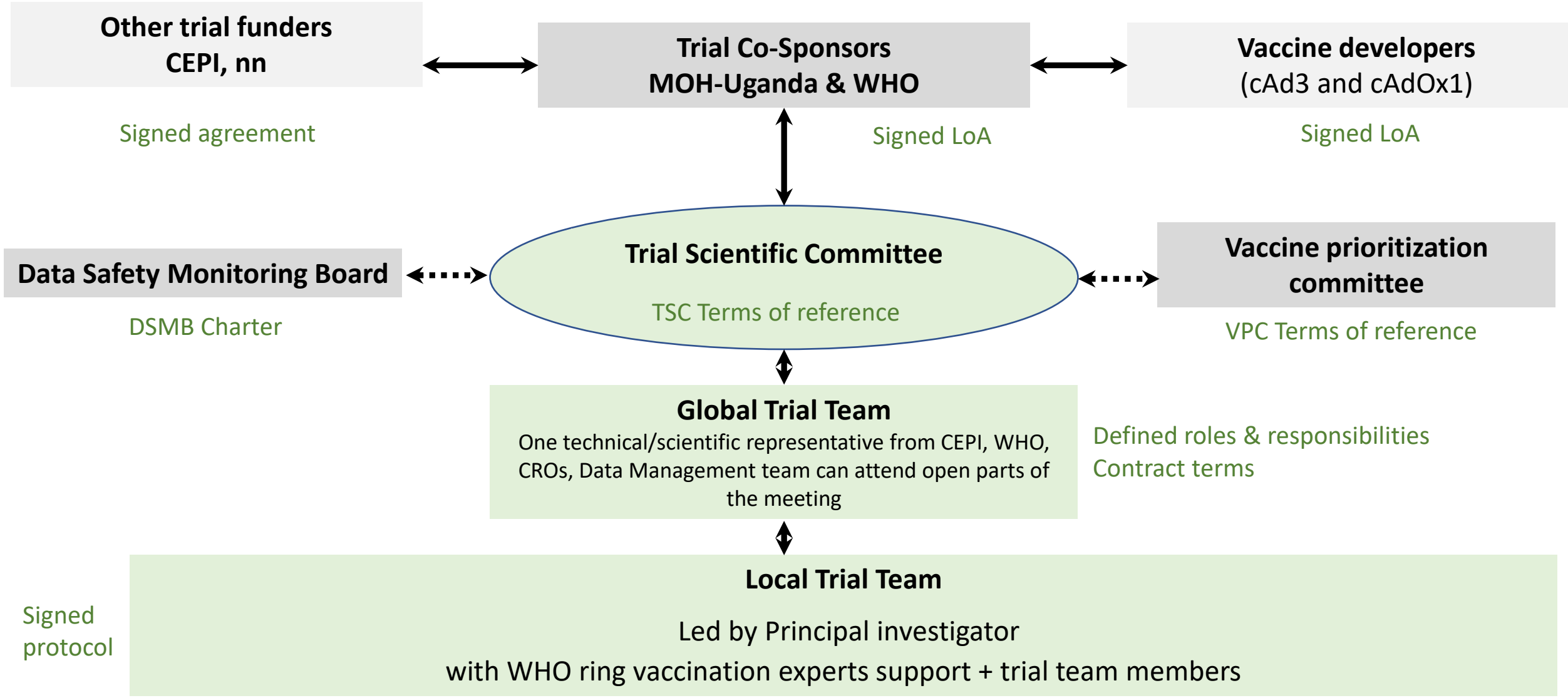
Sample size

The detailed information on transmission dynamics is not currently available.

Thus the decision about when to unblind the trial will be made by the Trial Scientific Committee without knowledge of previous allocation. It will be based on an assessment of the number of accumulated endpoints and epidemic trends.

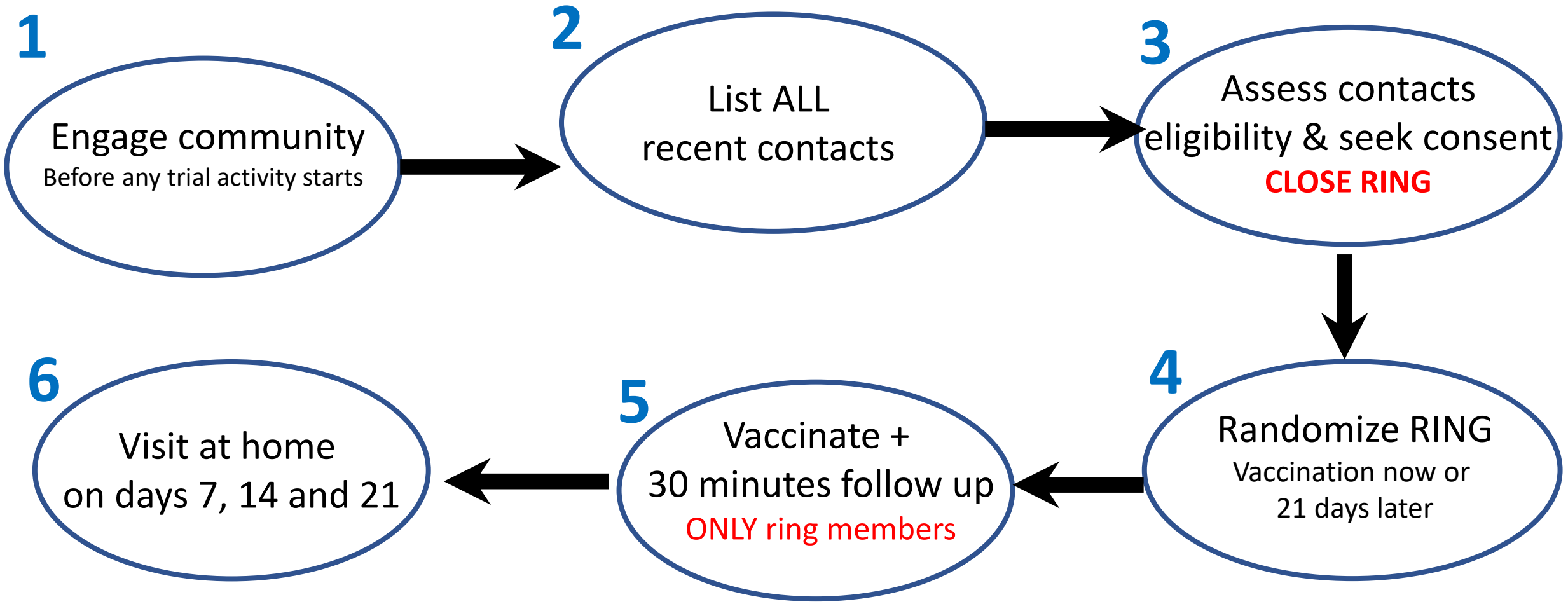
The final sample size achieved will depend on the number of new index cases accumulating during the study period.

Trial governance



Trial steps

A lab-confirmed case of SUVD is reported



TokomezaPlus

Objectives
Primary objectives:

1. To evaluate safety of SUDV vaccine(s) by assessing hematology, clinical chemistry and other soluble biomarkers as needed (e. g. inflammatory parameters).
2. To determine the immunogenicity of the Ebola Sudan Vaccine(s) candidates.

Secondary objectives:

1. To determine the durability of SUDV-specific induced responses in the ring trial
2. To determine the factors associated with optimal vaccine-induced responses in the ring vaccination trial
3. To determine the putative cross reactivity exerted by the SUDV vaccine candidates against other ebolaviruses (e. g. *Bundibugyo ebolavirus* (BUDV) and EBOV).

Solidarity against ebola

Exploratory objectives:

To determine the effect of SUDV vaccines on host gene expression.

To determine the T and B cell specific responses and immune profiling in response to vaccination.

To determine the effect of SUDV vaccines on the host metabolome.

To determine the effect of SUDV vaccines on host innate immune responses

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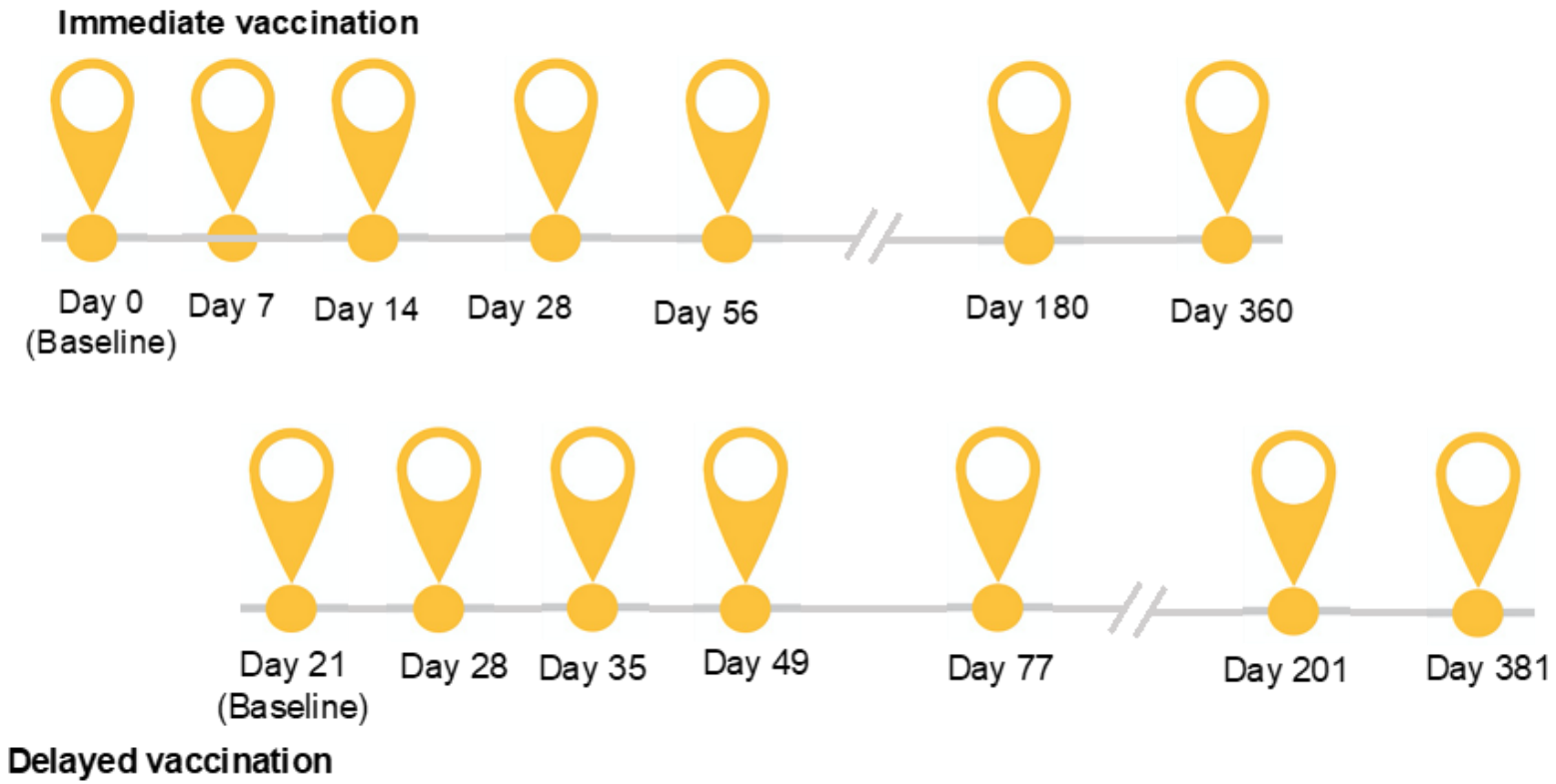
Blood sampling schedule for participants in immediate vaccination rings and delayed vaccination rings.



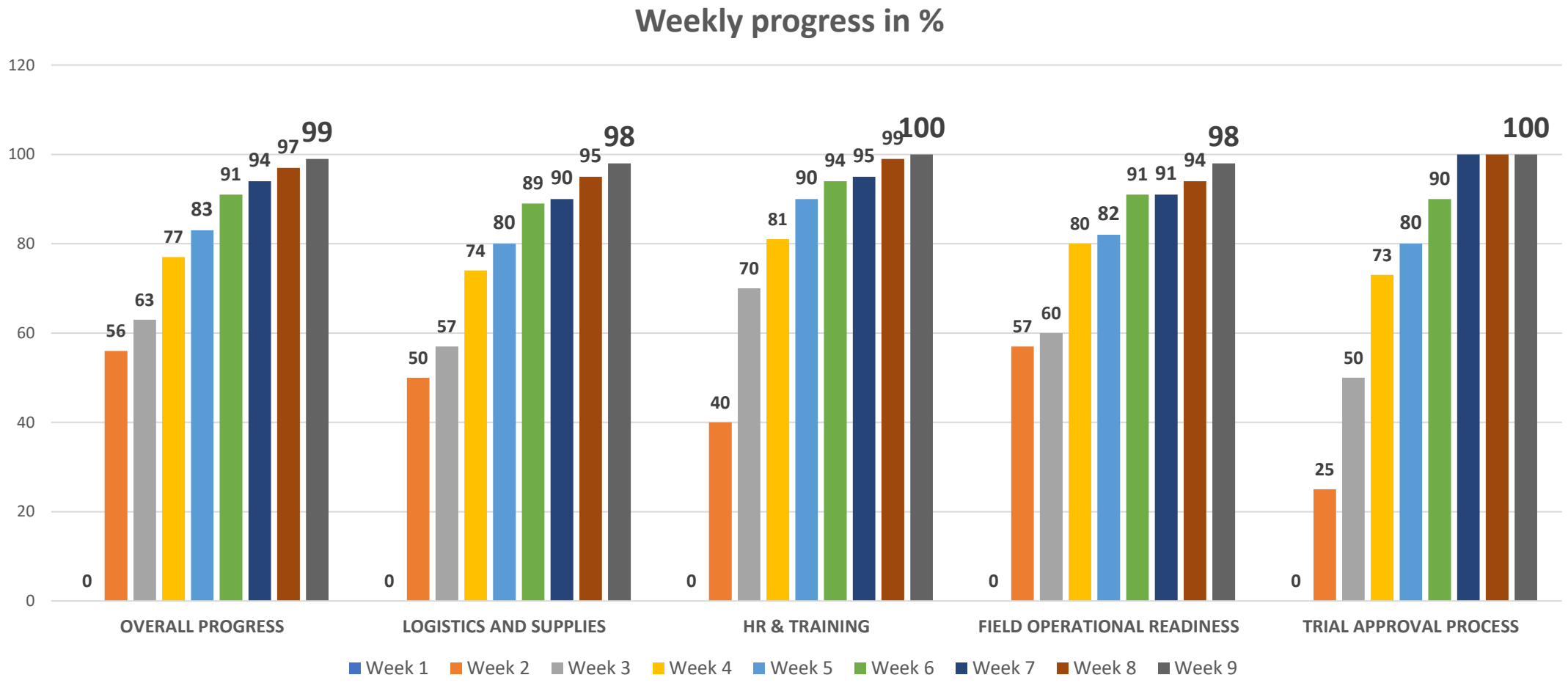
TRIAL implementation

13/12/2022

Trial Implementation Milestones by week

	Milestone	Time taken *
1	Principal Investigator appointment by MoH	1 week
2	Arrival of WHO technical assistance for the trial	2.5 weeks
3	Sub-Investigator appointments by MoH	3 weeks
4	Finalisation/Adaptation of generic protocol	3 weeks + 3days
5	Setting up an ultra-cold chain facility	6 weeks
6	IRB approval	8 weeks
7	Uganda National Council for science and technology approval	9 weeks
8	National drug Authority trial certificate	9 weeks
9	GCP and protocol training of staff	6 weeks
10	Dry runs	8 weeks
11	Wet runs	9 weeks
12	Arrival of 1st candidate vaccine in the country	11 weeks
13	Ring definition	11 weeks

Progress per week



Highlights trial implementation preparations

- As part of preparations of this trial the following was achieved:
  - 5256 doses investigational vaccines were received
  - 7 teams each comprising of 14 researchers were fully trained
  - 2 trial bases were secured renovated, furnished and complete with cold chains capacity- Field (Mubende) trial base at DHO offices and Central base at Mulago Hospital
  - Resources were mobilised with commitment from funders

Reception of the first SUDV candidate vaccine in country

Ministry of Health- Uganda ✓
@MinofHealthUG

Uganda has received 1200 doses of vaccines from @WHOUganda which will be used in the Tokomeza #Ebola vaccine trial. This is first batch of one of the three candidate Vaccines against the Sudan Ebolavirus.

12:01 · 08/12/2022 · Twitter for iPhone

WHO Uganda ✓ @WHOUganda · 2d

"This is a historic day for the country & the world of scientific health research. For the 1st time, vaccines 4 clinical trials are produced in less than 90 days after the start of an #EbolaOutbreak. This is a remarkable effort!" - Dr Charles Njuguna, Incident Manager @WHOUganda

WHO African Region and 4 others

Dr. Jane Ruth Aceng Ocero
@JaneRuth_Aceng

Today morning, together with @WHOUganda country representative, @tegegny, I visited the Principle investigator of the Sudan Ebola virus vaccine trial to assess the level of preparedness. I can comfortably say, #Uganda is ready for the vaccine trial.

32 · 25/11/2022 · Twitter for iPhone

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Key Lessons learned

1. Collaboration is key-both SS and SN- the case of support from Guinea physicians and Global vaccine organizations
2. Novel regulatory approvals mechanisms are key in emergencies- the case of the Uganda Joint Review mechanism
3. Government and political support- working with Ministry of officers and Ministry's co-sponsorship
4. Interdisciplinary teams
5. Past experience with Covid-19 emergency research teams- one epidemic should get us better ast epidemic research
6. Technology- electronic assessment of candidates for the teams

Thank you


THE REPUBLIC OF UGANDA
MINISTRY OF HEALTH
Hiding someone who has been in contact with an Ebola infected person is DANGEROUS to you and the entire community.
Report this to 0800-100-066 or call the nearest health facility for further assistance
Dr Jane Ruth Aceng Ocero
Minister for Health/Woman MP, Lira City