Ebola has demonstrated the ability to cause major disruption to society. Response in 2014-15 and subsequently has shown the resilience of African people, countries and investigators. Research to identify effective vaccines and therapeutics is an essential component of outbreak response.

Our common goal is to make plans and develop tools now so we are better prepared to act later. Have products available within 7-15 days of outbreak declaration. Coordination and collaboration across all levels (including MOH, WHO, developers, researchers) is essential as countermeasures are investigated and deployed in context of other public health measures. Involved countries must be and remain at the forefront of preparation and response efforts. There is strong political support for working together to find scientifically valid solutions based on the needed technical expertise.
Future efforts will build on past experience

Previous African studies have rigorously evaluated Ebola vaccines and therapeutics. African investigators already have many of the capabilities needed to lead the way forward.

For vaccines, the ring vaccination study performed in Guinea led to approval in many countries around the world of the VSV-vectored vaccine. This same vaccine was deployed in the DRC in over 300,000 individuals under “Expanded Access” to control large outbreaks including in 2018-20. Additional outbreaks led to development of a core protocol that will allow rapid evaluation of future vaccines in a way that promotes quality, equity, trust, and deployability.

For therapeutics, data has been collected under MEURI protocols before randomized trials could be implemented, and subsequent randomized trials have collected essential information regarding effective therapeutics against Ebola Zaire.

Experience has shown the importance of an African-centered approach, community engagement, sharing of capabilities and capacity building, and planning.

We don’t yet have known effective vaccines or therapeutics against other related filoviruses, so more work is needed. Critically, plans need to be made in advance of a future outbreak in order to be prepared.
Key elements of a flexible protocol for filovirus vaccines

Vaccines recommended for inclusion by Independent Working Group of Vaccine Prioritization

Phase 1, 2, 3 seamless
Covers both outbreak and inter-epidemic period
Multi-country, multi-center

Inclusion/Exclusion criteria
Many countries would like flexibility for pediatrics, pregnancy, vulnerable populations, ethics considerations, community engagement, etc. This may be accomplished via protocol addenda and country-specific SOPs.

Outbreak
Cluster randomized ring vaccination of direct contacts, immediate vs. delayed for efficacy
Discussion of appropriate delay time (21 d) considers need to obtain data on unproven interventions, low transmission rate, and eligibility of infected for therapeutics studies
Cases independently detected and verified
Assures unbiased case detection, supporting validity of trial results
May collect data across multiple outbreaks
Need for collaboration across countries

Inter-epidemic (HCW, FLW)
Individually randomized among vaccines (no placebo)
Maintain warm base and capacity

Both (as appropriate)
Safety & Immunogenicity
Phase I: up to 100, subject to DMC review
Dose finding
Phase II: up to 1000
Would like to make sure that safety is adequately evaluated before vaccine progresses to later stage evaluation
Value of collecting samples appropriate for robust evaluation of immunogenicity (pre vaccination, CMI, mucosal, etc.)

Overall: Enthusiasm for collaborative African-centered approach, where countries support each other to facilitate protocol implementation
Solidarity Partners Core protocol for therapeutics

1. Therapeutics prioritised by independent WHO Expert group

2. Pre-positioned: to enable inclusion of early cases in an outbreak

3. Streamlined core protocol
   a) **Conserved across outbreaks**: data from one outbreak contributes to findings in the next
   b) **Conserved across viruses**: since certain interventions might be applicable to more than one virus subtype

4. **Adaptive platform and factorial design**: test multiple interventions simultaneously and to assess combination therapies to identify the best treatment for a disease

5. Inclusion of control arm with no treatment

6. Adequate statistical analysis plan

7. **Minimal exclusion criteria**: recruit broad range of patients

<table>
<thead>
<tr>
<th>Evaluation domain</th>
<th>MARV</th>
<th>SUDV</th>
<th>EBOV</th>
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</thead>
<tbody>
<tr>
<td>Randomisation 1</td>
<td>Monoclonal antibody vs no additional treatment (1:1)</td>
<td>Monoclonal antibody vs no additional treatment (1:1)</td>
<td>Receive approved Mab</td>
</tr>
<tr>
<td>Randomisation 2</td>
<td>Antiviral vs no additional treatment (1:1)</td>
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<tr>
<td>Randomisation 3</td>
<td>Host directed therapy vs no additional treatment (1:1)</td>
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Addressing operational challenges

Protocol preapproval (MEURI and clinical trial) pending product information

Routine & event-based surveillance

MOH & key stakeholders (including investigators, NRAs, IRBs, ethics committees etc.) need prospective operational plan

If resources & experience exist: adapt to new outbreak (staff, labs, study-specific SOPs), reach out to countries that do not have resources or experience, collaborate internationally to support specific needs

Other capacity, including building research into the emergency operations center via incident management system, training

Community engagement is critical

Pre-position supplies

Strengthen clinical research capability, patient management. Lab (clinical & research)

Simulations can test processes before outbreaks

Procedures to facilitate sample transport (to allow sharing capacity), expert sharing

All countries need to prepare now to move forward together collaboratively