Randomised Evaluation of COVID-19 Therapy: the RECOVERY trial

Collaborators' Meeting

17th November 2020

Agenda

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1. Introductions
2. Update on progress
3. REGN-COV2
4. Tocilizumab
5. Aspirin
6. Other developments
7. Trial procedures
8. Q&A

Introductions

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- One of the central study team will talk to the agenda
- If you have questions please enter them into the “Q&A” on the right side of your screen.
- Questions may be answered directly or to the whole group

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PROGRESS UPDATE

Design

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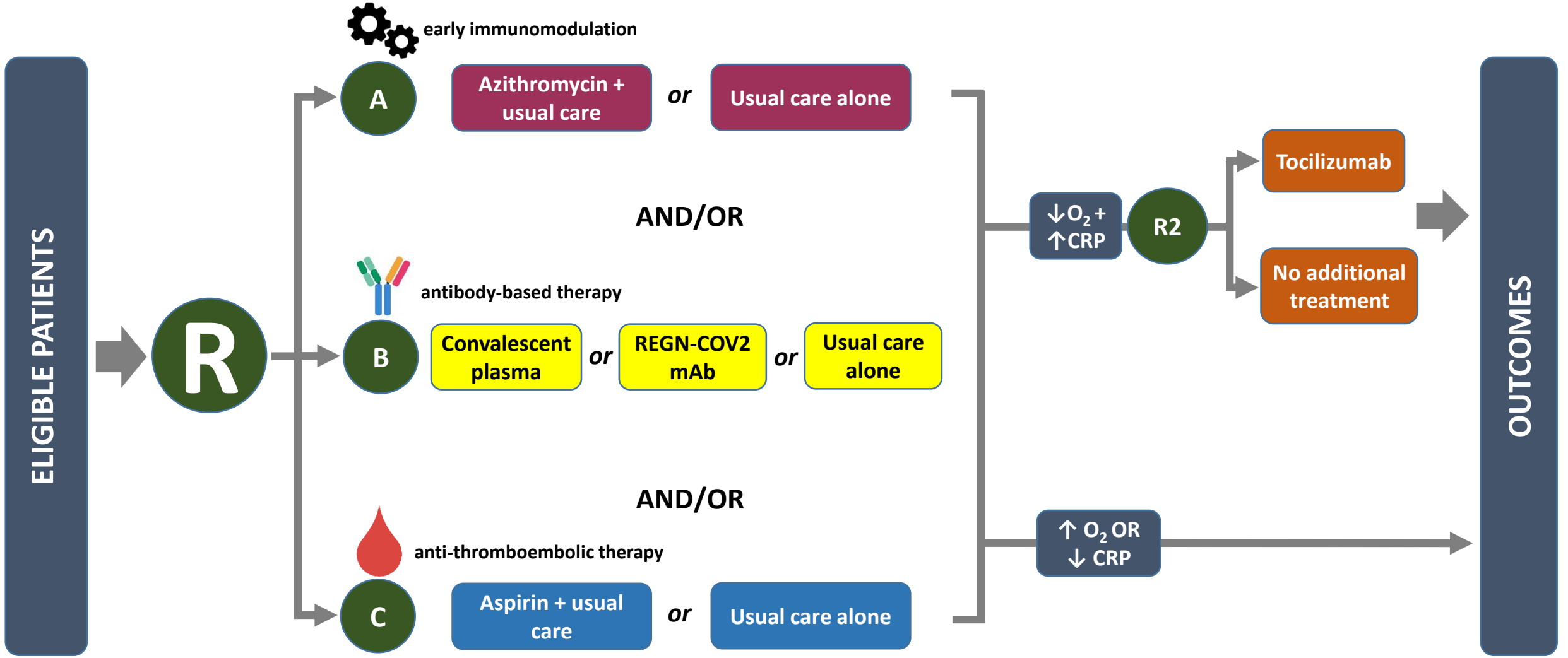

Recruitment by site and by time

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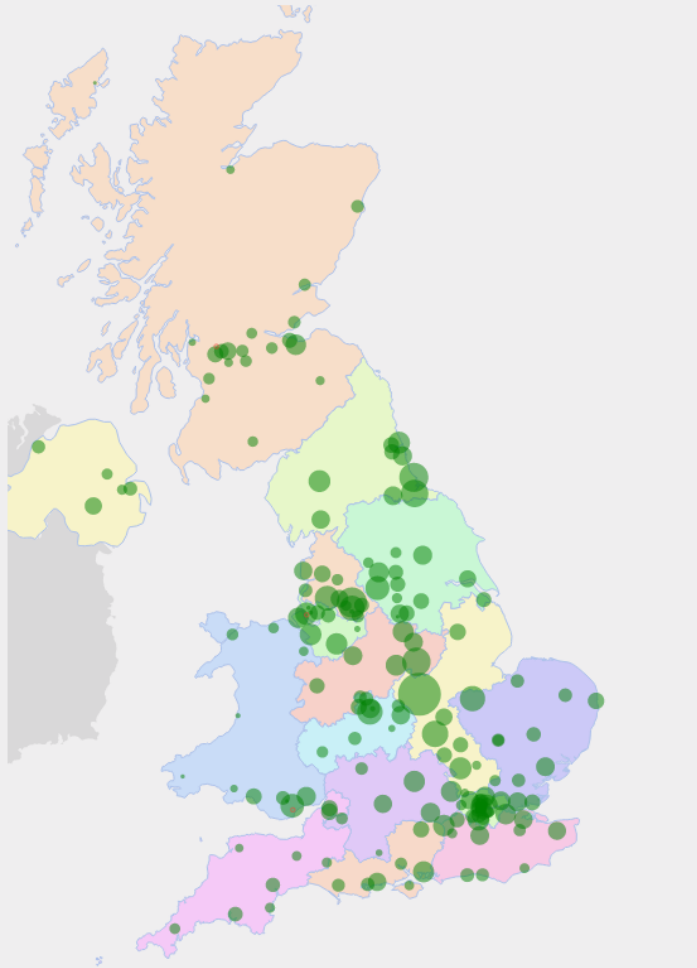
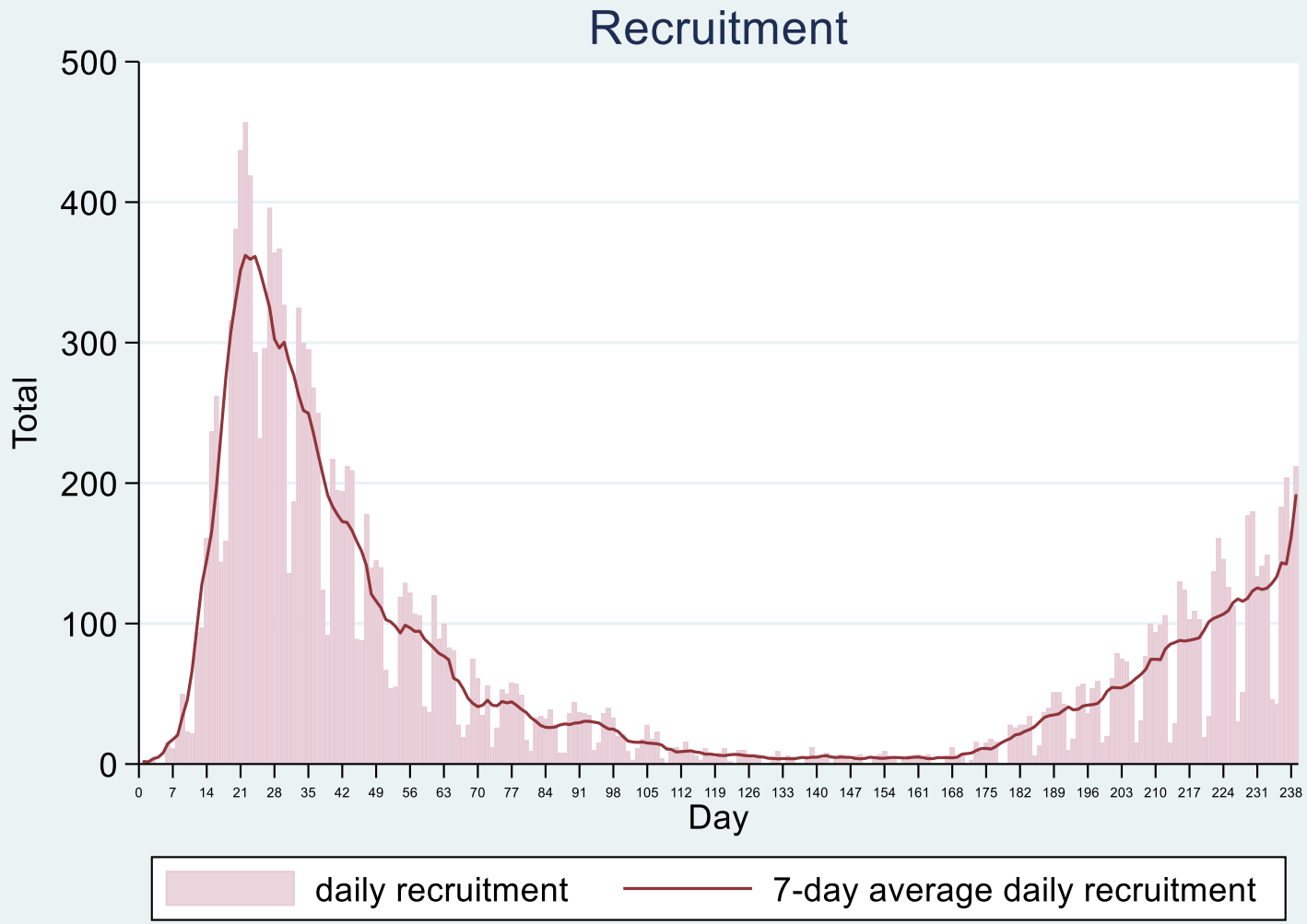
Active Sites	Recruiting Sites	Participants	Phase 2 rands.	Phase 3 rands.	Phase 4 rands.
176	173	17209	1798	4397	422





Recruitment

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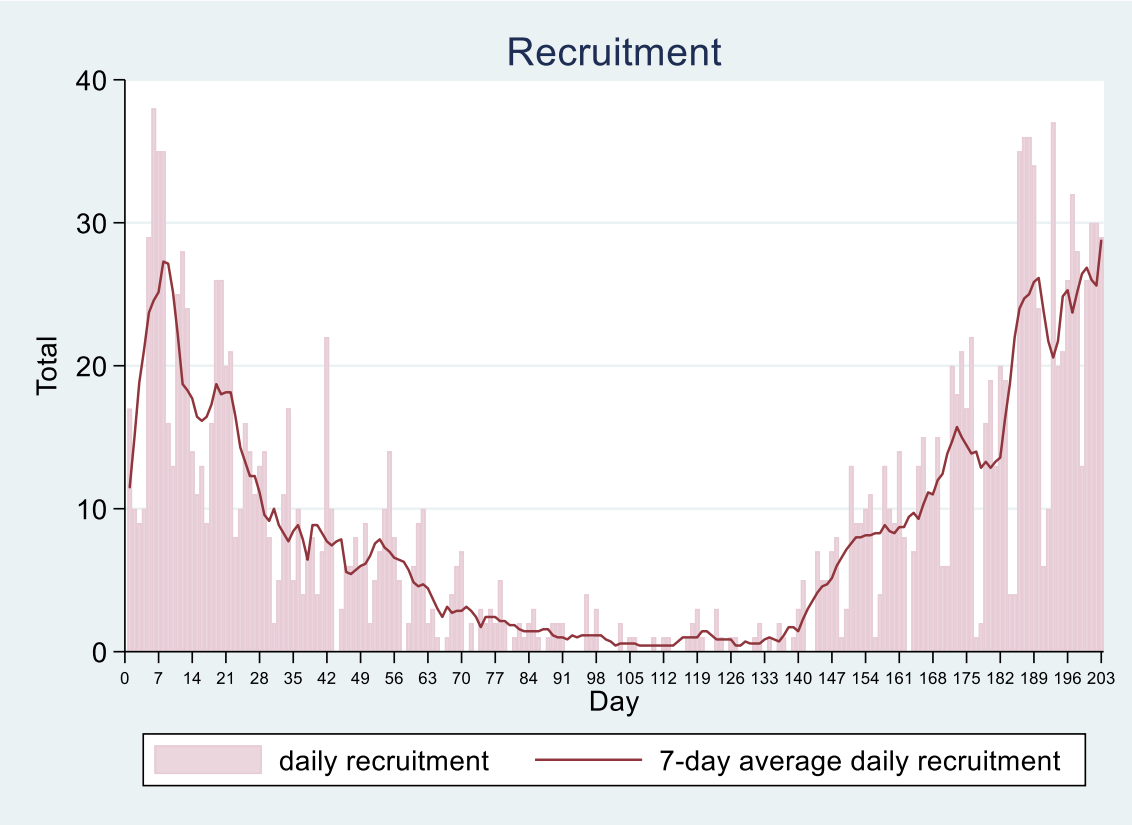
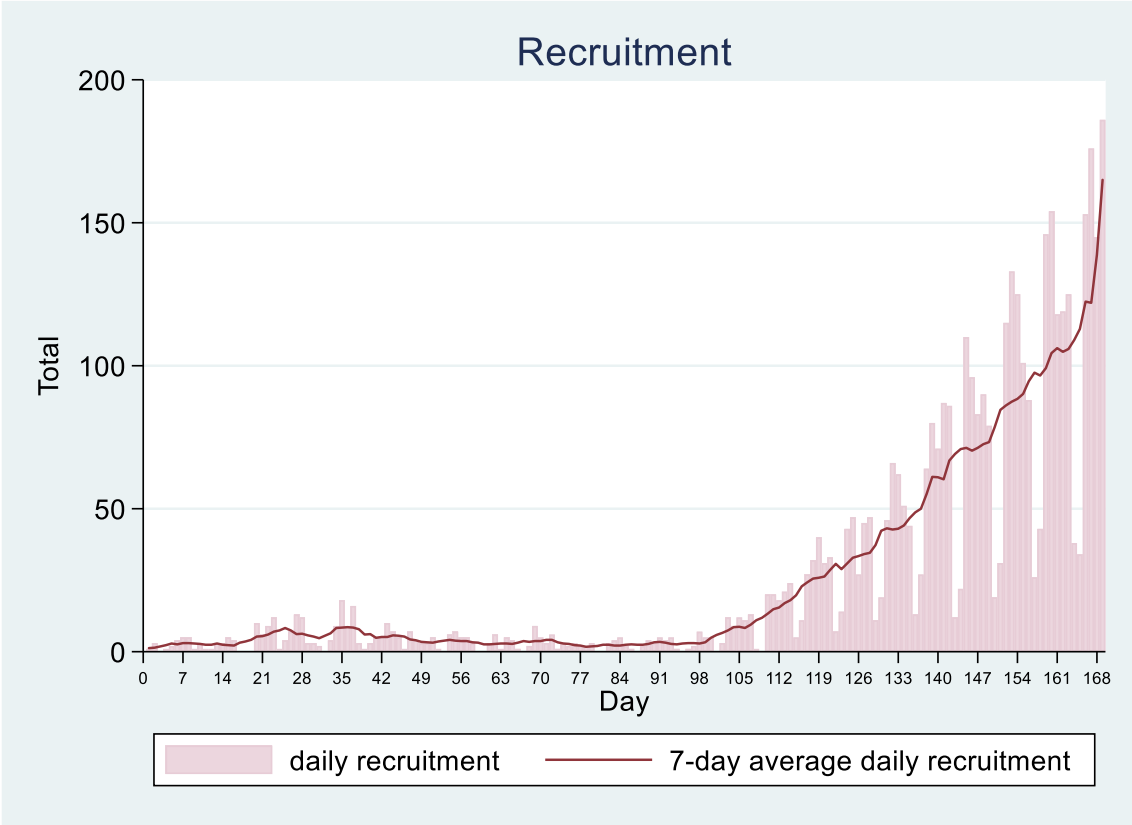
- Tocilizumab vs control



- Convalescent plasma vs REGN-COV2 vs control



Recruitment

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- As local outbreaks occur, please consider discussing with your teams how to ensure that all available admissions with Covid-19 are identified and enrolled if possible
  - Daily catch-up with admitting teams
  - Links with laboratory for all positive swabs among patients to be reported

- Average recruitment remains at about 12% of all COVID-19 admissions, but with significant variation between sites

How long until the next result?

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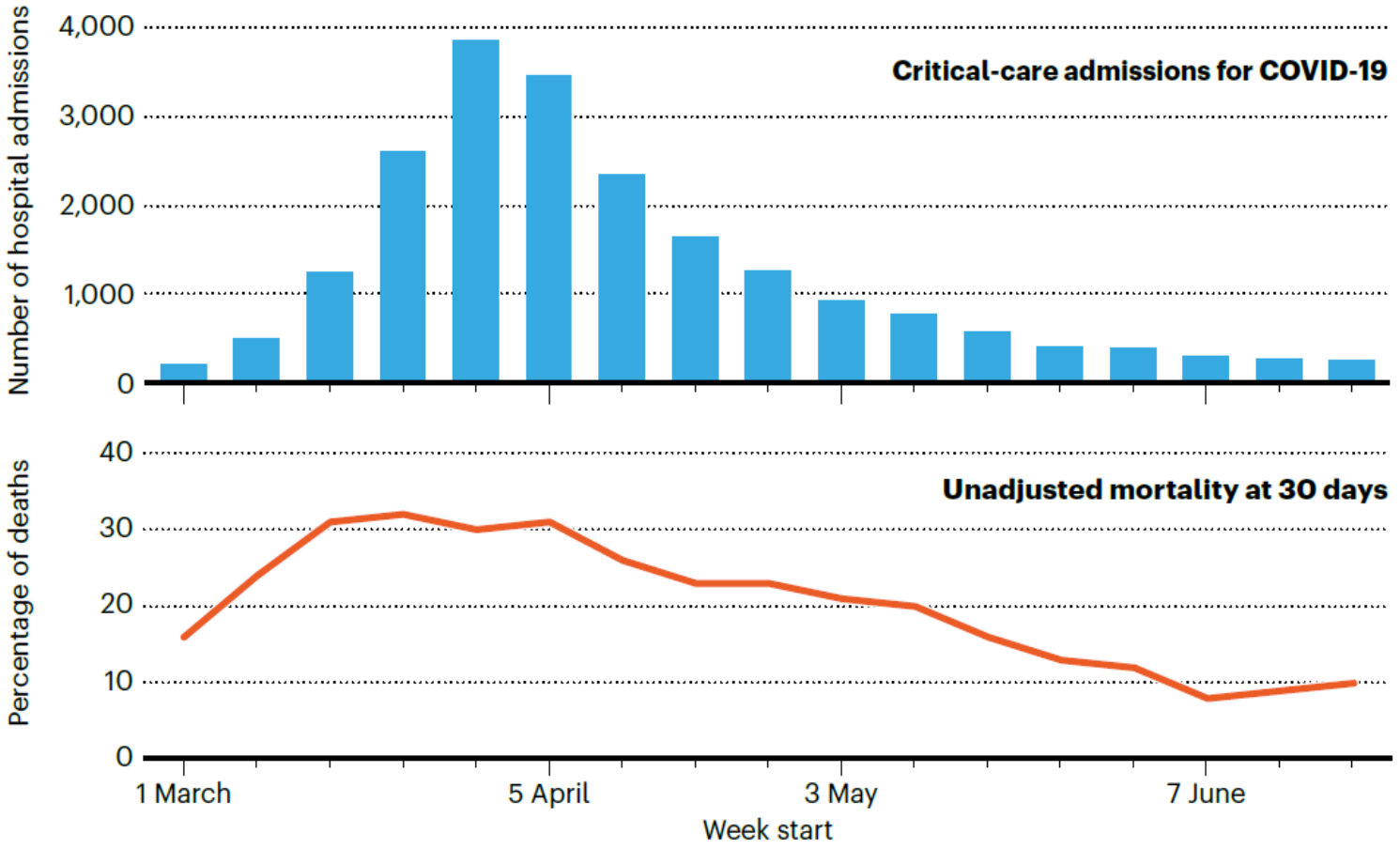
- Determined by recruitment rate and death rate



Recruitment

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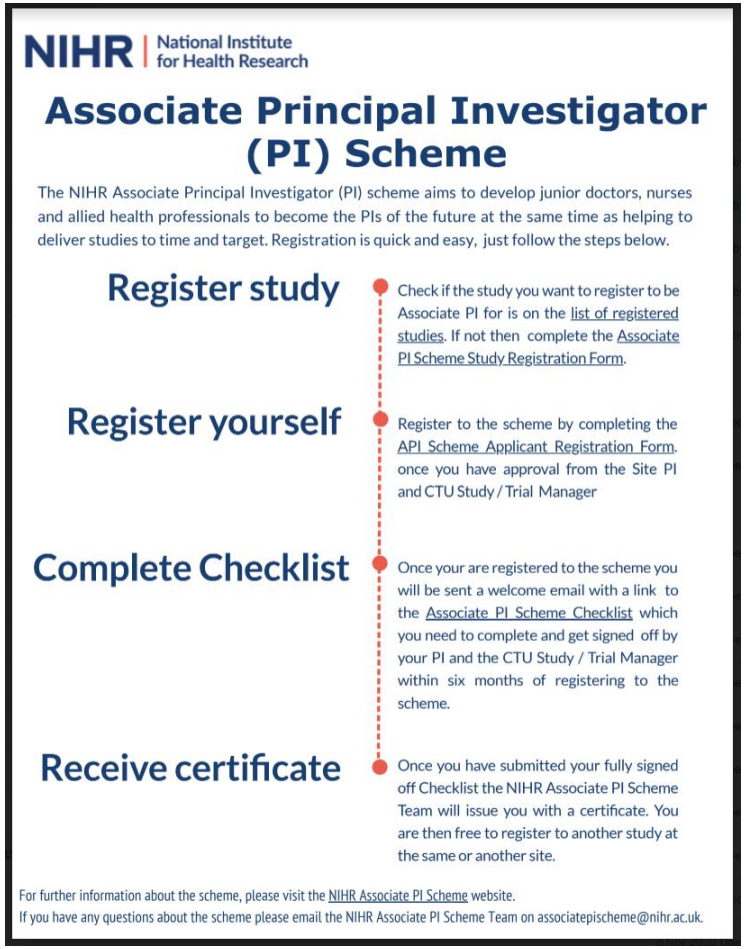
- Pilot of additional funding for weekend working in November underway at 6 trusts in England

- RECOVERY now active on Associate PI scheme
  - Webinars on 13th & 17th November
  - Further details at:

https://www.nihr.ac.uk/documents/associate-principal-investigator-pi-scheme/25040



NIHR | National Institute for Health Research

Associate Principal Investigator (PI) Scheme

The NIHR Associate Principal Investigator (PI) scheme aims to develop junior doctors, nurses and allied health professionals to become the PIs of the future at the same time as helping to deliver studies to time and target. Registration is quick and easy, just follow the steps below.

Register study
Check if the study you want to register to be Associate PI for is on the list of registered studies. If not then complete the Associate PI Scheme Study Registration Form.

Register yourself
Register to the scheme by completing the API Scheme Applicant Registration Form. once you have approval from the Site PI and CTU Study / Trial Manager

Complete Checklist
Once your are registered to the scheme you will be sent a welcome email with a link to the Associate PI Scheme Checklist which you need to complete and get signed off by your PI and the CTU Study / Trial Manager within six months of registering to the scheme.

Receive certificate
Once you have submitted your fully signed off Checklist the NIHR Associate PI Scheme Team will issue you with a certificate. You are then free to register to another study at the same or another site.

For further information about the scheme, please visit the NIHR Associate PI Scheme website.
If you have any questions about the scheme please email the NIHR Associate PI Scheme Team on associatepischeme@nihr.ac.uk.

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REGN-COV2

REGN-COV2

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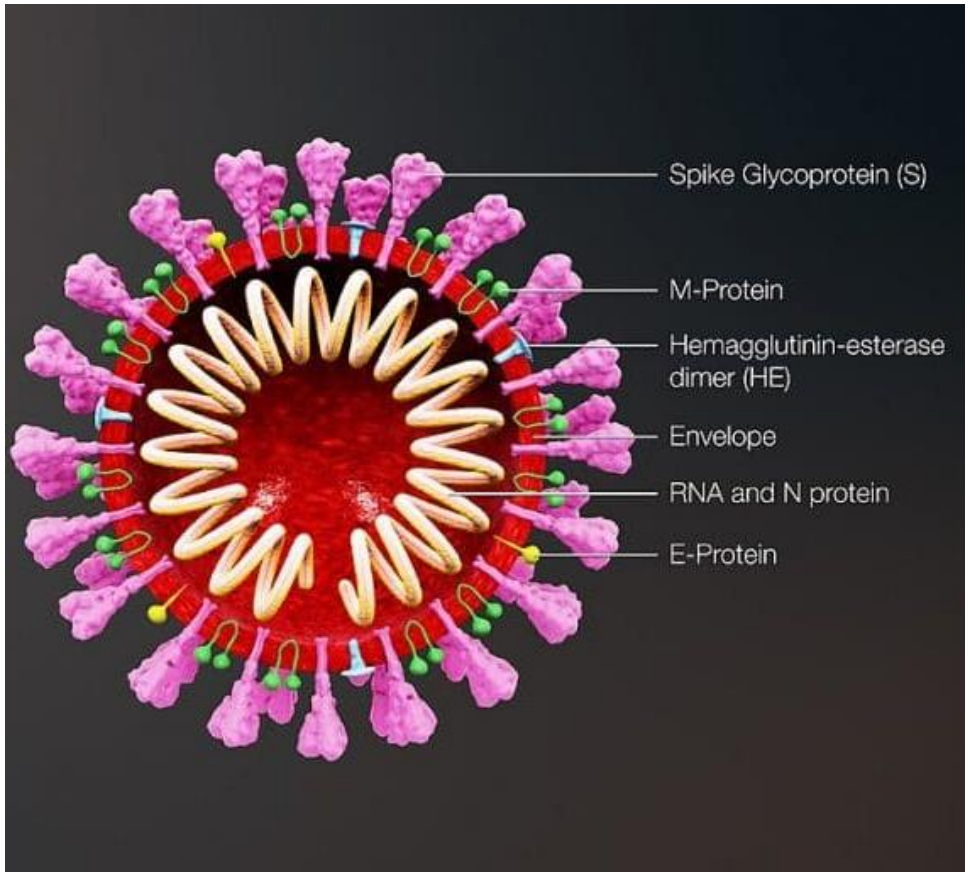
- REGN-COV2 is a mixture of two monoclonal antibodies (mAbs: REGN10933 and REGN10987)



- These are fully human antibodies directed against spike protein

- Two different antibodies mean that if virus mutates its spike protein such that one antibody doesn't bind so well, the other antibody probably still will

REGN-COV2 site setup

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1. Local PIs need to complete online training and confirmation form
   - They should ask other staff involved at site to also do this, but not require before site activation

2. Pharmacy need to be ready to support new arm
   - Review Pharmacy Manual on website and complete local risk assessment to determine where mAb will be prepared
   - Confirm staff details to RECOVERY team

3. >100 sites now in set-up process (with ~80 actively recruiting); still waiting to hear from ~50

REGN-COV2 dos and don’ts

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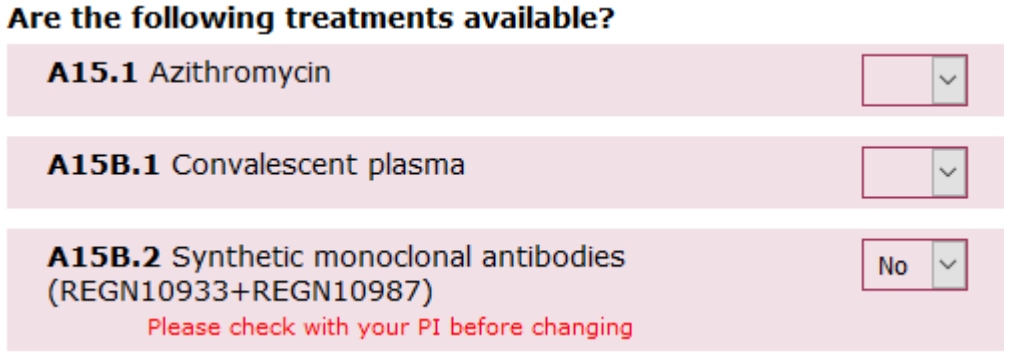
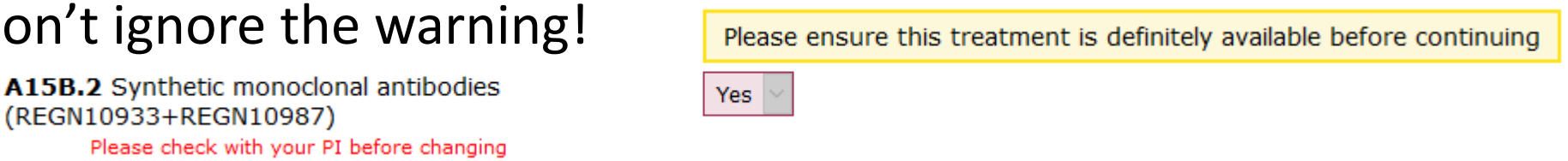
- Please **DO NOT** indicate REGN-COV2 is available if system suggests it is not *unless you are absolutely sure!*



- Please don’t ignore the warning!



- Otherwise the participant may be allocated a treatment they can’t have ☹

When to include REGN-COV2

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- REGN-COV2 should be administered as soon after randomisation as possible

- If being prepared in pharmacy, this may not be until next working day

- If delay is likely to be longer (e.g. at weekend), please indicate that mAb is unavailable on randomisation form so it will not be allocated

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TOCILIZUMAB

Tocilizumab

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- 1800 randomised
- Sufficient tocilizumab supply for 4000 randomised, but all now at sites
- Please ensure you consider this randomisation for appropriate participants:
  - On oxygen (or sats <92%)
  - CRP ≥75 mg/L

Aspirin

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- Increased risk of venous and arterial thrombosis observed in COVID-19, which may contribute to morbidity and mortality
- Platelets recognised as both activated by inflammation (making them more ‘sticky’) and also driving inflammation
- Aspirin 150 mg once daily recommended by CTAP antithrombotic subcommittee
- Added to protocol in V10.1 which went ‘live’ on 6th November 2020

Aspirin FAQs

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Q Why 150 mg?

A Potential risk of underdosing larger patients with 75 mg and bleeding risk little different

Q Should we give a PPI with aspirin?

A Gastroprotection can be used at the discretion of the treating physician

Q What about other VTE prophylaxis?

A Other VTE prophylaxis (e.g. heparin) should not be modified by allocation to aspirin or control

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OTHER DEVELOPMENTS

Other developments: RECOVERY international

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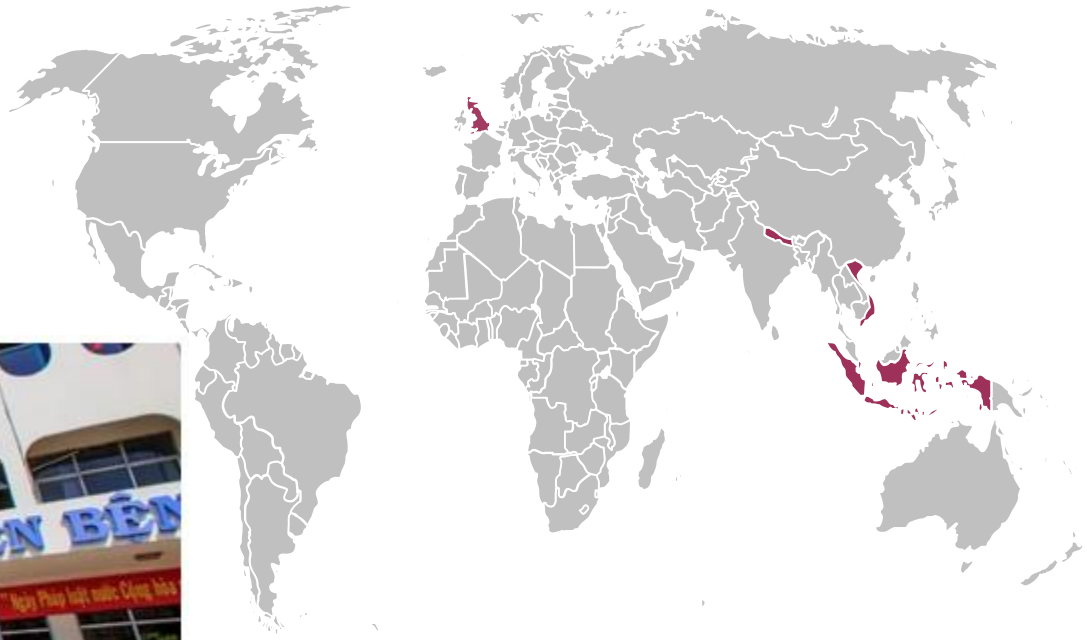
- Funding agreed by Wellcome

- Discussions are progressing with Vietnam, Indonesia and Nepal



Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

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TRIAL PROCEDURES

Serum samples

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- **All** participants entering antibody comparison (CP vs mAb vs control) need to have serum sample collected prior to randomisation

- Can be taken with G&S sample after consent prior to randomisation to limit venepunctures

- Must be taken for all participants in that comparison (regardless of allocation)

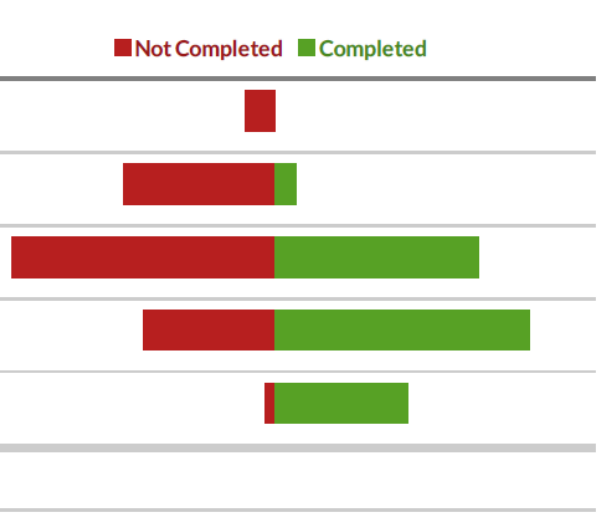
Completeness of follow-up

- Weekly reminders highlighting participants randomised >28 days ago without complete form **and also** those needing an Antibody Comparison 72h safety form

- Please do complete these as soon as possible

Follow-up form completion summary

Days Since Rand.	FU Not Completed	FU Completed	Total Rands.
7 ≤ 14	3 (100.0%)	0 (0.0%)	3
14 ≤ 21	15 (88.2%)	2 (11.8%)	17
21 ≤ 28	26 (56.5%)	20 (43.5%)	46
28 ≤ 35	13 (34.2%)	25 (65.8%)	38
> 35	1 (7.1%)	13 (92.9%)	14
Total	**58 (49.2%)**	**60 (50.8%)**	**118**



Carry on recruiting!

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- RECOVERY remains the largest global trial in COVID-19 and is an exemplar of what trials can do (both in and after pandemic)
- Current therapies are exciting, but need reliable data before they should be used routinely
- Thank you for your support!