WHO Chief Scientist updates

Member States Briefing Session

3 September 2020

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WHO guidelines and recommendations:

Ensuring rigor, quality, speed, and design for impact

2019 WHO Transformation decisions:

All Normative and Standard setting products follow a **fit-for-purpose quality-assured** process and include early assessment against **organizational needs/ priorities** and a link to **country impact**

Global Goods prioritization process

Establish a **three level mechanism** to **prioritize <u>all</u> norms & standards proposals** (including derivatives)

Fit-for-purpose standardized Quality Assurance

Ensure each Norms & Standards setting product follows a **standardized and quality assured development pathway** with **fit for purpose methodologies**

N&S process ownership

Create a "department" that **owns the N&S process**

- Supports methodological work & QA
- Ensures monitoring and evaluation
- Manages joint planning with support functions

QA: Agreed principles and 2 stage process across N&S, research, data

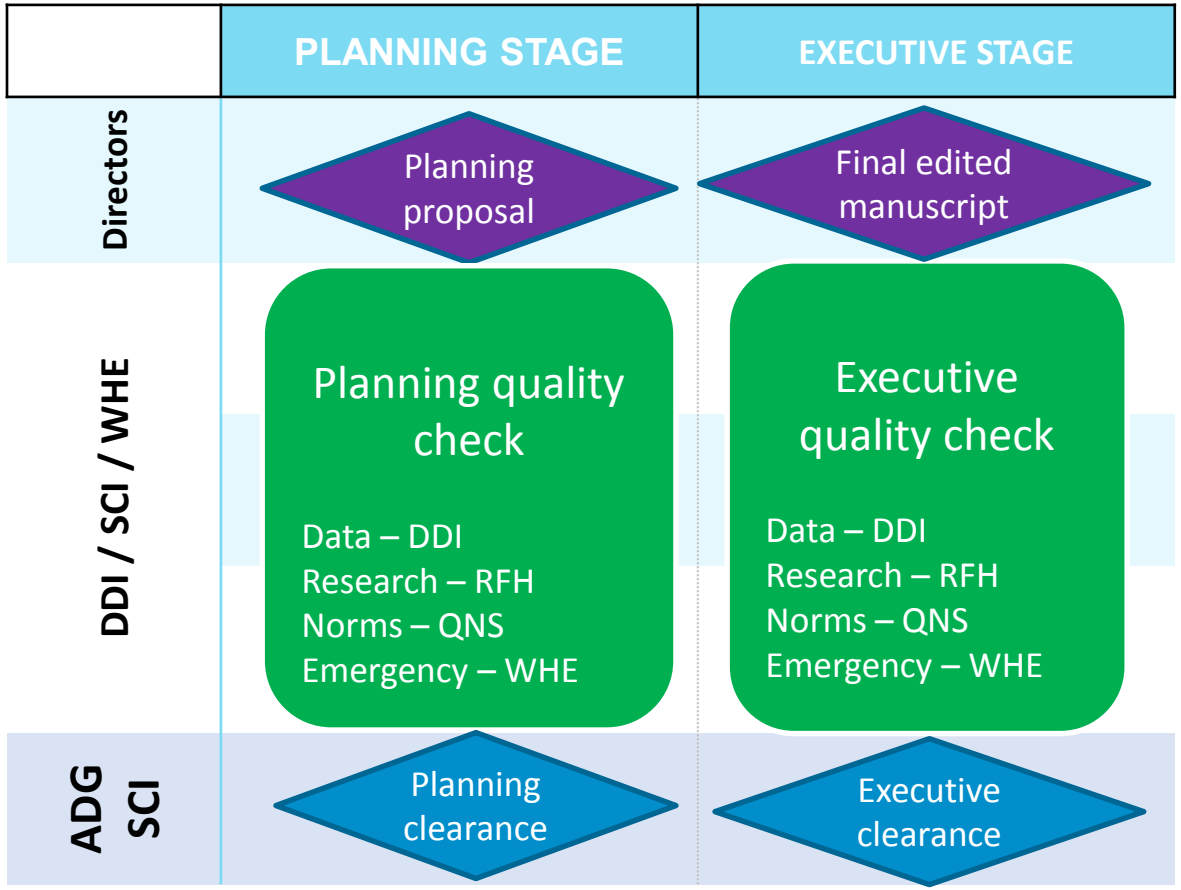
Agreed QA Principles

Clear Process: Were robust and comprehensive steps and procedures followed?

Suitability and execution of development methods: Were appropriate methods used and correctly executed?

Reporting and presentation: Is the right information provided and optimally presented?

Impact and evaluation: Is the product optimized for usability and impact?



PHEIC: More options for rigor and speed: SAGE – GRC - PRC

- **SAGE:** recommendations on vaccines use
- **GRC:** reviews ALL guidelines that
  - Include/provide a recommendation
  - Respond to a clinical or public health question of uncertainty
- **NEW PRC** reviews emergency rapid advice and/or interim guidance, where there is limited evidence, and where the time frames do not allow for a full GRC review. (Based on abbreviated GRC criteria).
- **Evidence Collaborative for COVID-19 Network (ECC-19):** Voluntary consortium of over 190 experts from 90+ organizations contributing to evidence retrieval

WHO Guidance for therapeutics and COVID-19

Evidence monitoring and synthesis:

- WHO collaborator provides **living network meta-analysis** on website (https://covid-nma.com/living_data/index.php)
- WHO is coordinating **prospective meta-analysis** of ongoing trials for certain therapeutics (i.e. corticosteroids, heparin, remdesivir, ritonavir/liponavir, hydrochloroquine.
- WHO collaborators MAGIC also conducting Living Network Meta-analysis on published data, as part of their methodologic support to guidance development.

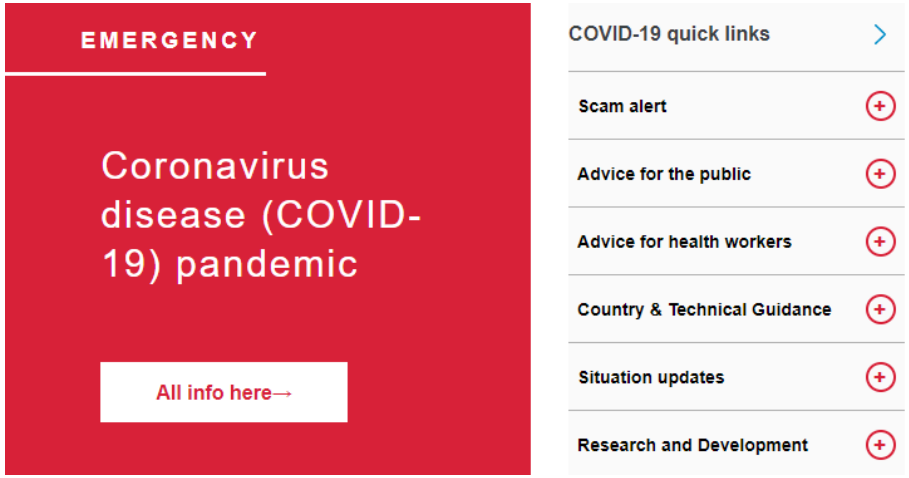
COVID-19: Expedited Guidance, Publications, Monitoring

Publications Review Cmte and Secretariat established by DDG, ExD-HEP, SCI/QNS on March, 18th 2020

Aims

To ensure:

1. **strategic publication** of technical documents and their appropriate and timely dissemination (strategic **prioritization** on the evolution of the pandemic and topic on which member states expect rapid guidance
2. **quality assurance** in spite of the accelerated process
3. **consolidation** of guidance by theme



✓*24-48 hour review turnaround*

✓*600+ drafts reviewed*

✓*200+ publications*

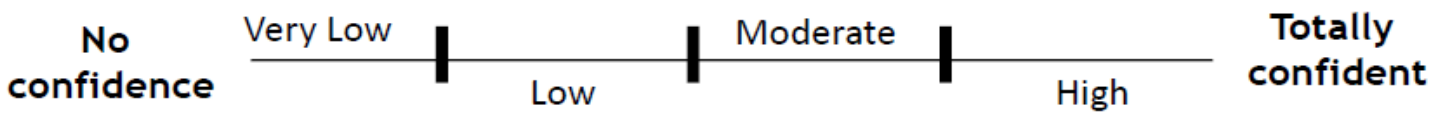
✓*HQ and Regional Committee*

✓*4 to 9 million downloads per month*

GRADE Background

- GRADE (*G*rading of *r*ecommendation, *a*ssessment, *d*evelopment and *e*valuation)
- Two components:

1. Grading evidence



2. Grading strength of recommendation

STRONG or WEAK

Recommendation implications

	Strong recommendation	Weak recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices are likely to be appropriate for different patients and therapy should be tailored to the individual patient's circumstances. Those circumstances may include the patient or family's values and preferences.
For policy makers	The recommendation can be adapted as policy in most situations including for the use as performance indicators.	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

WHO Guidance for Corticosteroids and COVID-19

RECOVERY preliminary results available **22 June**, peer-review publication on **17 July**.

WHO began to coordinate a **prospective meta-analysis** to synthesize evidence of 7 other trials conducted around the world, testing corticosteroids for COVID-19, in collaboration with principle investigators of each trial, with confidential sharing of data.

WHO convened **GDG on 6 July** with just RECOVERY data. GDG requested PMA results be made available to make recommendations. WHO re-convened **GDG again on 20 July** to formulate recommendations with PMA information.

WHO **publication review committee** gives provisional approval of guidance once all data publicly available.

Summary recommendations:

Recommendation 1:

We recommend systemic corticosteroids rather than no systemic corticosteroids for the treatment of patients with severe and critical COVID-19 (strong recommendation, based on moderate certainty evidence).

The evidence: *The panel made its recommendation on the basis of the moderate certainty evidence of a mortality reduction of 8.7% and 6.7% in patients with COVID-19 who are critically or severely ill. This is absolute risk reduction, transformed into NNT (11, 15 respectively)*

Recommendation 2:

We suggest not to use corticosteroids in the treatment of patients with non-severe COVID-19 (conditional recommendation, based on low certainty evidence).

Costs and access: systemic corticosteroid therapy is a low-cost intervention that is easy to administer and readily available globally

WHO Guidance for Corticosteroids and COVID-19

On **2 September**, coordinated hallmark coordination of publications:

WHO Living Guidance on Corticosteroids and COVID-19:
https://www.who.int/publications/i/item/WHO-2019-nCoV-Corticosteroids-2020.1

Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19 - A Meta-analysis. WHO REACT Working Group
https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2020.17023?guestAccessKey=ec87204d-c42d-4d34-bef5-077a40bc86b0&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=090220

Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19 –REMAP CAP
https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2020.17022?guestAccessKey=23fa39bc-68d3-4d4a-88ef-37c908849a05&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=090220

Effect of Hydrocortisone on 21-Day Mortality or Respiratory Support Among Critically Ill Patients With COVID-19 –CAPE COVID
https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2020.16761?guestAccessKey=87249cc0-d27a-4fd1-92de-82c71732a4c2&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=090220

Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19 -CoDEX
https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2020.17021?guestAccessKey=52805eb1-785a-4bcc-8d1d-9ca94a382711&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=090220

Convalescent plasma therapy and COVID-19

- WHO clinical research working group is now reviewing all ongoing trials on Convalescent Plasma therapy for COVID-19.

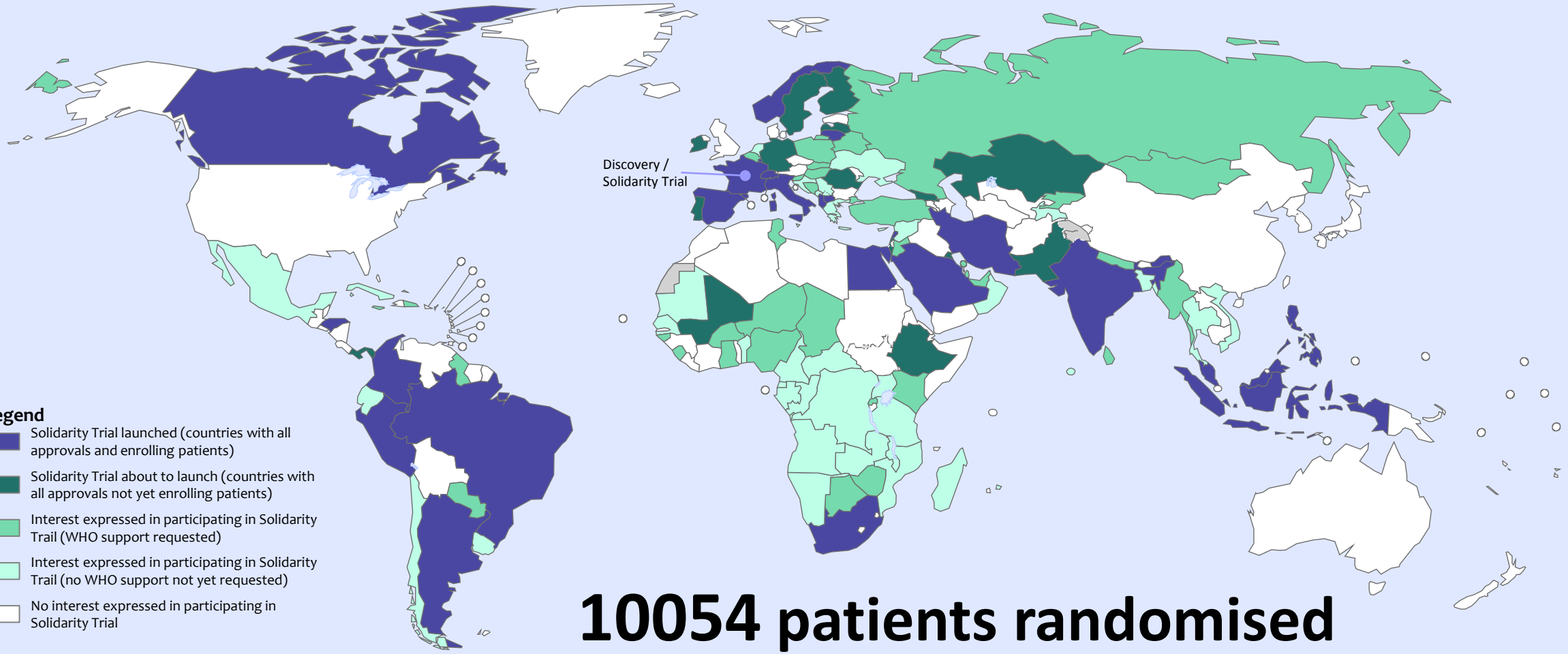
- In preparation for bringing studies together for pooling of evidence in a **prospective meta-analysis** (like corticosteroids). This will allow us to more rapidly see if there is any signals of true benefit or harm.
  * This will require similar strong coordination and collaboration between investigators.*

- At this time, WHO recommends that convalescent plasma be used in clinical trials; and if that is not possible, under MEURI protocols.

COVID-19: Where are we now with Solidarity Trials on Therapeutics ?

Solidarity Trial - Therapeutics

Over 450 hospitals in 27 countries enrolling patients, 12 other countries ready to start



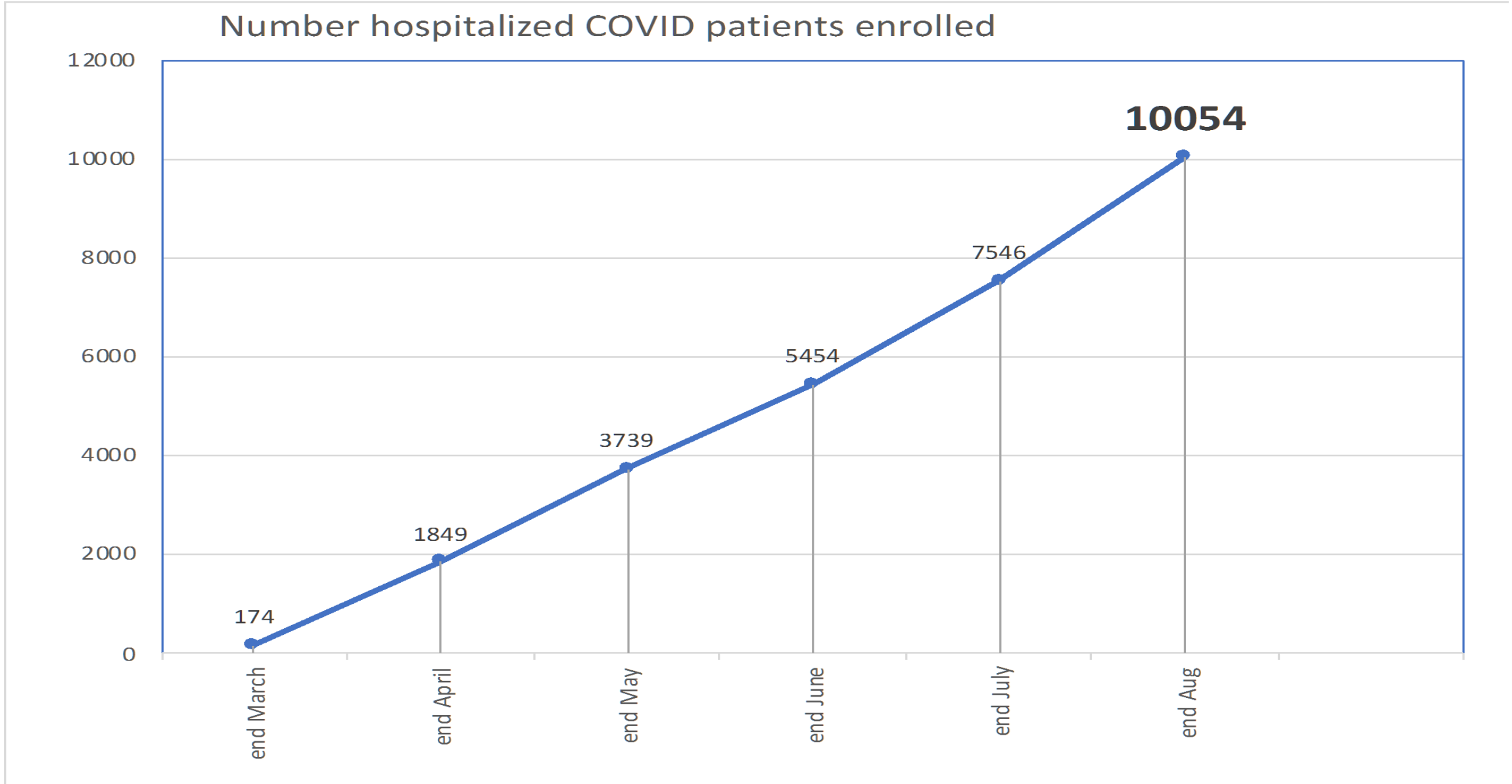
10054 patients randomised

World Health Organization

R&DBlueprint
Powering research to prevent epidemics

Solidarity Trial - Therapeutics

Over 450 hospitals in 27 countries enrolling patients (as of Sept 3, 2020)



COVID Potential treatments for solidarity trials

- **Immunomodulators: Protein kinase inhibitors**
- **Monoclonal Antibodies**

What have we learned from the therapeutics RCTs?

A worldwide effort to conduct RCTs.

BUT, coordination and size not optimal

Studies registered	1178
Completed	15
Recruiting	644
Not recruiting	515
Suspended	2
Terminated	2

https://www.covid-nma.com/dataviz/

WHY an international RCT of several candidate vaccines ?

Solidarity trial for vaccines

Evaluating several different candidate vaccines	Expeditiously enrolling participants at sites with high rates of COVID-19	Eliminating inefficiency of designing and conducting separate trials	International collaboration and countries' commitment
permitting selected vaccines to enter the trial whenever ready	flexible mix of fixed sites and pop-up sites	shared placebo group increases efficiency and attractiveness	fosters participation of sites with high COVID-19 rates
vaccines selection for trial assessed using a priori criteria	sufficient enrollment to assess efficacy and safety of all vaccines	If placebo can no longer be used, another vaccine becomes comparator	any effective vaccines will be tested at all sites
all vaccines selected for trial are eligible for testing at all sites	adaptive design accommodates unanticipated circumstances	ineffective vaccines don't much hinder evaluation of better vaccines	paves the way for international distribution of effective vaccines
INCREASING THE LIKELIHOOD OF FINDING SEVERAL EFFECTIVE VACCINES	**RAPID ACCUMULATION OF DATA TO SUPPORT RIGOROUS EVALUATION**	**RESULTS WITHIN 3-6 MONTHS AFTER EACH VACCINE IS READY FOR INCLUSION**	**FOSTERS INTERNATIONAL DEPLOYMENT WITH EQUITY OF ACCESS**