NIHR | Oxford Biomedical Research Centre

RECOVERY
Randomised Evaluation of COVID-19 Therapy

# Partnership and Collaboration:

# Lessons learned from the

# RECOVERY trial


**Martin Landray, University of Oxford,**

**on behalf of the RECOVERY Collaborative**


HDRUK
Health Data Research UK

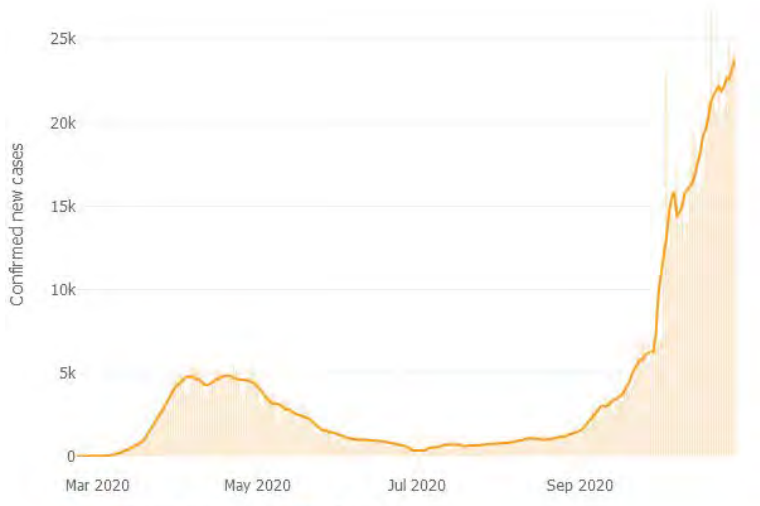
UKRI Medical Research Council

# Background

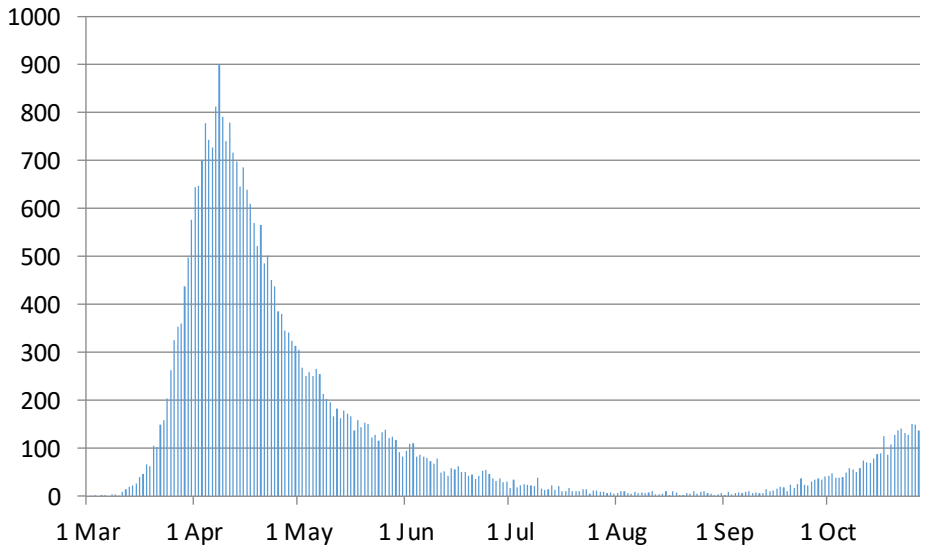
**Unprecedented clinical challenge:**

- Overstretched health service (availability of beds, staff, and ventilators)
- Huge time pressures and personal stress for frontline medical staff
- Large numbers of unwell, anxious, and often elderly patients

**UK New Cases**




**UK Deaths**



# Selection of treatments

**Huge uncertainty about treatment**

- Many candidate drugs
- Many opinions (from many sources)
- No reliable data (uncontrolled case series, inconclusive randomized trials)
- Unlikely to be a single “big win” but moderate benefits would be important

**Initial prioritisation principles**

- Potentially effective (based on prior pre-clinical & clinical data)
- Major safety issues understood
- Sufficient treatment available for large-scale recruitment
- Potential to rapidly scale up as a clinical treatment (if shown to be effective)

# RECOVERY trial - Design

- **Simple eligibility:** Hospitalised patients with SARs-CoV-2
- **Important outcome:** mortality (use of ventilation, duration of hospitalisation)
- **Randomization:** assigns patient between suitable and available treatments
- **Follow-up:** 1 page case report form + extensive linkage to NHS datasets via NHS DigiTrials

- **Repurposed antivirals**
  - Hydroxychloroquine
  - Lopinavir-ritonavir
- **Immunomodulatory**
  - Dexamethasone
  - Azithromycin
  - Tocilizumab
- **Targeted anti-SARS-CoV-2**
  - Convalescent plasma

RECOVERY RANDOMISED EVALUATION OF COVID-19 THERAPY (RECOVERY)

Hospital: Patient Name:

1. **Information about the study has been provided to me:** I confirm that I have read and understood the Participant Information Leaflet (V1.0 13-Mar-2020) I have had the opportunity to consider the information and ask questions. These have been answered satisfactorily.

2. **Voluntary participation:** I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected.

3. **Access to study data about me:** I give permission for relevant sections of my medical notes and information collected during the study to be looked at, in confidence, by authorised individuals from this hospital, the University of Oxford, and regulatory authorities to check that the study is being carried out correctly.

4. **Access to my medical information:** I agree that medical information collected by the doctors and hospitals which provide me with care and which may be located in local or national health and research organizations (including hospital admission, civil registration, audit and research data) may be provided to the study coordinating centre both during and for up to 10 years after the scheduled follow-up period. I understand that information that identifies me will be passed securely to such bodies to make this possible and that I can opt out of this at any time by writing to the coordinating centre team.

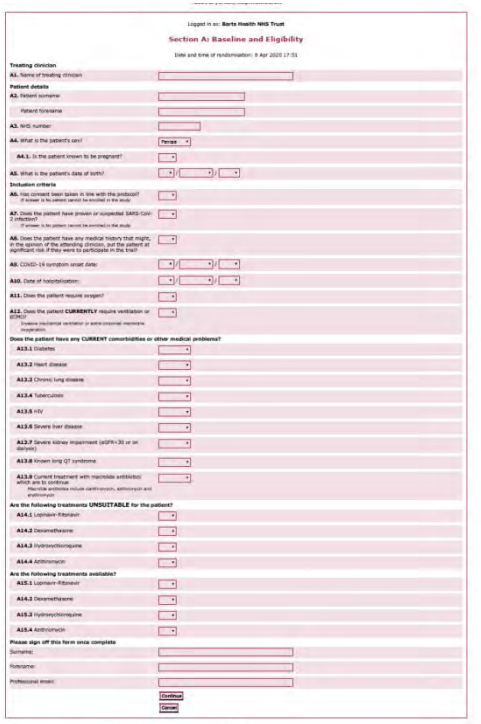
5. **Data stored on computer:** I understand that information about my progress in the study will be recorded on a computer database, and that this data will be stored on computers supervised by the University of Oxford. I understand that this information will be kept securely and confidentially.

6. **Agreement to take part:** I have read the information (or had it read to me), had an opportunity to ask questions and agree to take part in the above study.

PRINTED name of participant — Signature — Today's date

PRINTED name of person taking consent — Signature — Today's date

*1 copy for participant; 1 copy for researcher site file; 1 (original) to be kept in medical notes



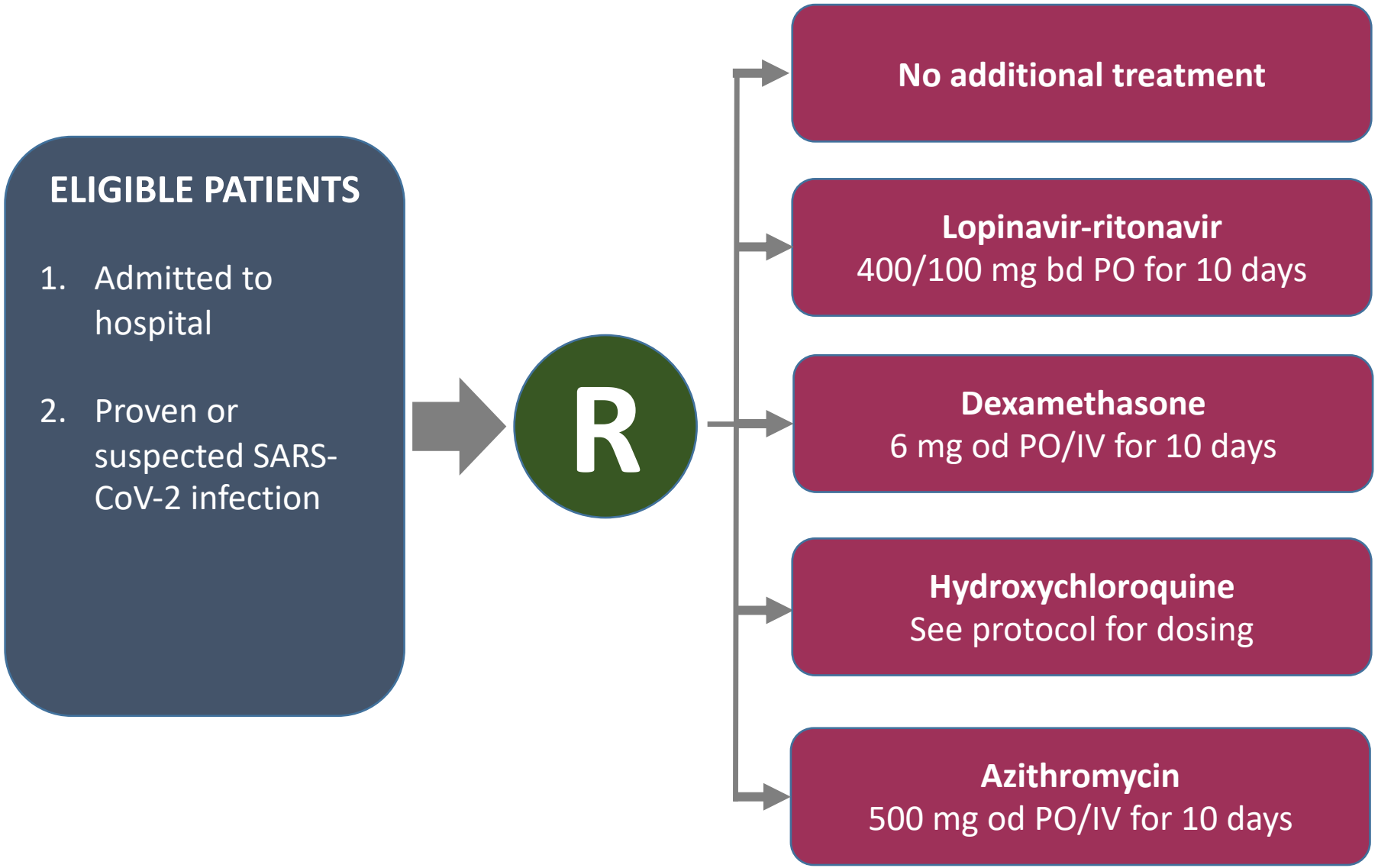
Section A: Baseline and Eligibility

# RECOVERY trial design

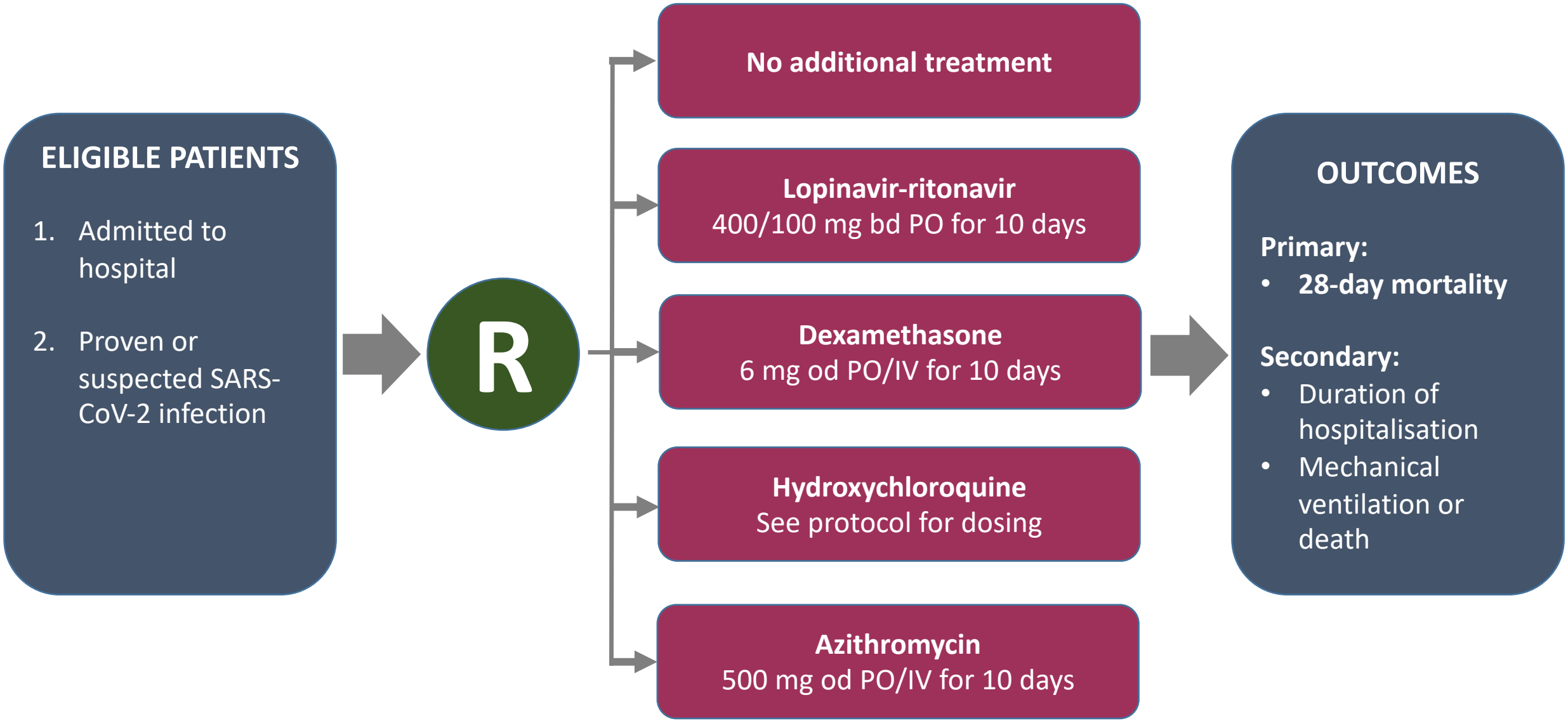
**ELIGIBLE PATIENTS**

1. Admitted to hospital
2. Proven or suspected SARS-CoV-2 infection

# RECOVERY trial design



# RECOVERY trial design



# Centrally collected routine data

## Hospitalisation datasets

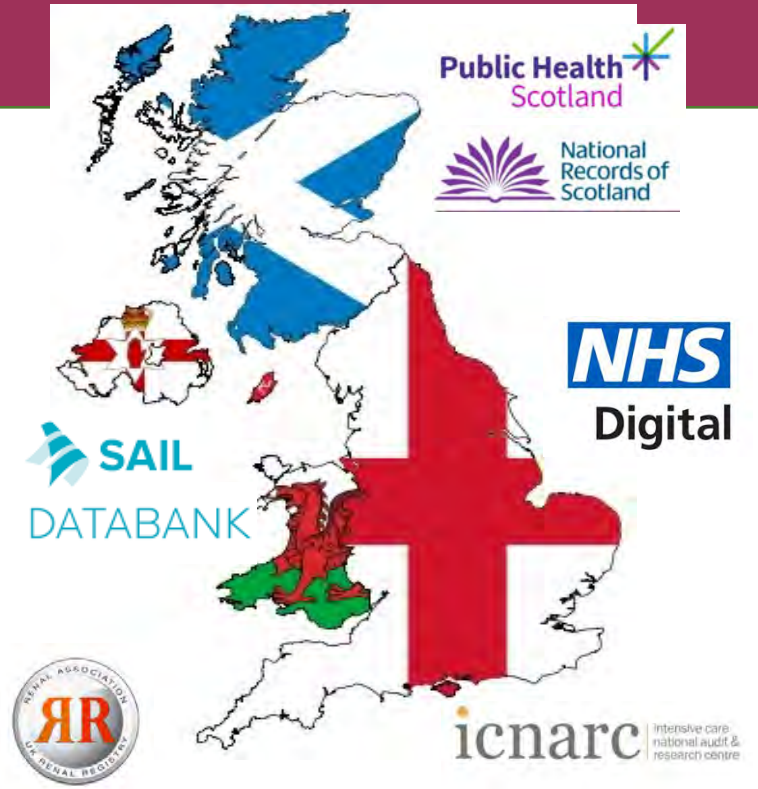
- ✓ Scottish Morbidity Records (SMR)
- ✓ Hospital Episode Statistics Admitted Patient Care (HESAPC)
- ✓ Secondary Uses Service Admitted Patient Care (SUSAPC)
- ✓ Patient Episode database for Wales (PEDW)

## Mortality datasets

- ✓ Personal Demographics Service
- ✓ Civil Registrations
- ✓ NHS Scotland Central Register PDS
- ✓ Welsh Demographics Extract

## Disease specific datasets

- ✓ UK Renal Registry
- ✓ Cancer Registry




## Primary care datasets

- ✓ Business Services Authority (BSA) prescribing and dispensing data
- ✓ General Practice Extraction Service (GPES) Data for pandemic planning and research (GDPPR)

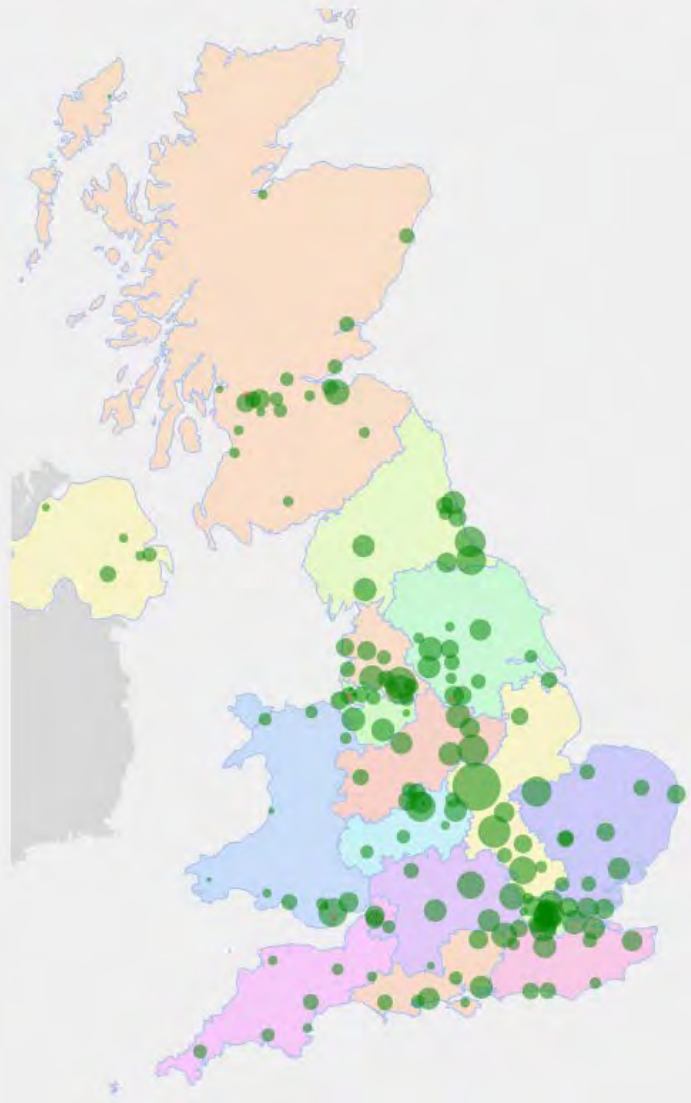
## Critical care datasets

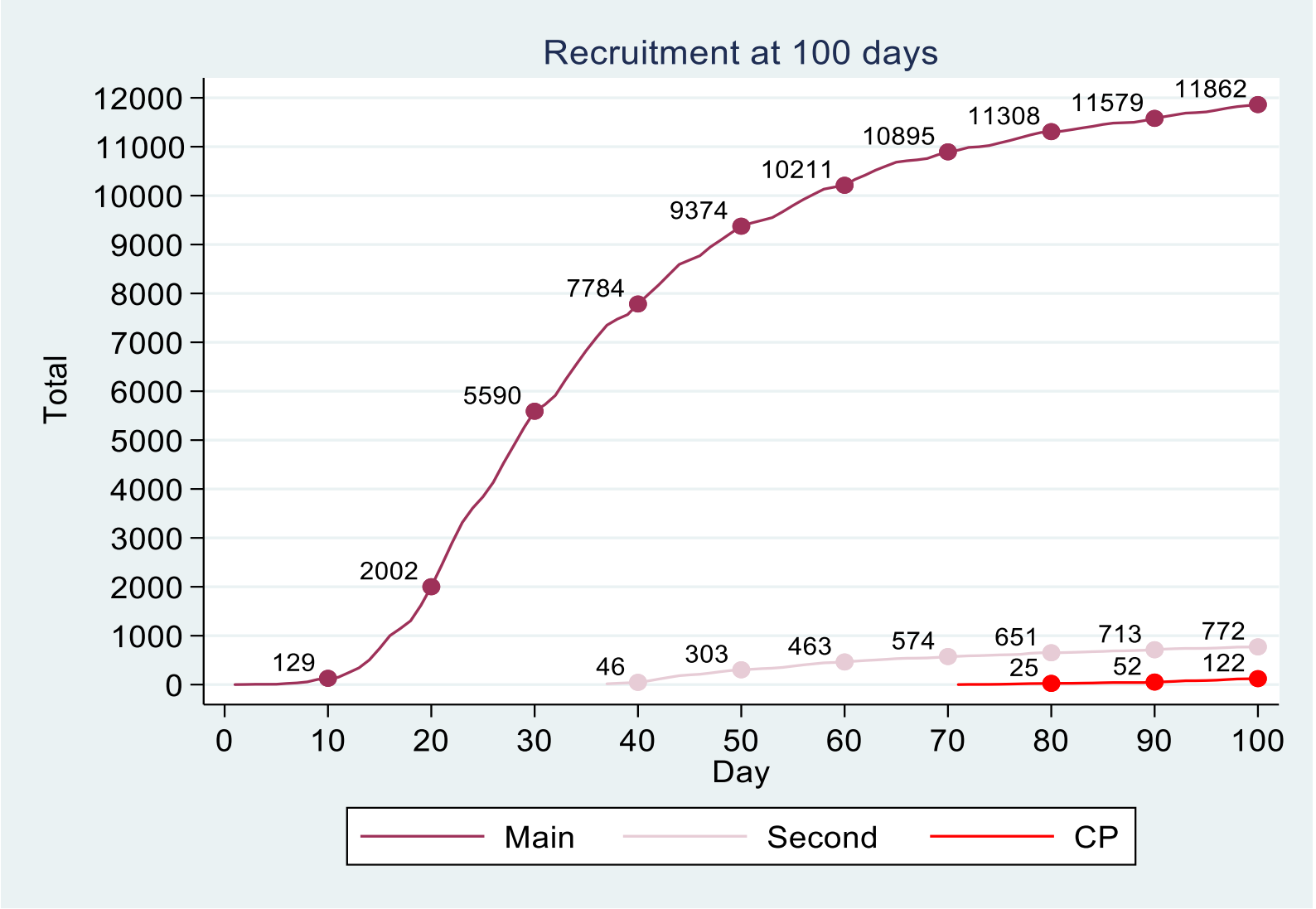
- ✓ Scottish Intensive Care Society Audit Group (SICSAG)
- ✓ Intensive Care National Audit and Research Centre (ICNARC)
- ✓ HES Critical Care Dataset (CCDS)
- ✓ PEDW Critical Care Dataset (CCDS)

## COVID datasets

- ✓ COVID-19 Hospitalisation in. England Surveillance System
- ✓ Second Generation Surveillance System (SGSS )
- ✓ Electronic Communication of Surveillance in Scotland (ECOSS)
- ✓ Welsh Results Reporting Service (WRRS)

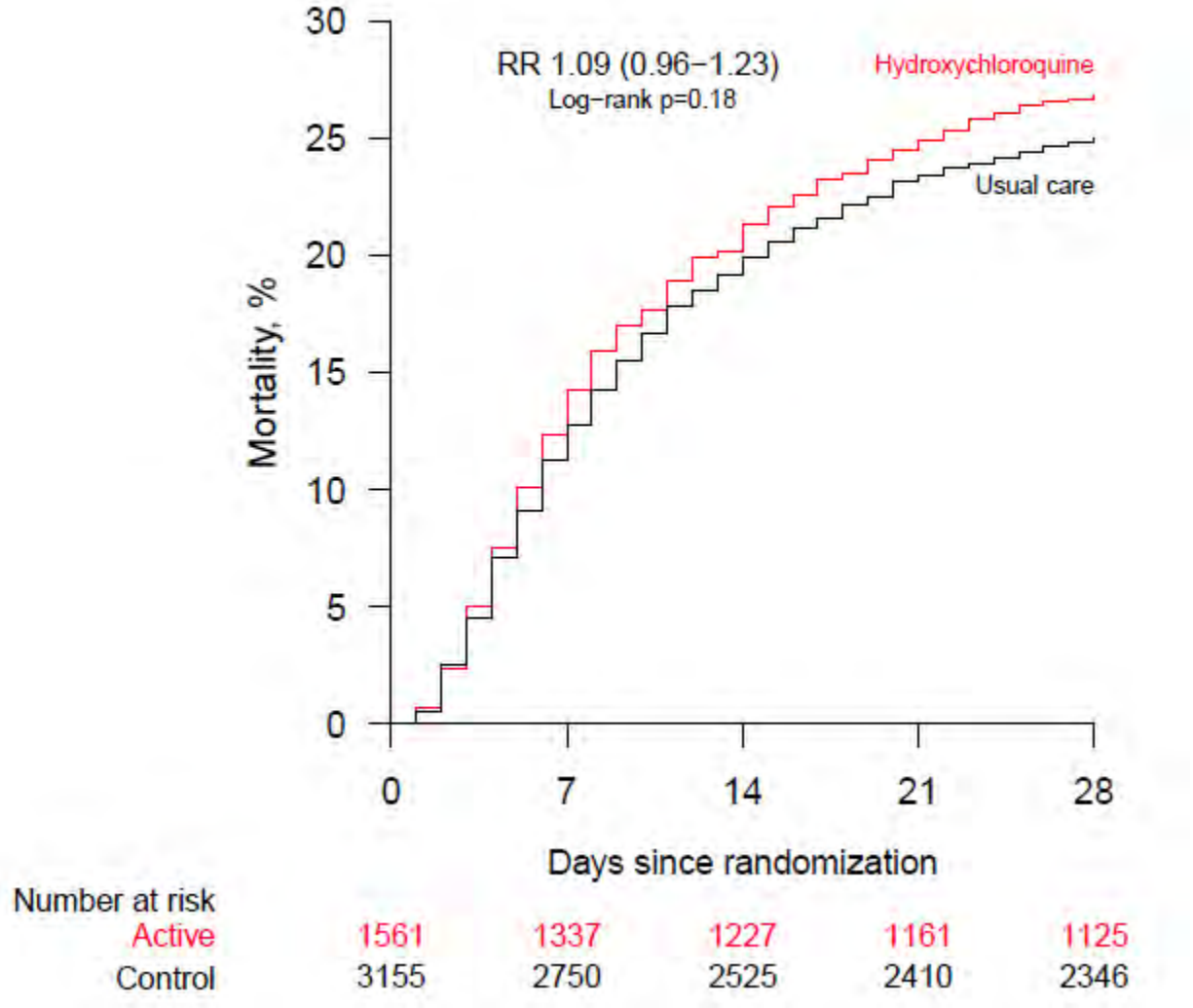
# RECOVERY – rapid and widespread recruitment





# Hydroxychloroquine:
## Widely recommended – shown to be ineffective

https://www.nejm.org/doi/10.1056/NEJMoa2022926

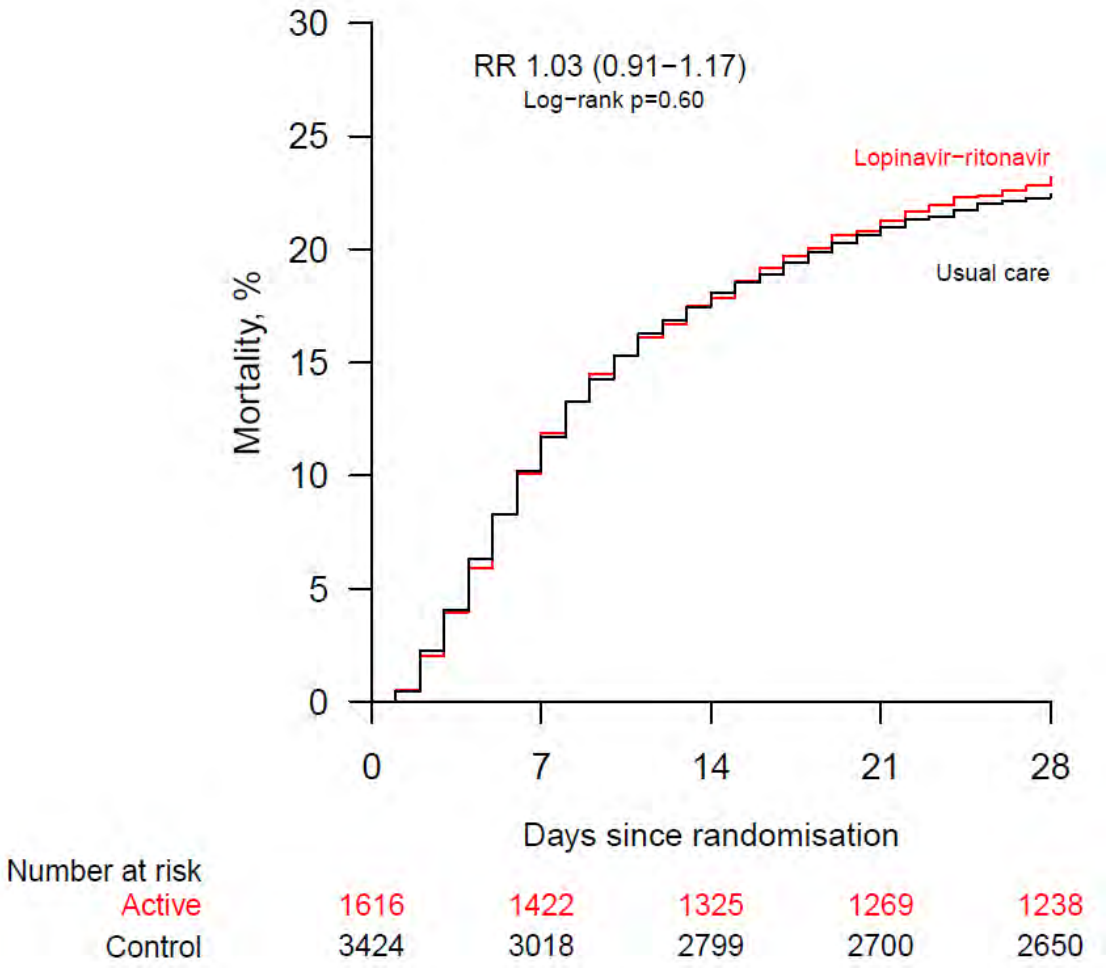


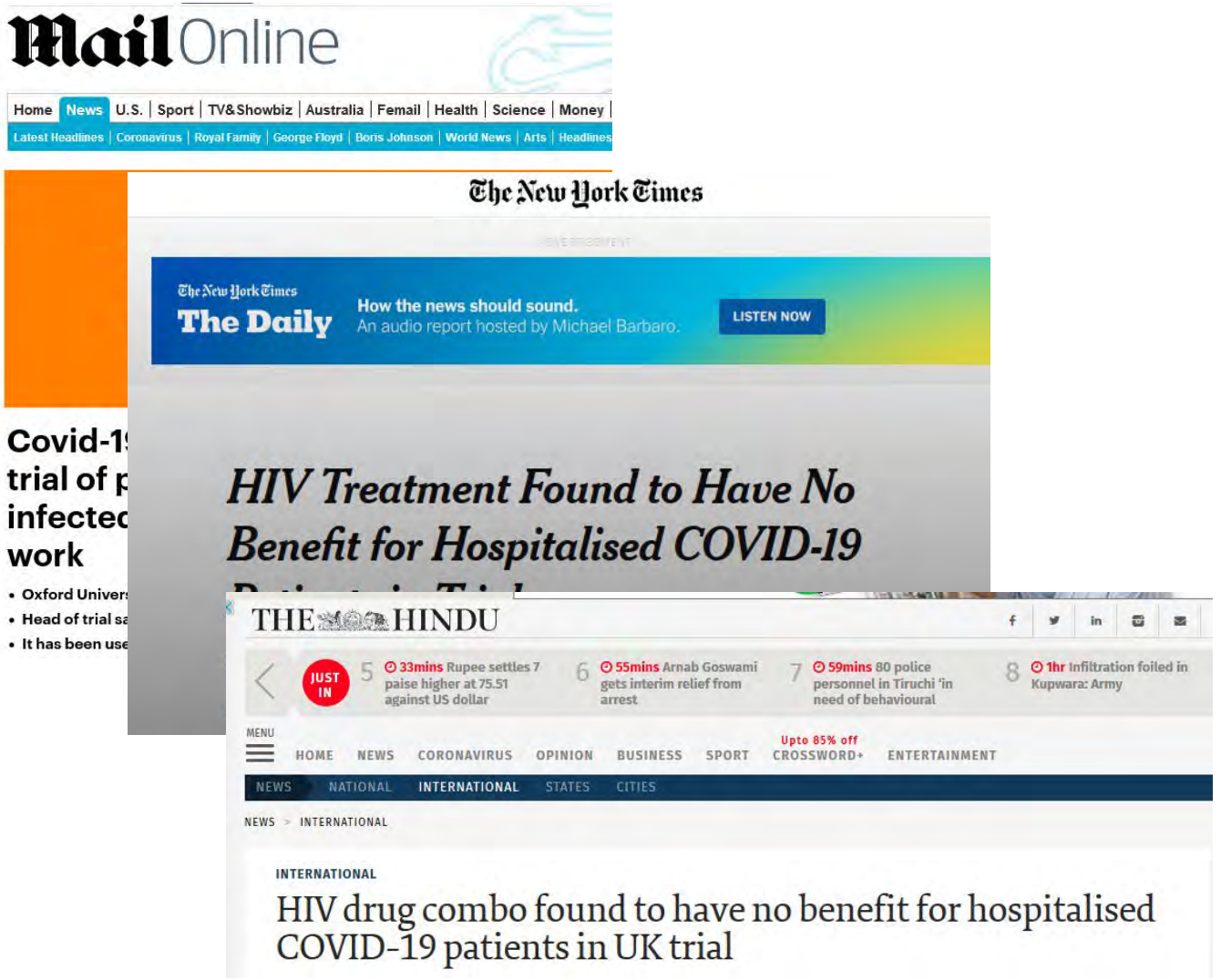


https://www.nejm.org/doi/10.1056/NEJMoa2022926

# Lopinavir-ritonavir:
## Widely recommended – shown to be ineffective

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32013-4/fulltext

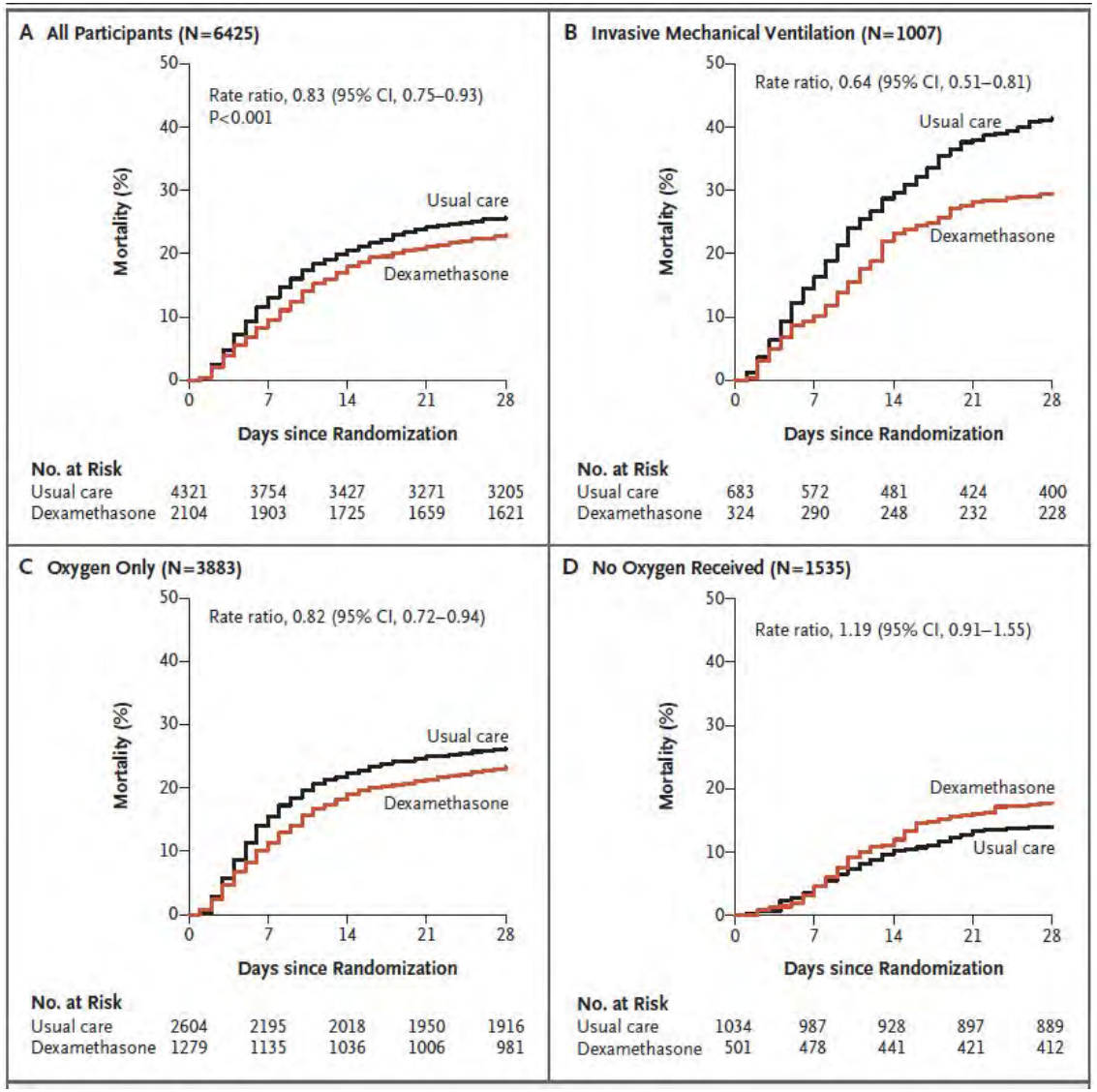


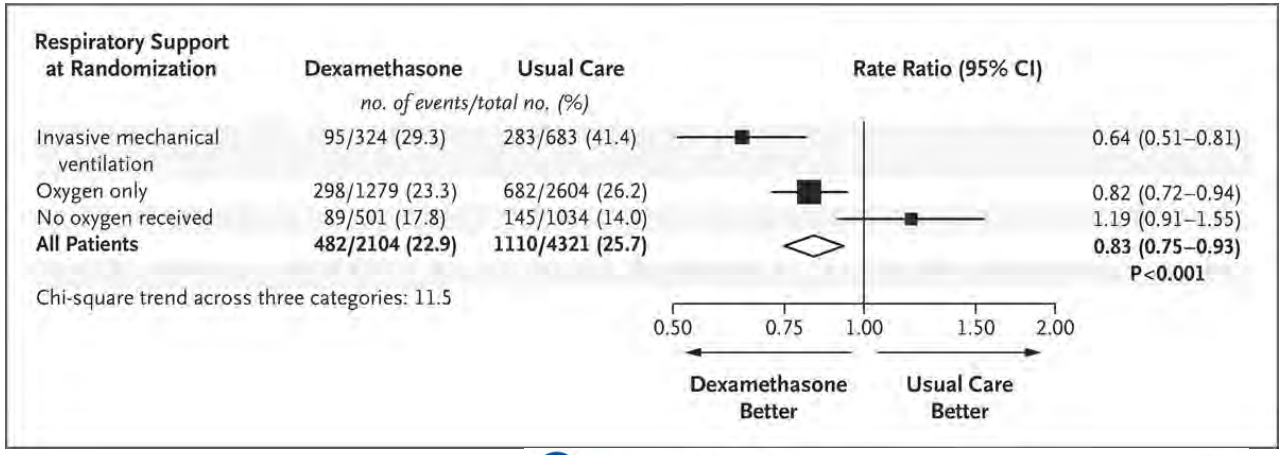



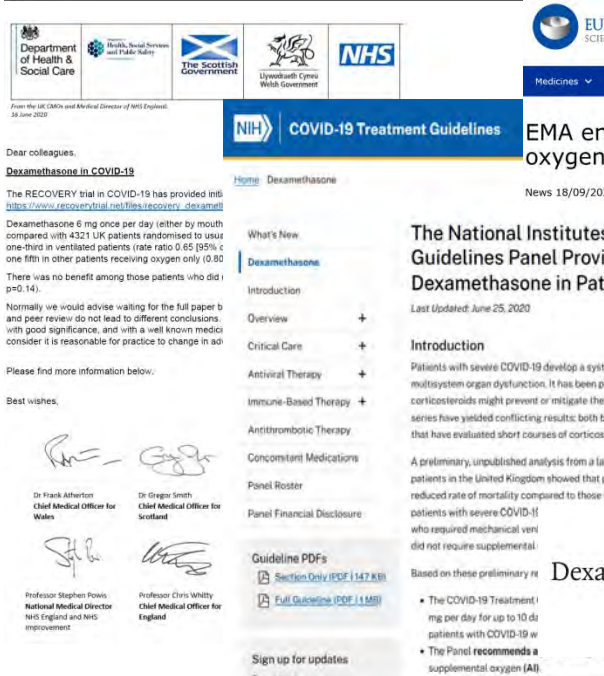
# Dexamethasone:

## Reduces mortality in patients requiring oxygen or ventilation

DOI: 10.1056/NEJMoa2021436




Opinion

# Where Is America's Groundbreaking Covid-19 Research?

The New York Times

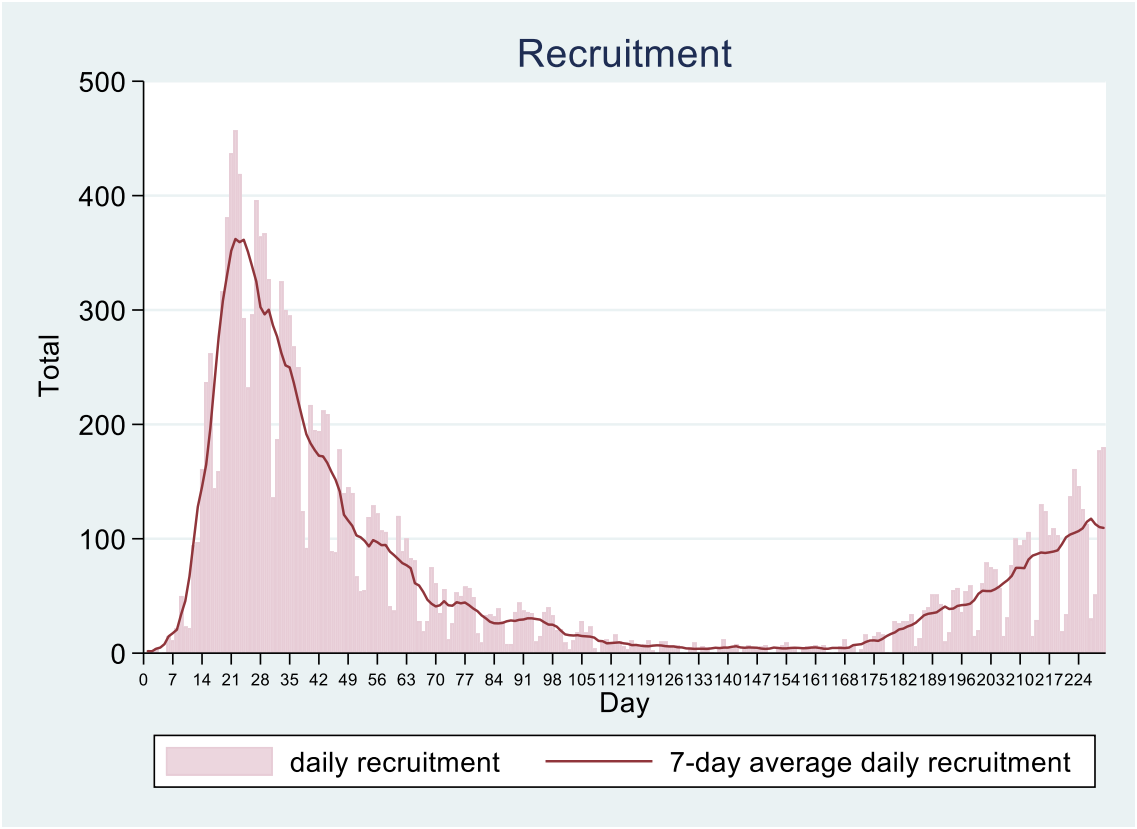
The U.S. could learn a lot from Britain.

By Ezekiel J. Emanuel, Cathy Zhang and Amaya Diana

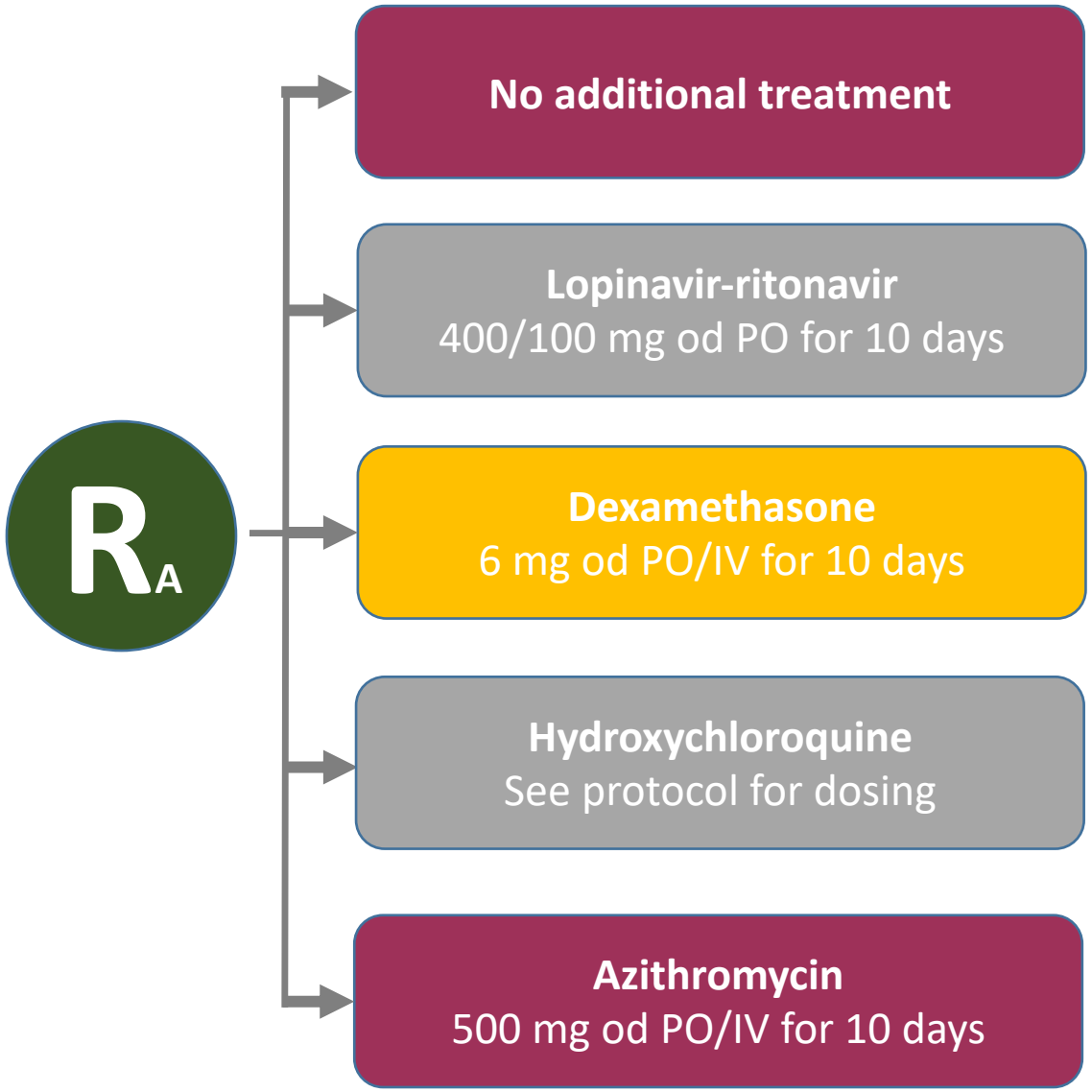
- First, the Recovery trials are **designed to be easy to take part in**
- Second, the Recovery **protocol was quickly approved** at the national level and **adopted by all hospitals** in Britain.
- Third, **background patient data provided by the National Health Service helped to simplify the research process.**
- Fourth, support from **leaders in government health care ensured widespread cooperation** by hospitals.
- Fifth, Britain has a **national system of research nurses** who were rapidly redeployed to work on Covid-19 research
- And last, the British effort was **incorporated as part of everyday clinical care in hospitals**.

https://www.nytimes.com/2020/09/01/opinion/coronavirus-clinical-research.html

# RECOVERY – the second wave is upon us




# RECOVERY – studying multiple treatments



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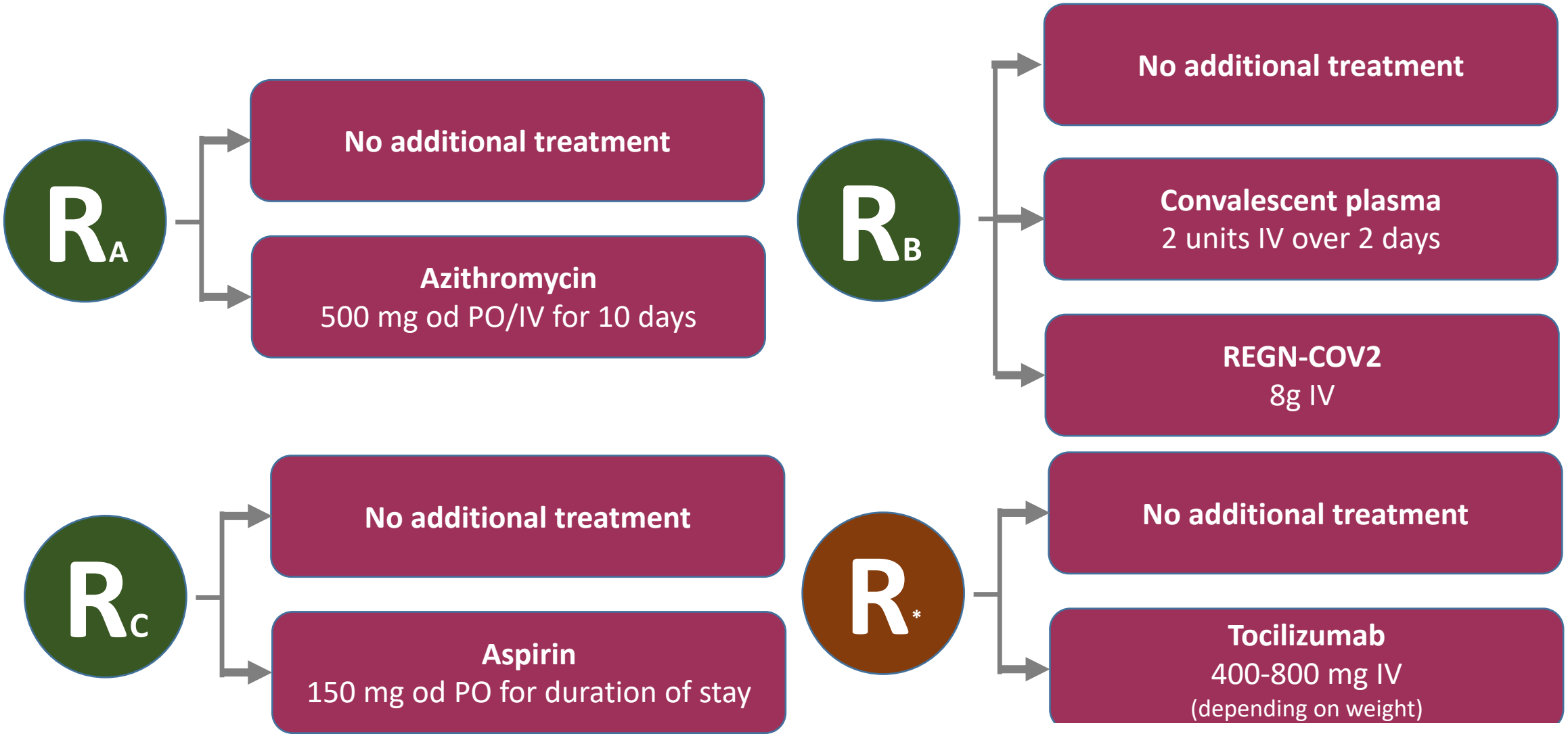



*If hypoxia + inflammation

# Randomised trials are an essential component of high quality clinical care

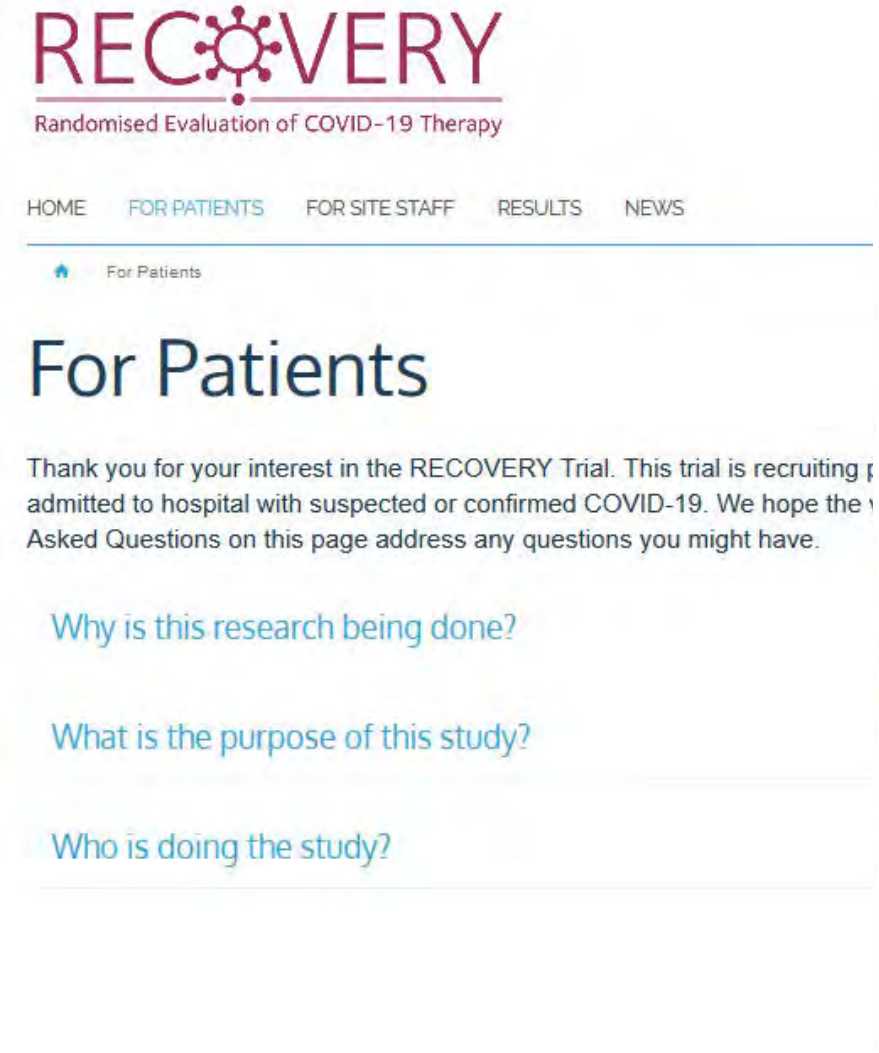
- Arbitrary use of unproven treatments must be avoided
- Large, randomized trials are a critical component of high quality clinical care
- Compelling results change practice

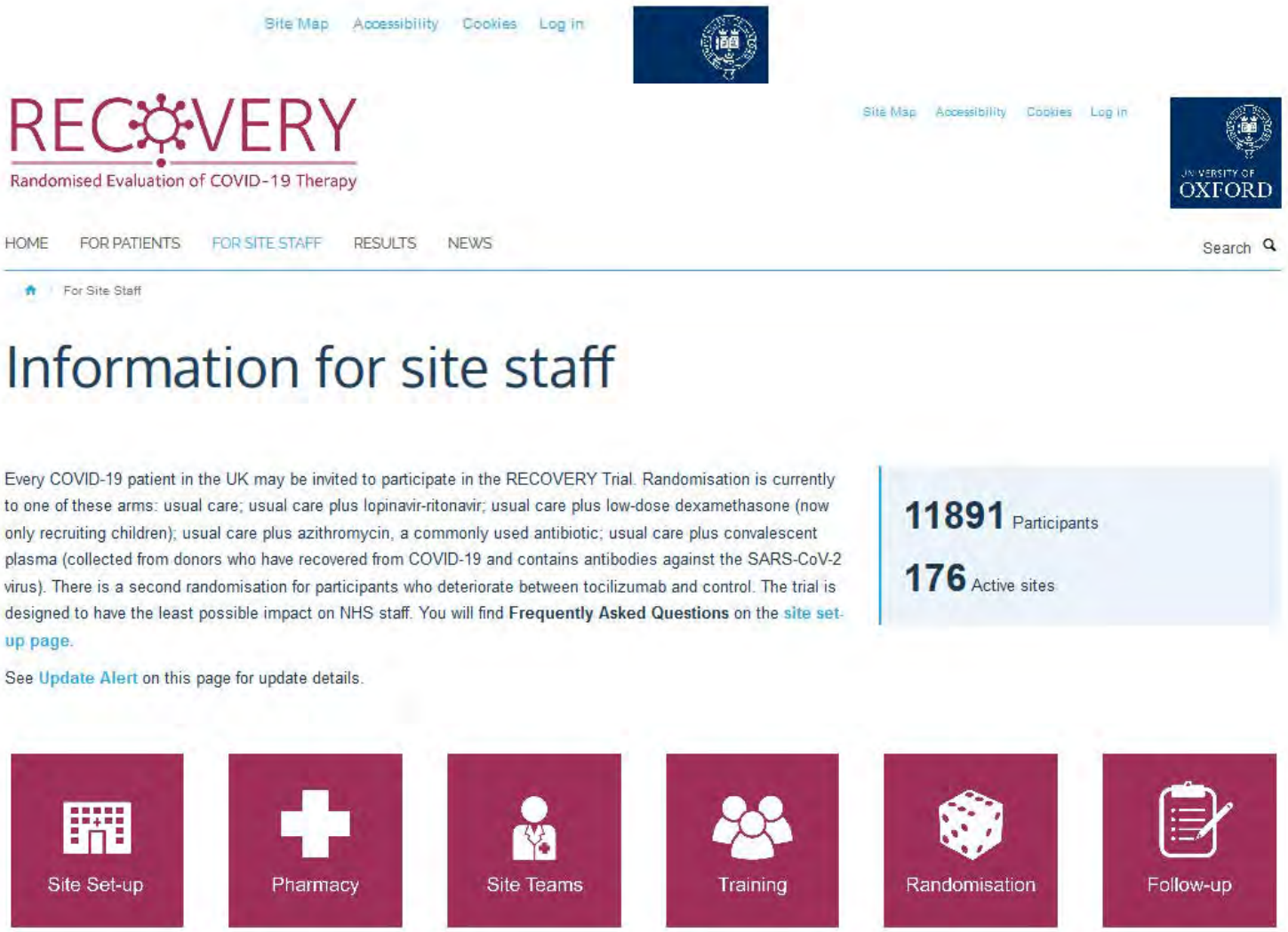
- But trials must be:
  - Feasible for patients and clinical staff
  - Inclusive of relevant patient groups
  - Focused on outcomes that matter

- Requires leadership, coordination, collaboration, fairness, and transparency

These lessons are important not only for the current COVID-19 pandemic but also for the tackling the burden of many other common diseases

# Communication: www.recoverytrial.net



# Huge thanks to the team...

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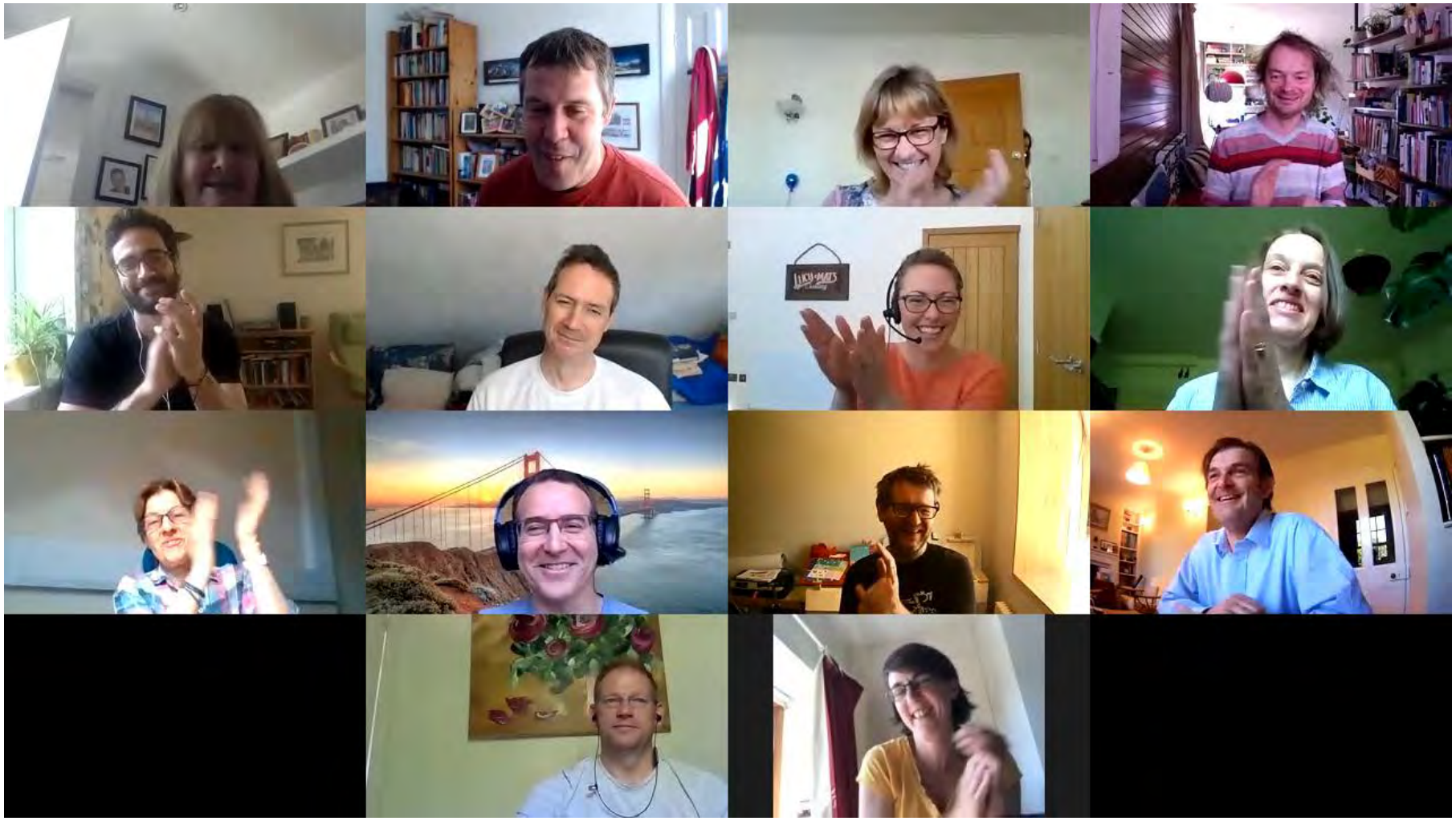

# Acknowledgements


- UK Research & Innovation
- Wellcome Trust
- Department for International Development
- National Health Service in England, Wales, Scotland, and Northern Ireland
- National Institute for Health Research
- Bill & Melinda Gates Foundation
- Department of Health & Social Care

- NIHR Clinical Research Network
- NIHR Oxford Biomedical Research Centre
- NHS DigiTrials
- Medical Research Council Population Health Research Unit

**with enormous thanks**

to the very many doctors, nurses, & other healthcare & research staff at over 176 NHS hospitals

and, most importantly

**to the thousands of patients who participate in this extraordinary project**