# Adaptive Platform Trials (APT) and REMAP-CAP Japan

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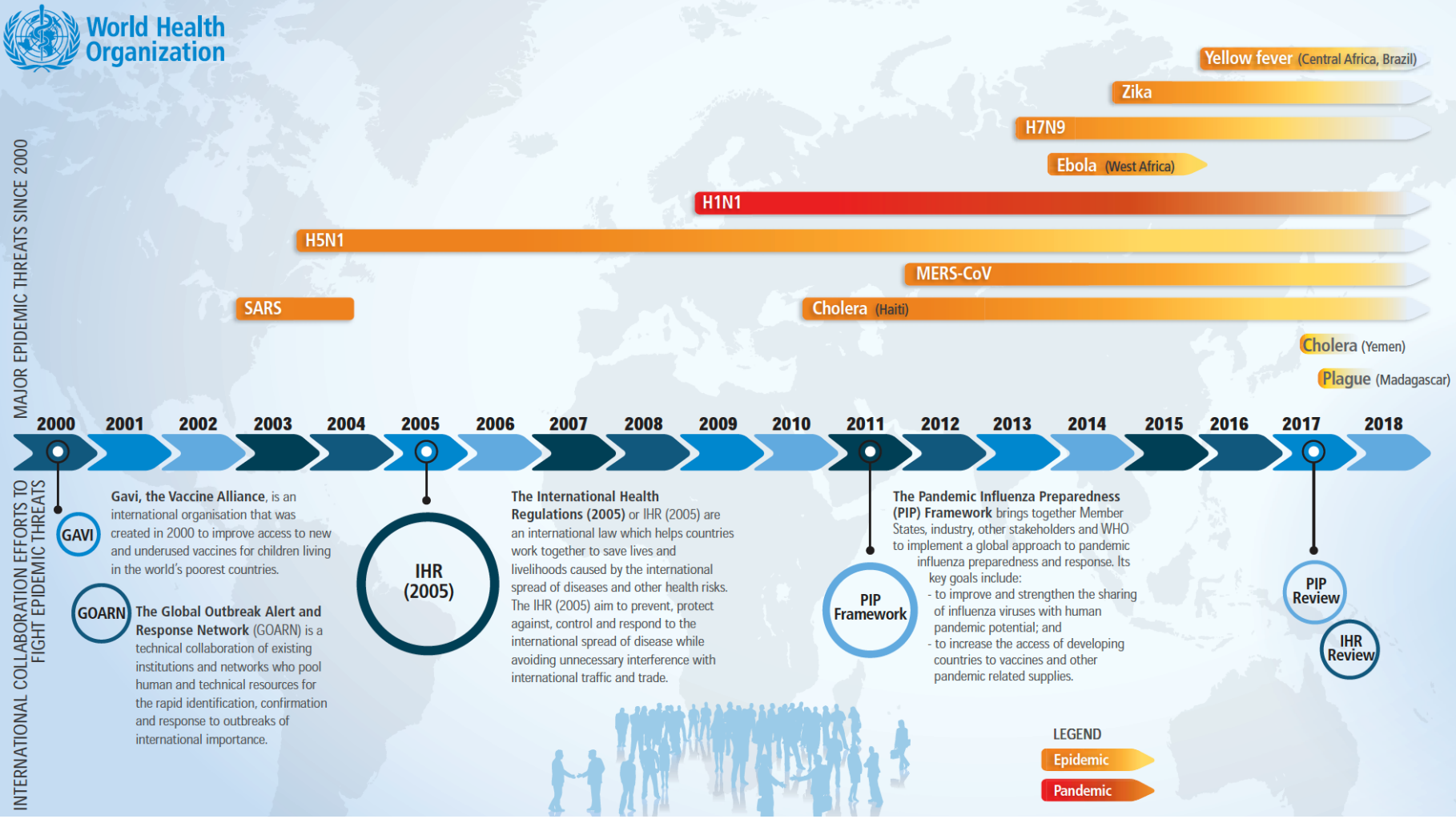
JICA COVID-19 Webinar Series
8th webinar, 21st Oct, 2021

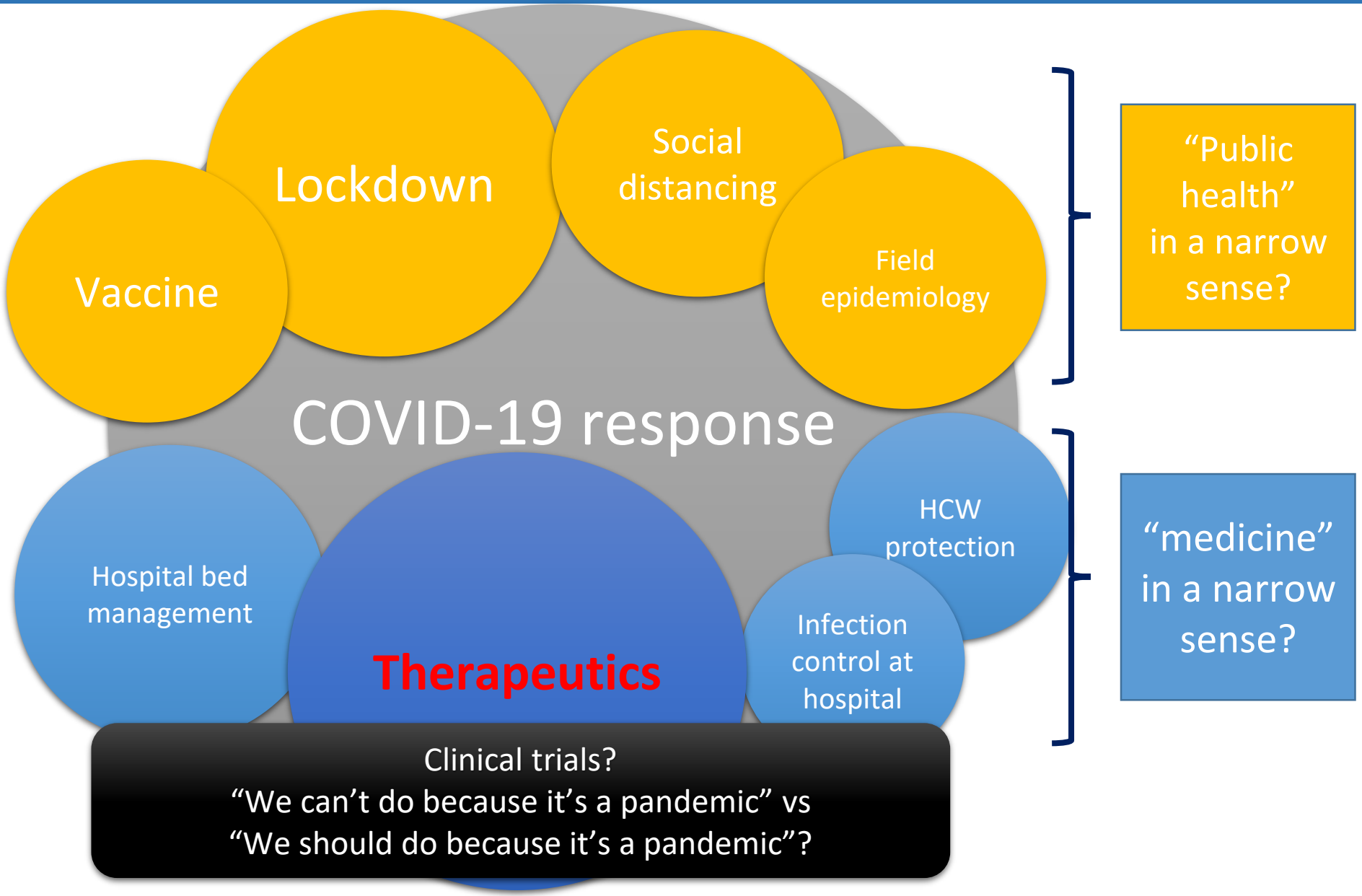
# (re-)emerging infections in 21st century

History repeats itself

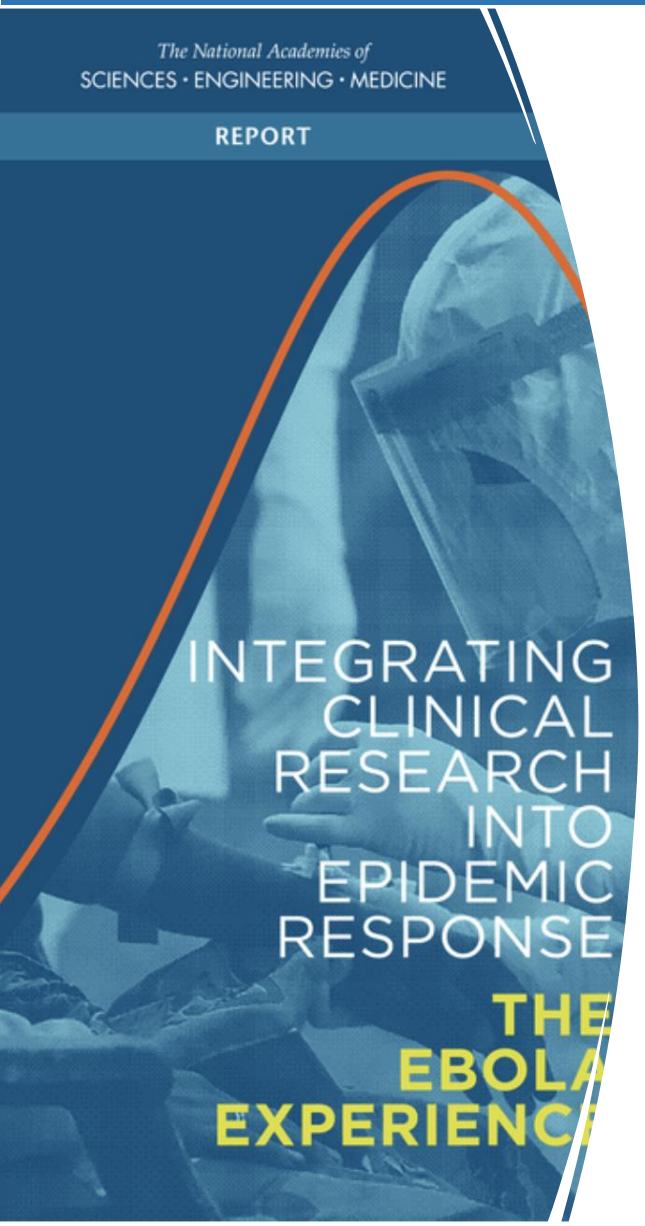



http://apps.who.int/iris/bitstream/handle/10665/272442/9789241565530-eng.pdf?ua=1

# What is “COVID-19 response”?



# Lessons learned from Ebola




## Recommendations made by Committee on Clinical Trials During the 2014-2015 Ebola Outbreak

Inter-epidemic (when no epidemic)

- Support the development of sustainable health systems and research capacities
- Facilitate capacity for rapid ethics reviews and legal agreements
- Enable the incorporation of research into national health systems
- Coordinate international efforts in research and development for infectious disease pathogens

Epidemic

- Provide resources to enable data collection and sharing
- Ensure that capacity-strengthening efforts benefit the local population
- **Establish and implement a cooperative international clinical research agenda**
  - **"Randomized trials are the preferable approach, and unless there are compelling reasons not to do so, every effort should be made to implement randomized trial design"**

# Therapeutic Clinical Trials for COVID-19

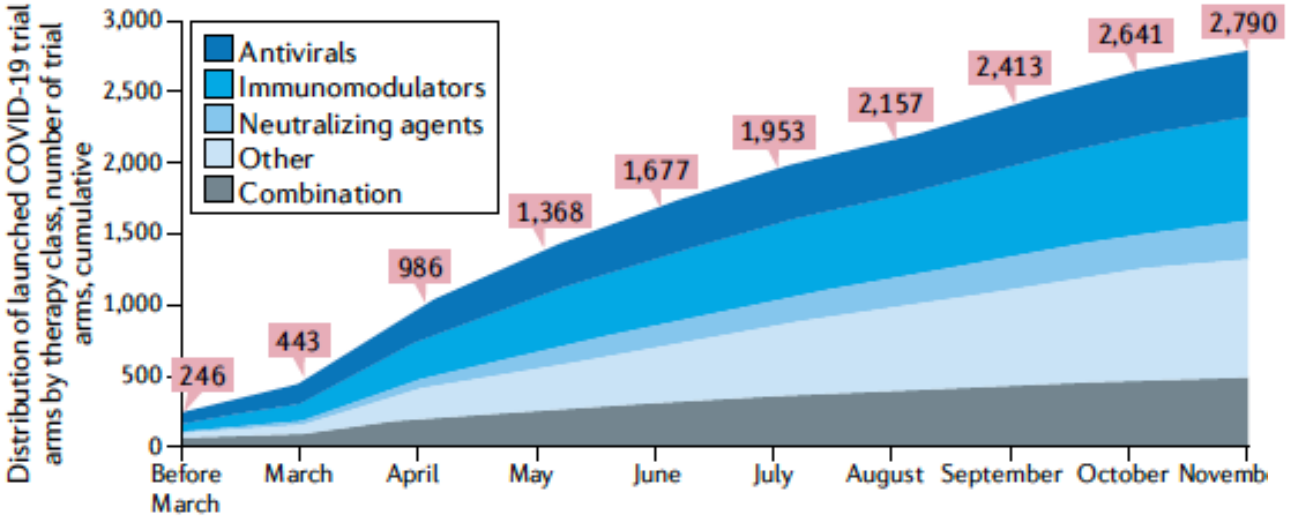
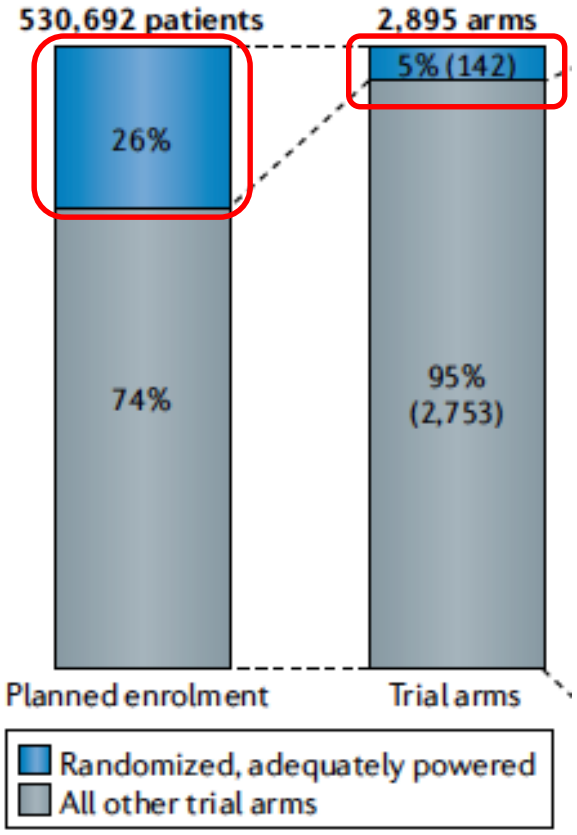



Fig. 1 | **Expansion of the clinical trial landscape for COVID-19 therapeutics in 2020.** Source ClinicalTrials.gov and WHO clinical trial registry. *As of 20 Nov 2020. See Supplementary informati for details.




*Nat Rev Drug Discov*. 2021;20(4):254-255.

# APTs contributing to WHO guideline

## 3. Background

As of 2 September 2021, over 218 million people worldwide have been diagnosed with COVID-19, according to the WHO dashboard *(13)*. The pandemic has thus far claimed more than 4.3 million lives *(13)*. Vaccination is having a substantial impact on case numbers and hospitalizations in a number of high-income countries, but limitations in global access to vaccines mean that many populations remain vulnerable *(13)(14)*. Even in vaccinated individuals, uncertainties remain about duration of protection and efficacy of current vaccines against emerging SARS-CoV-2 variants.

Taken together, there remains a need for more effective treatments for COVID-19. The COVID-19 pandemic – and the explosion of both research and misinformation – has highlighted the need for trustworthy, accessible and regularly updated living guidance to place emerging findings into context and provide clear recommendations for clinical practice *(15)*.

This living guideline responds to emerging evidence from RCTs on existing and new drug treatments for COVID-19. More than 4200 trials investigating interventions for COVID-19 have been registered or are ongoing (see section on emerging evidence) *(16)*. Among these are large national and international platform trials (such as RECOVERY, WHO SOLIDARITY, REMAP-CAP and ACTIV) that recruit large numbers of patients in many countries, with a pragmatic and adaptive design *(17)(18)(19)(20)*. These platform trials are currently investigating and reporting on numerous interventions, including antiviral monoclonal antibodies and immunomodulators. This rapidly evolving evidence landscape requires trustworthy interpretation and expeditious clinical practice guidelines to inform clinicians and health care decision-makers.

World Health Organization. Therapeutics and COVID-19 Living Guideline. 24 Sep 2021.

# Adaptive Platform Trials (APTs)

"the broad goal of finding the best treatment for a disease by simultaneously investigating multiple treatments"

**Table. General Characteristics of Traditional and Platform Trials[a]**

| Characteristic | Traditional Trial | Platform Trial |
|---|---|---|
| Scope | Efficacy of a single agent in a homogeneous population | Evaluating efficacy of multiple agents in a heterogeneous population; explicitly assumes treatment effects may be heterogeneous |
| Duration | Finite, based on time required to answer the single primary question | Potentially long-term, as long as there are suitable treatments requiring evaluation |
| No. of treatment groups | Prespecified and generally limited | Multiple treatment groups; the number of treatment groups and the specific treatments may change over time |
| Stopping rules | The entire trial may be stopped early for success or futility or harm, based on the apparent efficacy of the single experimental treatment | Individual treatment groups may be removed from the trial, based on demonstrated efficacy or futility or harm, but the trial continues, perhaps with the addition of new experimental treatment(s) |
| Allocation strategy | Fixed randomization | Response-adaptive randomization |
| Sponsor support | Supported by a single federal or industrial sponsor | The trial infrastructure may be supported by multiple federal or industrial sponsors or a combination |

[a] Platform trials and similar trials may also be called basket, bucket, umbrella, or standing trials.

Growing interests in APTs because of

"the need to rapidly evaluate multiple potential treatments"

"the ethical imperative to achieve the best possible outcomes in trial participants"

JAMA. 2015;313(16):1619.

# APTs and Global Health

## Clinical Trials in Global Health 2

### Randomised trials at the level of the individual

*Jay J H Park, Nathan Ford, Denis Xavier, Per Ashorn, Rebecca F Grais, Zulfiqar A Bhutta, Herman Goossens, Kristian Thorlund, Maria Eugenia Socias, Edward J Mills*

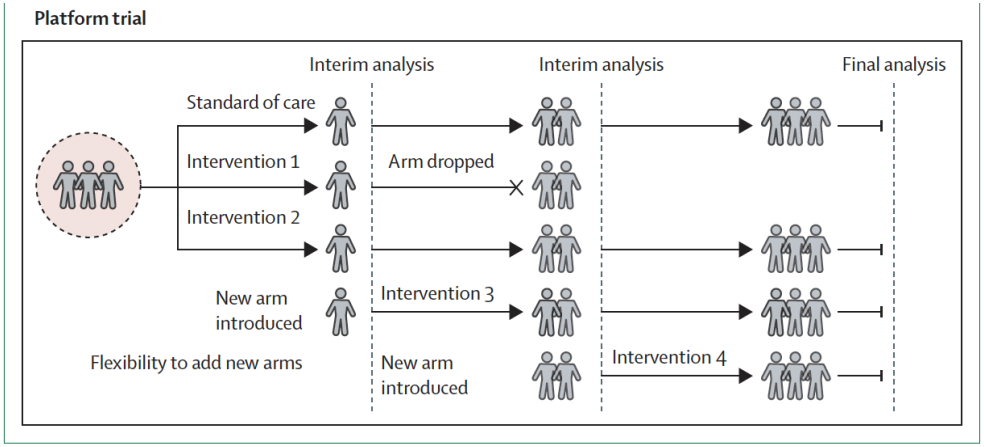
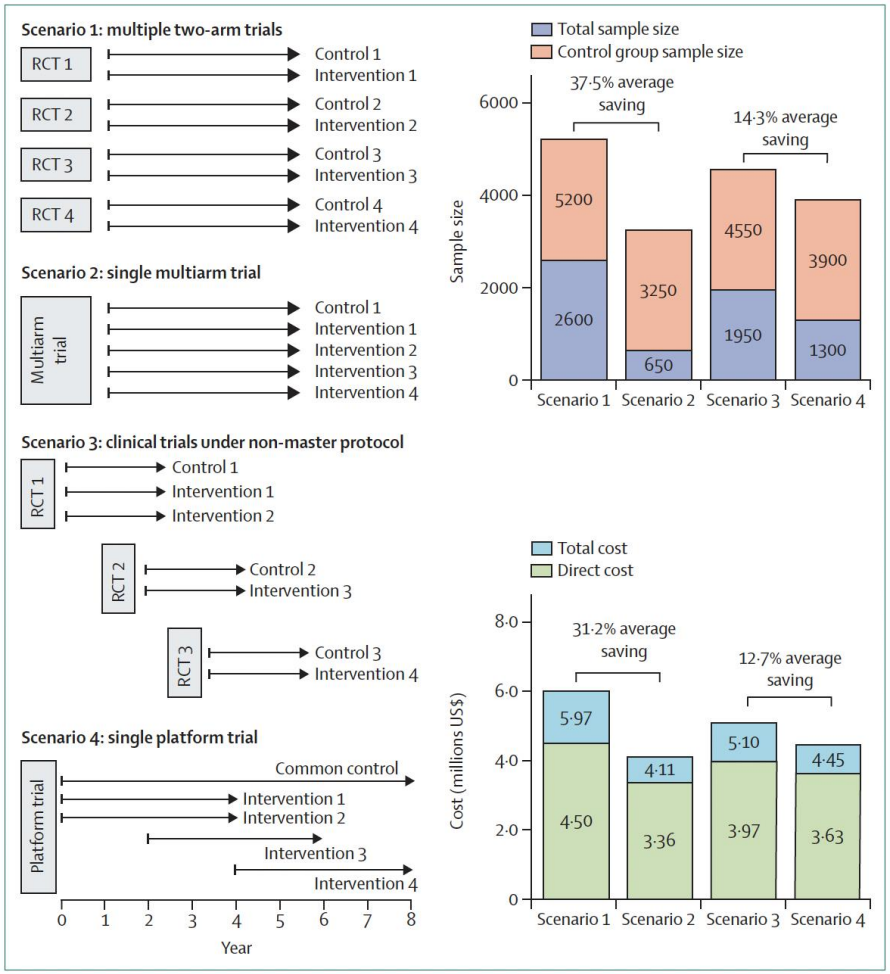



*Figure 1:* **Master protocols: basket trials, umbrella trials, and platform trials**




*The Lancet Global Health*. 2021;9(5):e691-e700.

# Resilient, Dynamic, Research Ecosystem

Clinical Trials in Global Health 4

## How COVID-19 has fundamentally changed clinical research in global health

Jay J H Park, Robin Mogg, Gerald E Smith, Etheldreda Nakimuli-Mpungu, Fyezah Jehan, Craig R Rayner, Jeanine Condo, Eric H Decloedt, Jean B Nachega, Gilmar Reis, Edward J Mills

- Refers to SOLIDARITY, REMAP-CAP and RECOVERY as an example of APTs
- Importance of pre-existing resource-efficient trial sites and capacity
- RECOVERY: 12000 patients enrolled in a short span of 4 months in UK due to “the national-level buy-in and cooperation”
- Plan ahead for the worst case scenario

*The Lancet Global Health*. 2021;9(5):e711-e720.

# REMAP-CAP

**16,851**

Patient randomizations

**15,106**

Patients randomizations with COVID-19

**50**

Current or completed interventions in 14 domains

**9,411**

Total patients

**8,359**

Patients with COVID-19

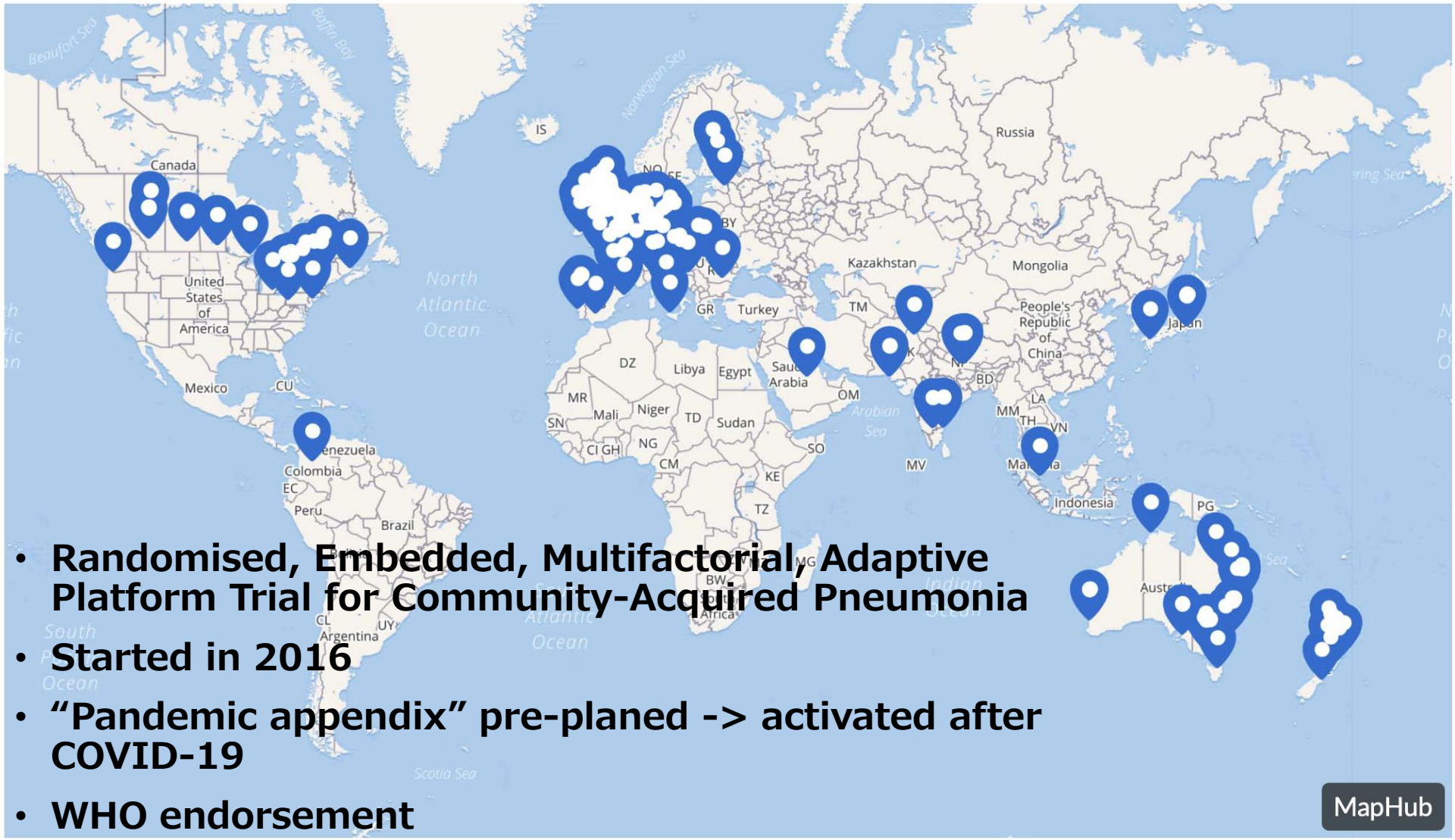
**339**

Active Sites
（21 countries）

As of 15th Oct, 2021

https://www.remapcap.org

# Global Network of REMAP-CAP




- **Randomised, Embedded, Multifactorial, Adaptive Platform Trial for Community-Acquired Pneumonia**
- **Started in 2016**
- **“Pandemic appendix” pre-planed -> activated after COVID-19**
- **WHO endorsement**

# Clinical Trials as Public Goods

Letter to the Editor | Open Access | Published: 14 April 2021

**Why participation in an international clinical trial platform matters during a pandemic? Launching REMAP-CAP in Japan**

REMAP-CAP JAPAN

NEBNEG to SEBSEG

"neither evidence-based nor evidence-generating"

"sensibly evidence-based and sustainably evidence-generating"

# Thank you

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