# Building Resilience Against Outbreaks & Pandemics

## Research to identify sustainable solutions

The 3rd Global Research and Innovation Forum

World Health Organization

R&DBlueprint
Powering research to prevent epidemics

# Critical research to ensure **equitable and fast access to high-quality and affordable therapeutics** while ensuring people's trust

## Update and priorities

Dr. Marco Cavaleri
EMA

# Only a handful of platform trials were informative

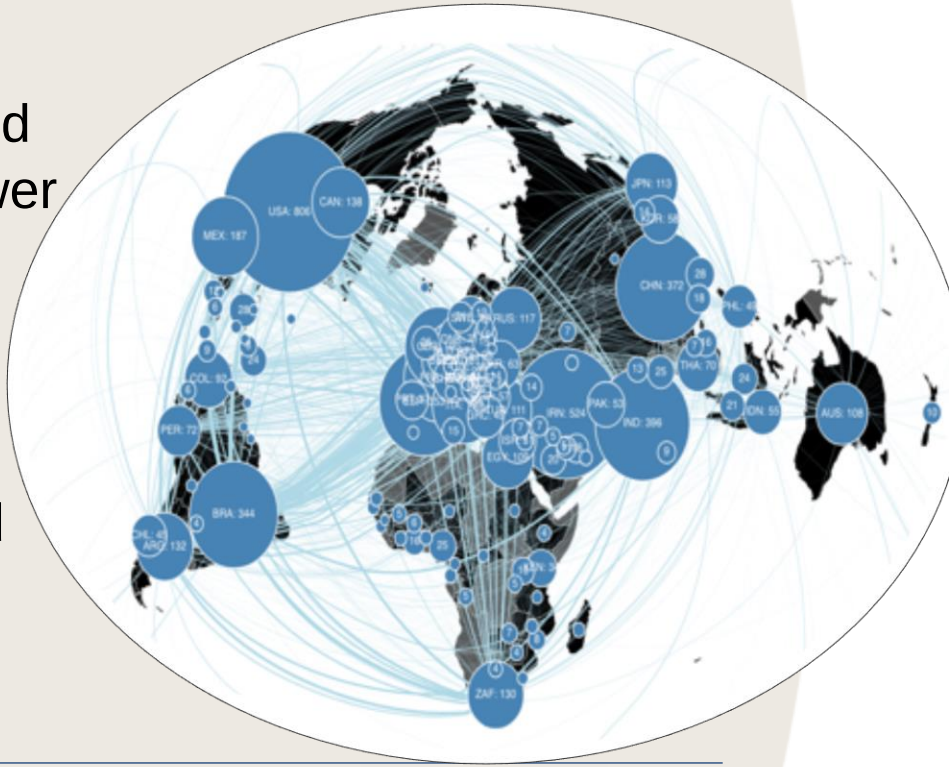


As of Aug 02, 2023 there were 4634 randomized trials of COVID-19 treatments

Most trials were **not informative** and some were too small to be able to answer confidently **key public health** questions.

Some of the treatments evaluated maybe should have not been prioritised

Improvements are needed in the **South and in the North**!



Regarding access to candidate therapeutics during outbreaks and pandemics, some have emphasized the importance of **speed** and sometimes **cost** in responding to future pandemics.

It is equally important to take a broader view that recognizes the primary importance of **quality**, **equity** in availability, and **trust** in the products safety and efficacy.

# Being prepared to integrate research during outbreaks

Data-driven decisions by **open collaborative scientific networks**

**MOH in the driving seat**
designates researchers

Support of
**local research capacity**

**Local researches contribute**
to the process

Landscapes of candidates

Target Product Profiles

**Independent process**
for prioritization

A virtual process to ensure
**therapeutics are available**
for outbreak evaluation

Pre-outbreak **trial design**

Pre-approved
**CORE protocol**

**Legal, regulatory and insurance** framework

Support of local
research capacity

## Research and innovation priorities for other areas

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# Inter-epidemic research for Filovirus family

An example, leading toward a Viral family approach


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WHO R&D Blueprint

Filoviruses research meeting

Strategic agenda for Filoviruses research and monitoring (AFIRM)

WHO reference number



30 March 2022, virtual consultation
Geneva, Switzerland

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# Outbreaks research for Filovirus family

An example, leading toward a Viral family approach

3 November 2022 | Statement

**Global health agencies outline plan to support Ugandan government-led response to outbreak of ebola virus disease**

15 NOVEMBER 2022

**Sudan Ebolavirus – Experts deliberations. Candidate treatments prioritization and...**

October & November 2022

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# A WHO Global Committee for prioritization of candidate treatments for evaluation during outbreaks



Established in early 2020
Independent experts, transparent, data-driven, with a priori defined criteria

| Pathogen | Number of products reviewed | Type of product |
|---|---|---|
| COVID-19 | Over 20 | • Antiviral<br>• Inmunomodulators<br>• Antimalarials |
| Sudan ebola virus | 7 | • MAbs cocktail and MAb<br>• Antiviral<br>• Therapeutic to target host response |
| Marburg | 3 | • MAbs cocktail and MAb<br>• Antiviral |

# An existing open collaborative scientific network (MARVAC) was triggered immediately after Sudan ebolavirus outbreak declaration



**8 consultations on candidate treatments** were held between Aug-Nov 2022

Approx 50 scientists per meeting

(and 500+ for global consultations)

- clinicians/researchers from the Uganda MOH, ETCs,
- filovirus experts, clinical trial experts, developers

Topics discussed included

1. Evidence regarding different investigational therapeutic agents
2. Study design and opportunities for implementation of a clinical trial.
3. Proposed CORE protocol based on the prioritized trial design options.

**Prioritization of Treatment Study Designs**

There was consensus on the need for randomization to evaluate the safety and efficacy of these investigation therapeutics with minimal bias.

Experience from previous trials such as PALM and PREVAIL was considered. Table 2 summarizes the different study designs discussed during the meetings among a group of trialists and Ugandan researchers.

As of October 31, 2022, some treatments are provided in Uganda under MEURI protocol or compassionate use. Experts agreed that study designs 1-3 were credible and would provide evidence of efficacy, while design 4 should be excluded.

Ugandan clinicians and other experts determined that study design 3 was the most feasible given the local context, while still maintaining the benefits of randomization. The proposed study design includes secondary randomization to dexamethasone for all participants.

**Table 2. Summary of Proposed Trial Design Options**

| Option | Trial Design Option | Strengths | Limitations |
|---|---|---|---|
| 1 | Standard of care (SOC) + Monoclonal versus SOC + Antiviral versus SOC + Monoclonal + Antiviral versus SOC alone (Full Factorial) design Secondary randomization corticosteroids | Including a SOC arm will permit the most valid and interpretable estimation of potential treatments effect. This design is efficient and could provide the results relatively quickly. | As the candidate therapeutics are already in use, the SOC arm was considered less acceptable for a disease with very high baseline mortality. |
| 2 | SOC + Monoclonal versus SOC + Monoclonal + Antiviral versus SOC alone Secondary randomization corticosteroids | Including a SOC arm will permit the most valid and interpretable estimation of potential treatments effect. This design will provide understanding on the impact of the monoclonal and the synergistic impact of the combination therapy. | As the candidate therapeutics are already in use, the SOC arm was considered less acceptable for a disease with very high baseline mortality. The design does not provide direct information on the effect of the antiviral alone. |
| 3 | SOC + Monoclonal versus SOC + Antiviral versus SOC + Monoclonal + Antiviral Secondary randomization corticosteroids | If an SOC alone arm cannot be implemented, this design can provide evidence on any differential effect of monoclonal antibodies vs antiviral, and on any efficacy of the two combined | If the synergistic effect of a monoclonal plus an antiviral is low, the sample size could increase. |

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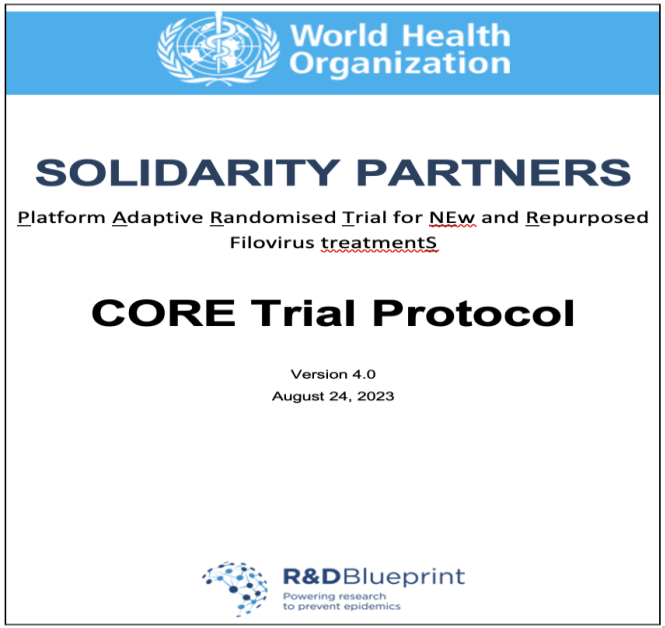
# An existing open collaborative scientific network (MARVAC) was triggered immediately after Marburg outbreak declaration

## 4 consultations on candidate treatments were held between Feb – Jul 23

Approx 30-50 participants and 500+ for global consultations

Items discussed included

- Review of available vaccines and therapeutics, status, and availability
- Review a CORE trial protocol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SOLIDARITY PARTNERS

Platform Adaptive Randomised Trial for NEw and Repurposed Filovirus treatmentS

CORE Trial Protocol

Version 4.0

August 24, 2023

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With special thanks to Peter Horby, Amanda Rojek, Martin Landray, and colleagues at the Univ of Oxford for developing the full protocol based on the outputs of the global consultations

# Being prepared to integrate research during outbreaks



The planned objectives of the future scientific workshops are to:

- **Continue to foster collaboration** for evaluating candidate therapeutics within outbreak responses, led by clinical trial networks and research teams.
- **Give the opportunity to national researchers and authorities to contribute to design of trial protocols** for candidate vaccines and therapeutics towards final consensus on key trial design attributes.
- **Develop an action plan per pathogens for collaborative network** of designated researchers in "at risk" countries via engagement in a framework for clinical research preparedness to ensure clinical research is promptly integrated into future outbreak responses.

# Maximizing our research efforts to inform strategic actions

**is critical to control outbreaks and prevent future pandemics.**

*"A systematic approach that studies treatments against representative pathogens from families with known pandemic potential to be better prepared vs. emerging or reemerging pathogens".*

Innovative approaches and emerging technologies, e.g. Mab platforms, broad-spectrum antivirals or host-therapies, can help select among available candidate treatments for prototype pathogens.

# Thank you

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