Randomised Evaluation of COVID-19 Therapy: the RECOVERY trial

Collaborators' Meeting

4th January 2022

Agenda

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1. Introductions
2. Update on progress
3. Current active comparisons:
   - Empagliflozin
   - High-dose corticosteroids
   - Sotrovimab
4. Trial procedures
5. Future plans
6. Pregnancy update
7. 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

Recruitment by time

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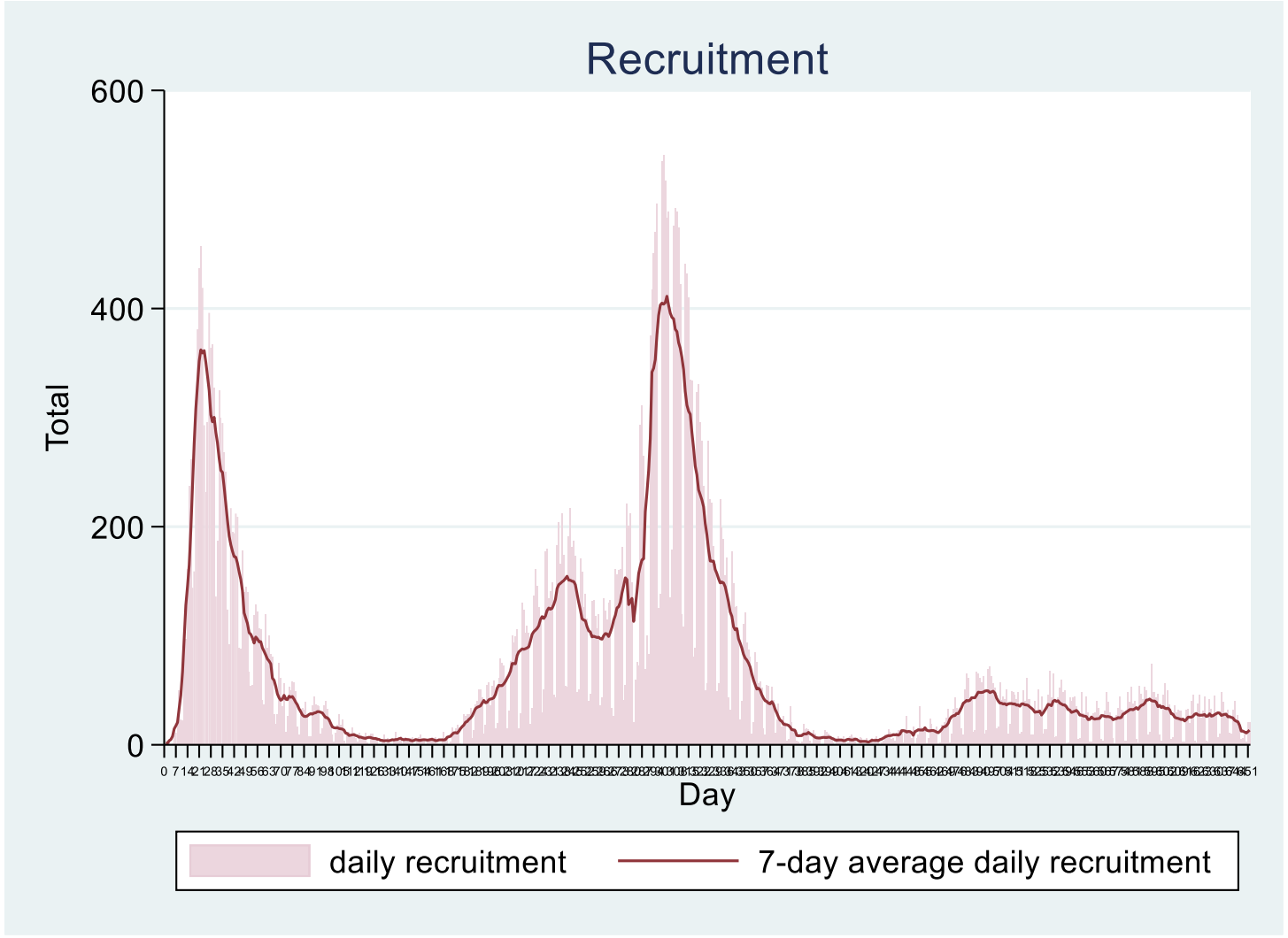

Current numbers in comparisons

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- Baricitinib *vs* usual care: 8156 (recruitment now closed)
- Empagliflozin: ~2750
- High-dose corticosteroids: ~860

Recruitment

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- We recognise up to ⅓ of admissions *with* COVID-19 are 'incidental' diagnoses (ie, patient was admitted for something else)
- Such patients are eligible if they develop symptoms of COVID-19 during admission
- Staff absences mean that situation is just as challenging as in January 2020 even though numbers being admitted is not as high
- Thank you for trying to embed RECOVERY into standard clinical care so recruitment can cause minimal disruption

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CURRENT DESIGN

Current comparisons for adults with COVID-19

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ELIGIBLE PATIENTS

High-dose corticosteroids (hypoxic)

E — High dose steroids *or* Usual care alone

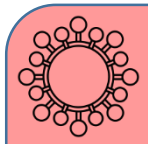
SGLT-2i comparison

F — Empagliflozin *or* Usual care alone

Baseline data collected
Participants enter ≥1 comparisons

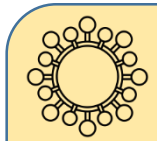
R

Outcomes collected at earliest of death, discharge or 28 days



Antiviral 1

J — Sotrovimab *or* Usual care alone



Antiviral 2

K — Molnupiravir *or* Usual care alone

OUTCOMES

Eligibility

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1. Hospitalised

2. Viral pneumonia syndrome
   - or PIMS-TS in children

3. Confirmed SARS-CoV-2 infection
   - PCR (hospital or community) or in-hospital lateral flow test

4. No medical history that might put the patient at risk if s/he were to participate

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EMPAGLIFLOZIN

SGLT-2 inhibitors and Empagliflozin (empa)

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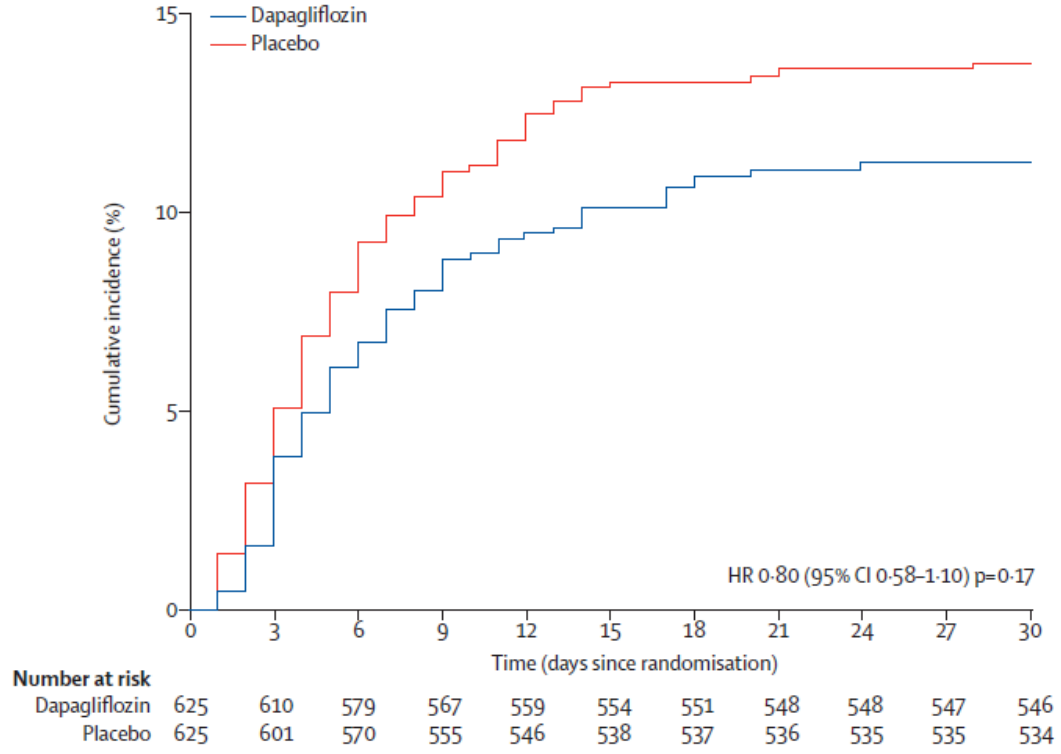
- Empagliflozin is an SGLT-2 inhibitor (SGLT-2i)

- SGLT-2i may have beneficial effects in COVID-19
  - Shift in energy metabolism from glucose (which SARS-CoV-2 may rely on) to lipids
  - Improve endothelial function
  - Anti-inflammatory effects

- DARE-19 trial compared dapagliflozin with placebo among 1250 patients hospitalised for COVID-19 with another 'risk factor' (eg, diabetes, cardiovascular disease)



Empagliflozin in RECOVERY

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- **Dose: 10 mg once daily for up to 28 days** (stopped at discharge if sooner)

- **Exclusions:**
  - Patients at risk of ketoacidosis (eg, type 1 or post-pancreatectomy diabetes mellitus; history of ketoacidosis; current blood ketones ≥1.5 mmol/L or urine ketones ≥2+)
  - Pregnancy or breast-feeding

- **Important monitoring of ketones for participants with diabetes**
  - Twice daily blood ketones (or once daily urine ketones if blood ketone testing not available) or if clinical concern

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HIGH-DOSE CORTICOSTEROIDS

High-dose corticosteroids

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- RECOVERY demonstrated benefits of 6 mg dexamethasone for hypoxic patients with COVID-19
- Additional immunomodulation (tocilizumab) has been shown to be beneficial
- Higher doses of corticosteroids may be beneficial, but risks also may be increased

High-dose corticosteroids

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- **Eligibility:** adult patients <u>with hypoxia</u>
  - on supplemental oxygen or SpO_2 <92% on air

- **Usual care:** should include dexamethasone 6 mg
- **High-dose arm:** 20 mg dexamethasone once daily for 5 days, then 10 mg once daily for 5 days (stopped at discharge if sooner)

- **Pregnant/breastfeeding women:** should receive equivalent doses of prednisolone/hydrocortisone

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SOTROVIMAB

Monoclonal antibodies can improve clinical outcome

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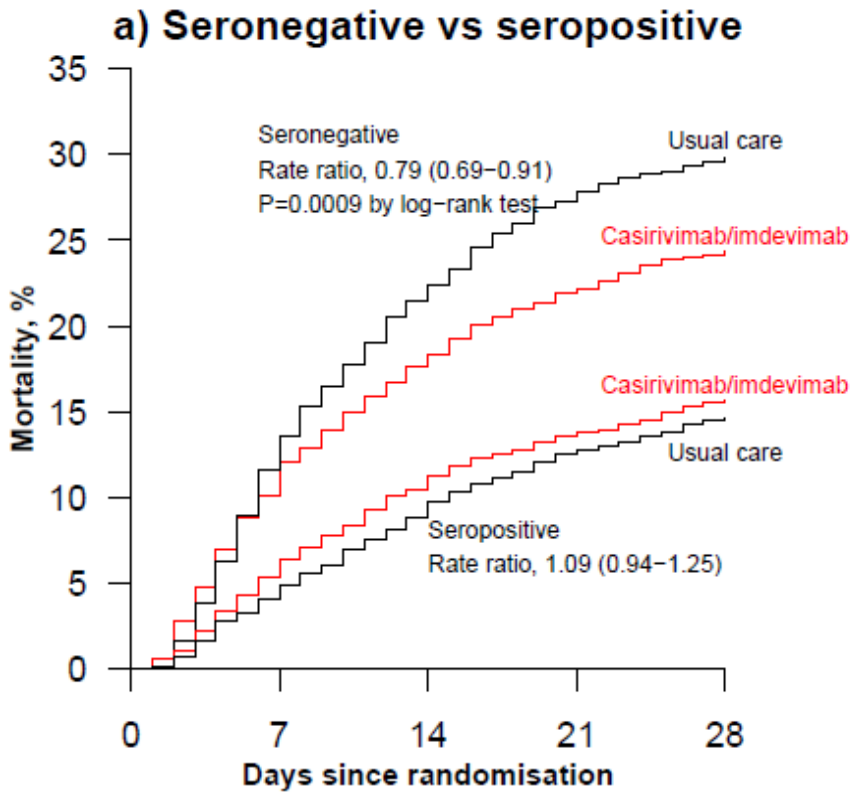

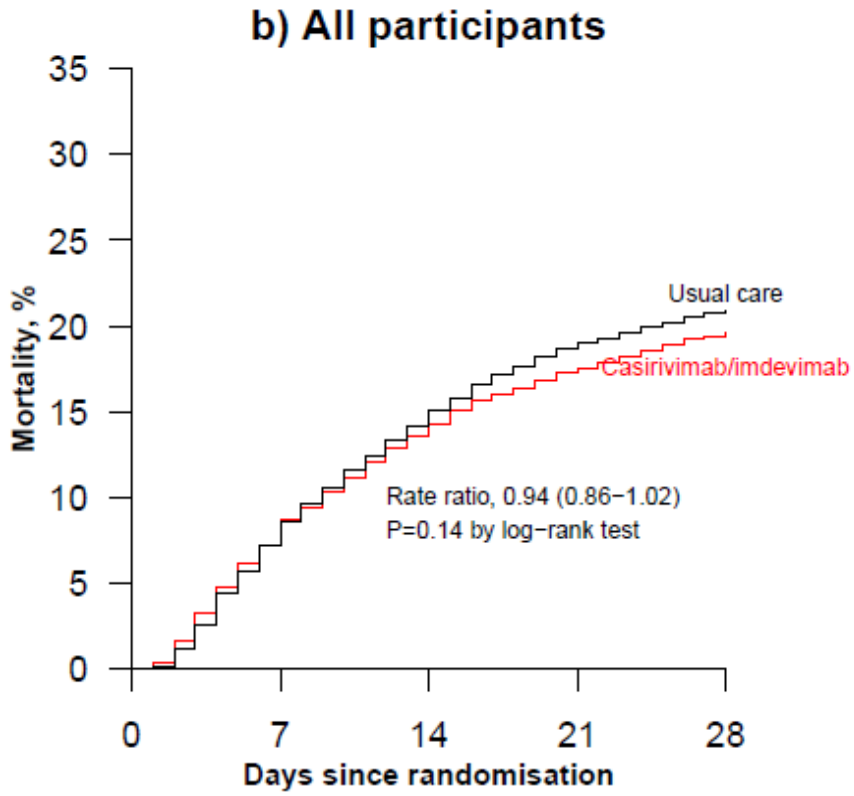

No. at risk, Seronegative

Casirivimab/imdevimab	1633	1431	1328	1266	1230
Usual care	1520	1310	1176	1094	1064

No. at risk, Seropositive

Casirivimab/imdevimab	2636	2456	2329	2261	2214
Usual care	2636	2504	2376	2298	2249

No. at risk

Casirivimab/imdevimab	4839	4394	4122	3968	3868
Usual care	4946	4508	4186	3992	3899

Variants and monoclonal antibodies

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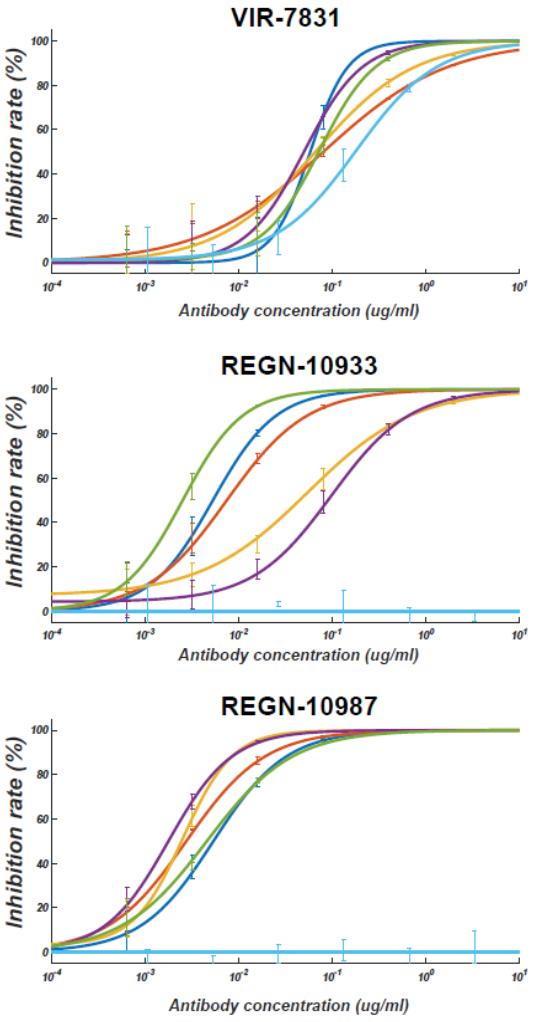
- Because each monoclonal antibody binds to its own specific part of the spike protein, mutations in the binding site can alter the potency of these treatments
- Ronapreve is highly effective against previous variants, but has very little activity against Omicron
- Sotrovimab has preserved efficacy against Omicron



Cao et al. BioRxiv 2021

Sotrovimab

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- Derived from an antibody identified in a patient who had SARS-CoV-1 infection
- Thought to bind to part of the spike protein which is more “conserved” so may be less likely to mutate in future variants
- Is fully human, but has had Fc portion modified to increase its half-life after infusion

Efficacy of sotrovimab

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- Among **outpatients** in the COMET ICE trial, sotrovimab reduced need for hospitalisation or death by 85%

- Assessed in NIH ACTIV-3-TICO trial among **inpatients**, but abandoned for futility
  - However, pre-specified analysis did not take into account serostatus, so effects like that seen with Ronapreve in RECOVERY would have been missed

- There remains uncertainty around benefits of sotrovimab for **inpatients**

Sotrovimab in RECOVERY

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- All adult participants are potentially eligible, including those who have received sotrovimab previously
  - Adolescents ≥12 years old and ≥40 kg are also eligible
  - Pregnant or breast-feeding women are eligible after discussion with them
  - No exclusions around liver or kidney function

- Dose is **1000 mg** in 100 mL 0.9% saline or 5% dextrose given over 1 hour given as soon as possible after randomisation

Requirements for participation

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- Site PI must complete online training
  - Cascade to other relevant staff
- Provide CCO with addresses for:
  - Delivery of IMP (and days on which it can be received)
  - Delivery of sample kits
- CCO will request shipment of IMP once these details received
  - Comparison will be activated in IT system once receipt of shipment confirmed

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TRIAL PROCEDURES

Biological sampling in RECOVERY

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- Only for participants in antiviral comparisons
- RECOVERY has demonstrated that knowledge of baseline serostatus is crucial to understand effects of monoclonal antibody therapies
- Measuring effects on viral load may help reduce time it takes to accept sotrovimab as a treatment for hospitalised patients
- Swab samples also provide opportunity to assess whether resistance develops to antivirals

Biological sampling in RECOVERY

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	Serum sample	Nose swabs
Baseline (**Day 1** - <u>after</u> consent, <u>before</u> randomisation)	✓	✓
Day 3	✗	✓
Day 5	✗	✓

Serum samples used to measure antibody levels and possibly viral antigen
Swabs used to measure viral load and presence of resistance markers

Biological sampling in RECOVERY

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- Kits currently being manufactured and will be sent to participating sites soon
- All materials provided (except for vacutainer)
- Samples should be labelled with participant ID and time/date of collection
  - No requirement for processing in hospital so do NOT send to hospital lab
- Can be returned using standard post (full instructions on website)

Consent training

- Consent training materials have been updated

- **All staff** who will continue to obtain consent for RECOVERY are required to complete new training (and online confirmation form)

Consent monitoring

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- It has always been intention to monitor consent process, but delayed until now
- All sites have been asked to review a random sample of 20-40 consent forms and provided tool for completion
- We recognise current pressures so please say is more time is required

Completeness of follow-up

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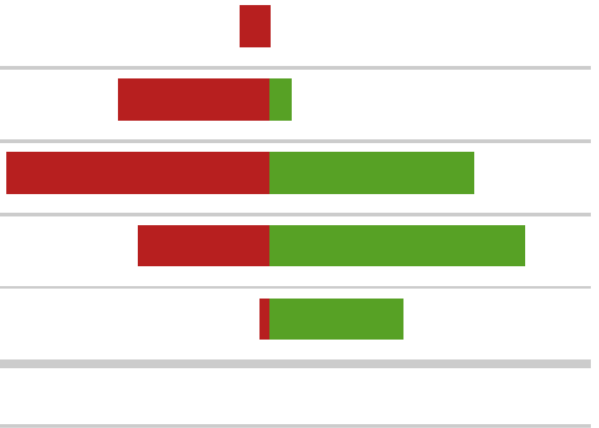
- Weekly reminders highlighting participants randomised >28 days ago without complete form

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**



- Baricitinib arm now closed to recruitment, so complete follow-up is essential

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FUTURE PLANS

Future COVID arms

- Molnupiravir arm will be activated once supply is agreed with DHSC
- Paxlovid was given a license by MHRA on 31st December and will be considered for RECOVERY
- Further immunomodulatory therapies await results of baricitinib comparison

RECOVERY international

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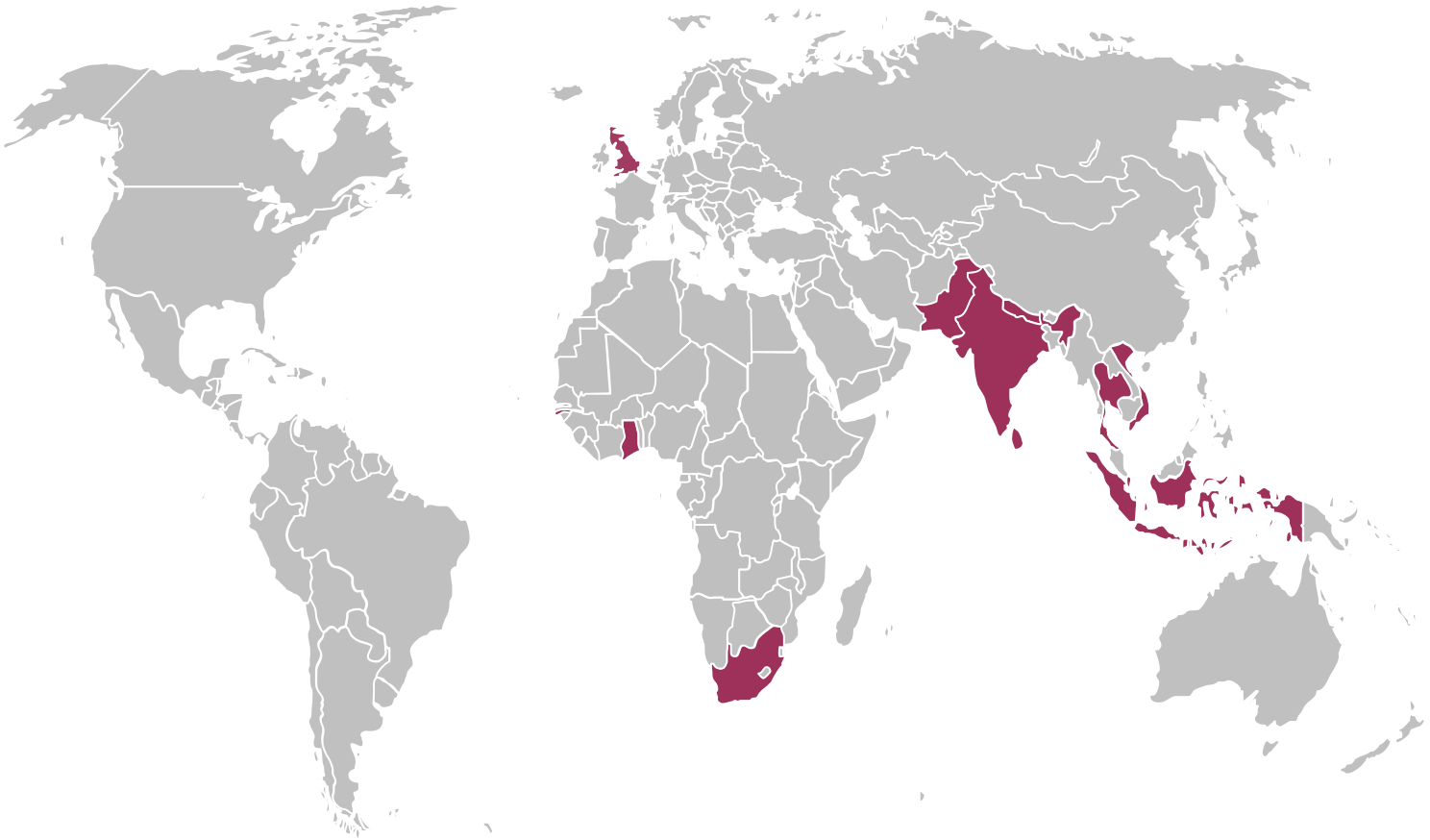

Carry on recruiting!

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- January 2022 will be a challenging time in the NHS
- In January 2021 over 10,000 participants were recruited in equally challenging (but different) circumstances
- We are extremely grateful for your efforts to recruit to RECOVERY as part of the clinical care pathway and help us identify new treatments as we care for patients with COVID-19

Randomised Evaluation of COVID-19 Therapy: the RECOVERY trial

Collaborators Meeting for Pregnancy

4 January 2022

RECOVERY for pregnant women

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1. Update on covid-19 and pregnancy
2. Update on new arms and adaptations
3. Q&A

Covid-19 and pregnancy

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RESEARCH

OPEN ACCESS

Check for updates

Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study

Marian Knight,[1] Kathryn Bunch,[1] Nicola Vousden,[2] Edward Morris,[3] Nigel Simpson,[4] Chris Gale,[5] Patrick O'Brien,[6] Maria Quigley,[1] Peter Brocklehurst,[7] Jennifer J Kurinczuk,[1] On behalf of the UK

BMJ: first publ

PLOS ONE

PUBLISH ABOUT BROWSE

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: A national cohort study using the UK Obstetric Surveillance System (UKOSS)

Nicola Vousden, Kathryn Bunch, Edward Morris, Nigel Simpson, Christopher Gale, Patrick O'Brien, Maria Quigley, Peter Brocklehurst, Jennifer J Kurinczuk, Marian Knight, on behalf of the UKOSS

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CSH Cold Spring Harbor Laboratory BMJ Yale

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Comments (3)

Impact of SARS-CoV-2 variant on the severity of maternal infection and perinatal outcomes: Data from the UK Obstetric Surveillance System national cohort

Nicola Vousden, Rema Ramakrishnan, Kathryn Bunch, Edward Morris, Nigel Simpson, Christopher Gale, Patrick O'Brien, Maria Quigley, Peter Brocklehurst, Jennifer J Kurir, Marian Knight

doi: https://doi.org/10.1101/2021.07.22.21261000

Morbidity and Mortality Weekly Report

Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–October 3, 2020

Laura D. Zambrano, PhD[1,*]; Sascha Ellington, PhD[1,*]; Penelope Strid, MPH[1]; Romeo R. Galang, MD[1]; Titilope Oduyebo, MD[1]; Van T. Tong, MPH[1]; Kate R. Woodworth, MD[1]; John F. Nahabedian III, MS[1]; Eduardo Azziz-Baumgartner, MD[1]; Suzanne M. Gilboa, PhD[1]; Dana Meaney-Delman, MD[1]; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team

Maternal, Newborn and Infant Clinical Outcome Review Programme

MBRRACE-UK

Saving Lives, Improving Mothers' Ca

Rapid report: Learning from SARS-CoV-2-related and associated maternal deaths in the UK

Maternal, Newborn and Infant Clinical Outcome Review Programme

MBRRACE-UK
Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK

Saving Lives, Improving Mothers' Care

Rapid report 2021: Learning from SARS-CoV-2-related and associated maternal deaths in the UK

June 2020-March 2021

EDITORIALS

Check for updates

Include pregnant women in research—particularly covid-19 research

Adapting interventions and changing attitudes will drive scientific progress

Marian Knight,[1] R Katie Morris,[2] Jenny Furniss,[3] Lucy C Chappell[4]

The UK Confidential Enquiries into Maternal Deaths have repeatedly highlighted inequities in the medical treatment of pregnant and postpartum women, noting

or breastfeeding allows safety concerns to be allayed for women, their families, and healthcare professionals.

1 National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK

2 Institute of Applied Health Research, University of Birmingham, Birmingham, UK

3 UK Obstetric Surveillance System

BMJ: first published a

RESEARCH

OPEN ACCESS

Check for updates

FAST TRACK

Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis

John Allotey,[1,2] Elena Stallings,[3,4] Mercedes Bonet,[5] Magnus Yap,[6] Shaunak Chatterjee,[6] Tania Kew,[6] Luke Debenham,[6] Anna Clavé Llavall,[6] Anushka Dixit,[6] Dengyi Zhou,[6] Rishab Balaji,[6] Siang Ing Lee,[1] Xiu Qiu,[7,8,9] Mingyang Yuan,[1,7] Dyuti Coomar,[1] Madelon van Wely,[10] Elizabeth van Leeuwen,[11] Elena Kostova,[10] Heinke Kunst,[12,13] Asma Khalil,[14] Simon Tiberi,[12,13] Vanessa Brizuela,[5] Nathalie Broutet,[5] Edna Kara,[3] Caron Rahn Kim,[5] Anna Thorson,[5] Olufemi T Oladapo,[5] Lynne Mofenson,[15] Javier Zamora,[3,4,16] Shakila Thangaratinam,[2,17] for PregCOV-19 Living Systematic Review Consortium

BMJ: first published as 10.1136/bmj.m33

UKOSS
UK Obstetric Surveillance System

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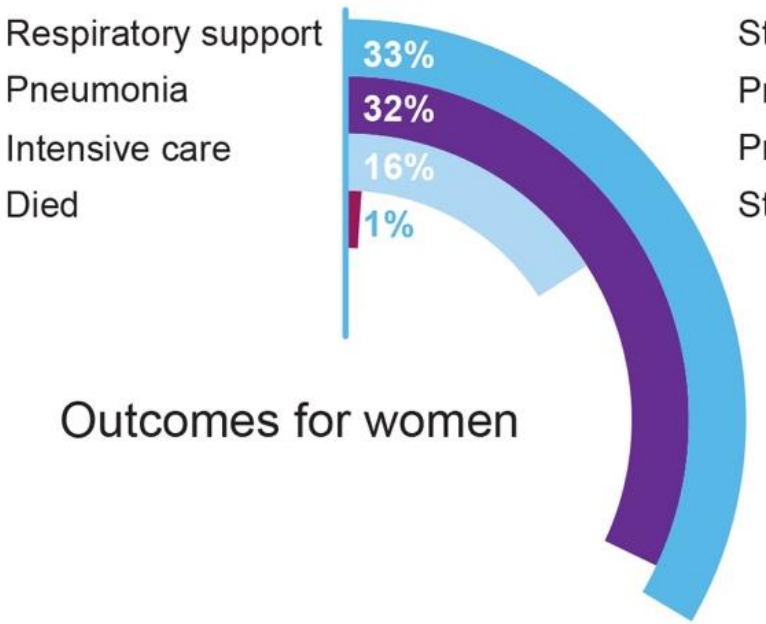
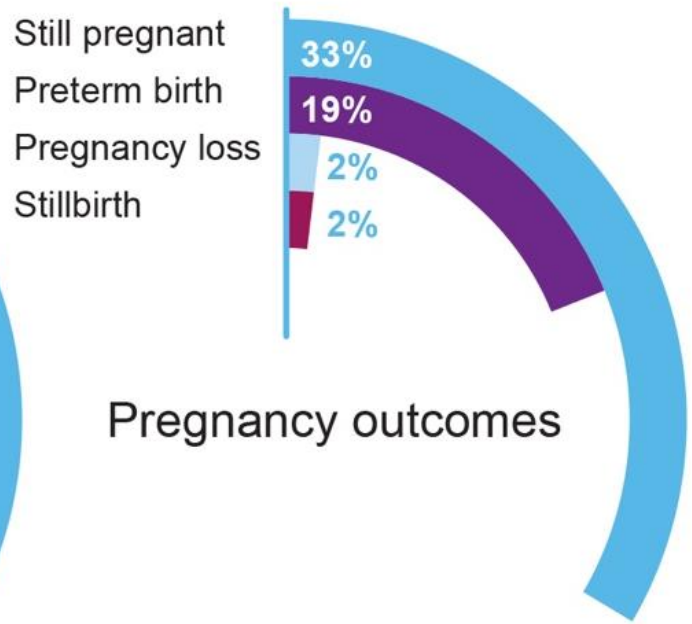
Outcomes of COVID-19 Delta for 1436 pregnant women admitted to hospital with symptoms

16th May 2021 to 31st October 2021



Outcomes for women



Pregnancy outcomes

Who is at greatest risk?

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- Risk of admission and risk of severe infection is greatest in:

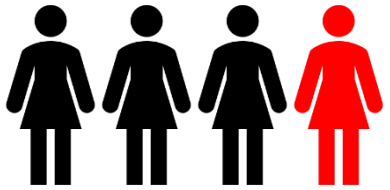
➢aged over 35	x 2.1	
➢BMI > 30	x 2.7	risk of
➢pre-existing comorbidity	70%	ICU admission[1]
➢non-White ethnicity	66%	
➢Third trimester	83% of those admitted	

https://www.medrxiv.org/content/10.1101/2021.07.22.21261000v1

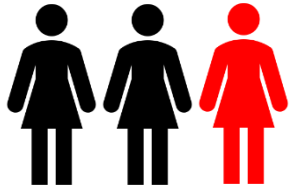
Disease severity

The proportion of hospitalized symptomatic women with moderate to severe COVID-19 has increased

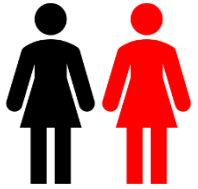
- First wave:



- Alpha variant:



- Delta variant:

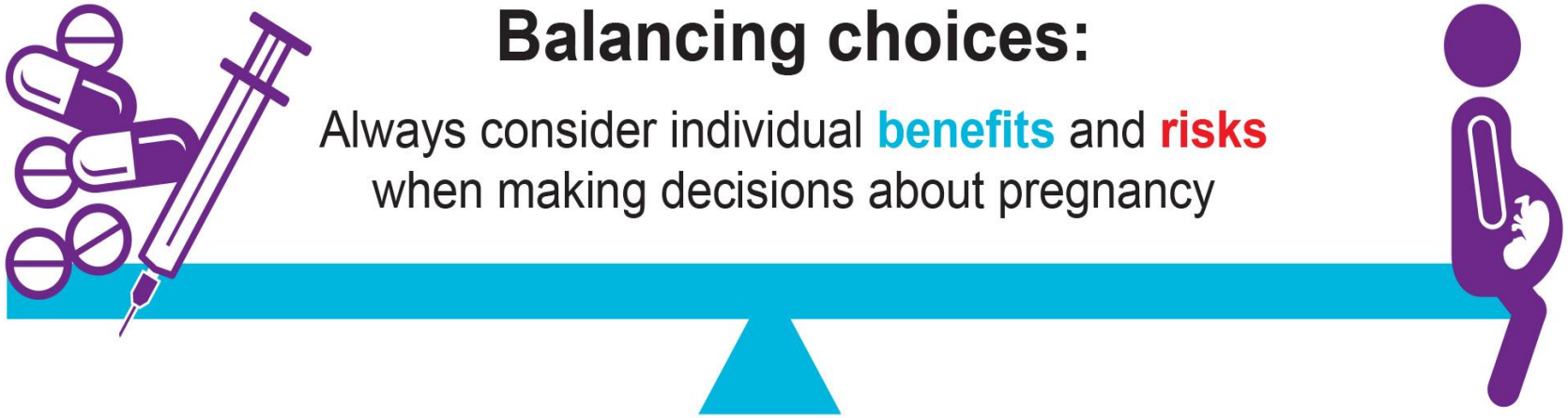


Pregnant and postpartum women appear disproportionately severely affected compared to non-pregnant people of reproductive age

https://www.medrxiv.org/content/10.1101/2021.07.22.21261000v1

Covid-specific medical therapies in pregnant women

- Covid-specific medical therapies are still used infrequently, even for women who are critically ill
- Steroids for maternal indication administered to only around a quarter of pregnant women admitted to intensive care



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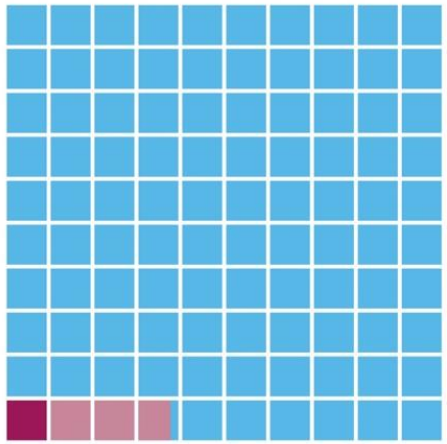
Hospital admissions with symptomatic COVID-19 in pregnancy

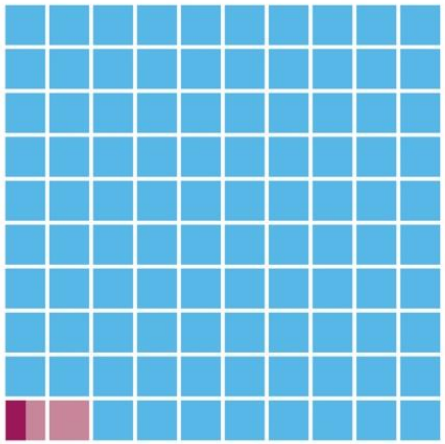
16th May 2021 to 31st October 2021

1436 pregnant women admitted to hospital with symptomatic COVID

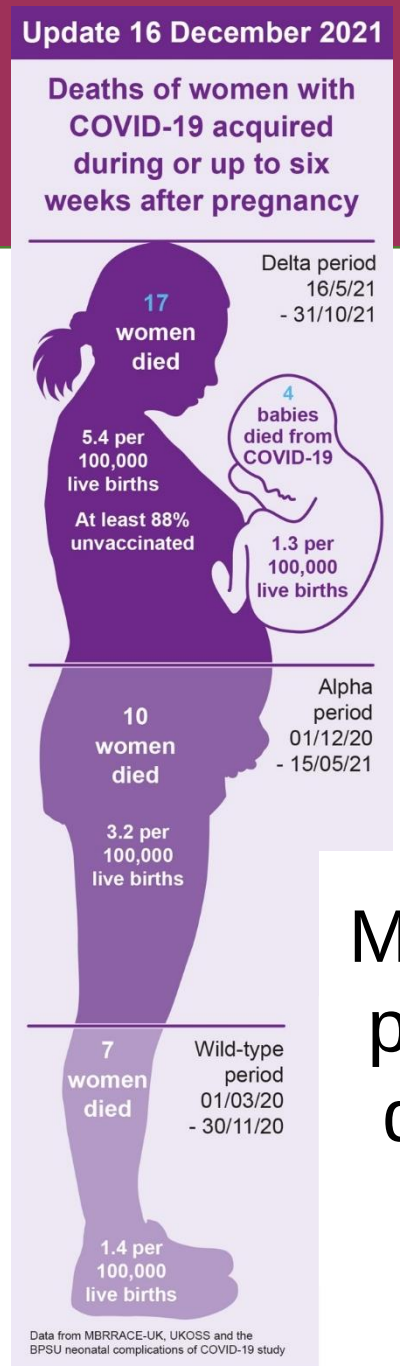


96.3% unvaccinated
2.6% one dose
1.1% two doses

230 of whom (16%) were admitted to intensive care



97.9% unvaccinated
1.7% one dose
0.4% two doses



MBRRACE-UK
Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK

Maternal deaths during pregnancy or up to 42 days after pregnancy with COVID-19

Update from UKOSS this week

Nuffield Department of POPULATION HEALTH
Medical Sciences Division
UNIVERSITY OF OXFORD

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UK Obstetric Surveillance System

Notifications by week

ICNARC data (critical care)

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ICNARC report on COVID-19 in critical care:

England, Wales and Northern Ireland

31 December 2021

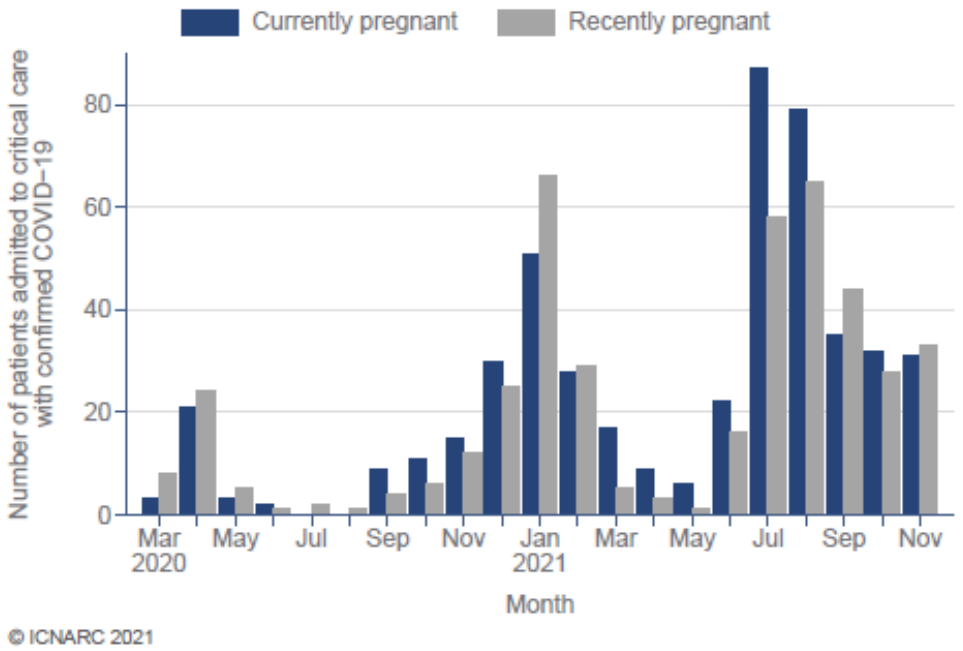

Figure 31. Numbers currently and recently pregnant

Monthly trend in the number of women reported to be currently or recently pregnant on admission to critical care.

Demographics	Patients with confirmed COVID-19 Admitted 1 May 2021 to date (N=13,058)	Admitted 1 Sep 2020-30 Apr 2021 (N=25,849)
Currently or recently pregnant, n (% of females aged 16-49) [N=2115]		
Currently pregnant	316 (14.9)	169 (7.4)
Recently pregnant (within 6 weeks)	257 (12.2)	150 (6.6)
Not known to be pregnant	1542 (72.9)	1970 (86.1)

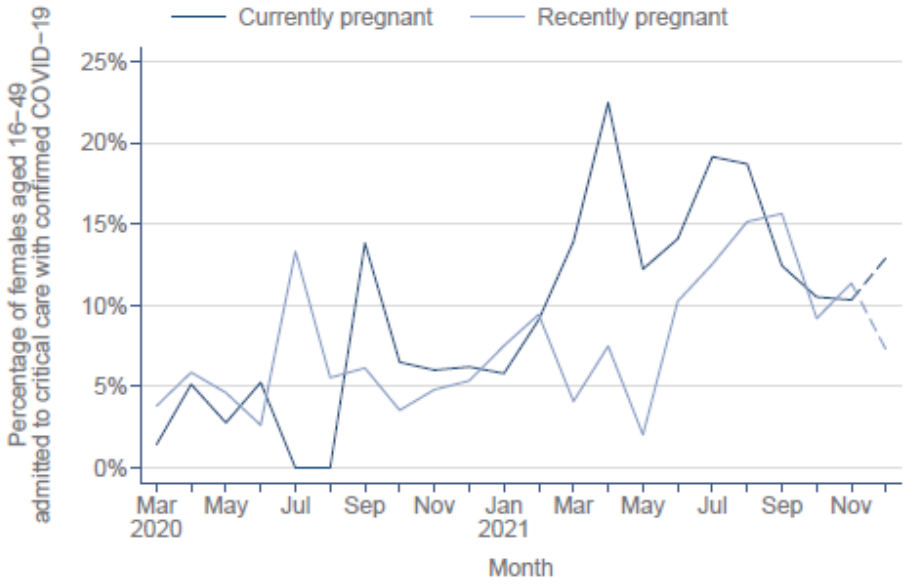

Figure 32. Percentages currently and recently pregnant

Monthly trend in the percentage of women aged 16-49 years reported to be currently or recently pregnant on admission to critical care.

Covid-19 and pregnancy: headlines

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- Covid-19 affects pregnant women – now moved into JCVI ‘at risk’ group
- Additional risk factors previously identified (ethnic minority groups, increasing gestation, higher maternal age, high BMI, pre-existing comorbidities)
- Impact on preterm birth continues to be major impact
- Ongoing evidence of increased maternal risk (ICU admission and maternal morbidity) and increased perinatal risk (stillbirth, neonatal death) – we don’t yet know with omicron, but likely to be similar in unvaccinated

- RECOVERY trial is one of few trials to include pregnant women, and has changed clinical practice, including for pregnant women

Covid-19 and pregnancy: RCOG

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THE ROYAL COLLEGE OF MIDWIVES

Royal College of Obstetricians & Gynaecologists

Coronavirus (COVID-19) Infection in Pregnancy

Information for healthcare professionals

Version 14: Published Wednesday 25 August

Quick reference summary of acute COVID-19 management in pregnancy

Quick reference only, see section 6 for further detail.

- Assess – admit, or discharge with clear advice about symptom deterioration and specific contact details.
- Oxygen to maintain saturations above 94%, escalating with e.g. nasal prongs, masks, CPAP, IPPV, ECMO
- No antibiotics unless additional bacterial infection suspected.
- LMWH for VTE prophylaxis
- Steroids if oxygen is needed (e.g. oral prednisolone 40 mg once daily or IV hydrocortisone 80 mg twice daily, with intramuscular dexamethasone 6 mg twice daily for four doses followed by oral prednisolone as below if fetal lung maturity is also required).
- MDT review – is escalation required? Does birth need expediting?
- Strongly consider tocilizumab (400 mg/600 mg/800 mg single IV infusion depending on weight) if C-reactive protein at or above 75 mg/l or in ICU.
- Strongly consider REGEN-COV monoclonal antibodies (8 g single IV infusion) in those with no SARS-CoV-2 antibodies.

Remdesivir should only be considered for those who are not improving or who are deteriorating.

Azithromycin, hydroxychloroquine and lopinavir/ritonavir have been shown to be ineffective and should not be offered.

Eligibility and outcomes (adults)

RECOVERY
Randomised Evaluation of COVID-19 Therapy

Eligibility criteria:

1. Hospitalised
2. Viral pneumonia syndrome (e.g. fever, cough, or shortness of breath with compatible chest X-ray findings not thought related to another cause)
3. **Confirmed SARS-CoV-2**
4. No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if they were to participate in the trial

Outcomes:

1. All-cause mortality by 28 days after randomisation
2. Duration of hospitalisation; need for mechanical ventilation or death

Current for adults with COVID-19

RECOVERY
Randomised Evaluation of COVID-19 Therapy

ELIGIBLE PATIENTS

High-dose corticosteroids (hypoxic)

E — High dose steroids *or* Usual care alone

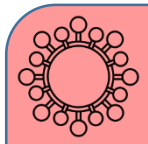
SGLT-2i comparison

F — Empagliflozin *or* Usual care alone

Baseline data collected
Participants enter ≥1 comparisons

R

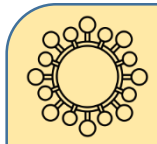
Outcomes collected at earliest of death, discharge or 28 days



Antiviral 1

J — Sotrovimab *or* Usual care alone

Protocol V21.1



Antiviral 2

K — Molnupiravir *or* Usual care alone

OUTCOMES

Current for pregnant adults with COVID-19

RECOVERY
Randomised Evaluation of COVID-19 Therapy

ELIGIBLE PATIENTS

High-dose corticosteroids (hypoxic)

E — High dose steroids *or* Usual care alone

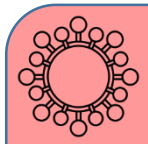
SGLT-2i comparison

F — Empagli[illegible] Usual care alone

Baseline data collected
Participants enter ≥1 comparisons

R

Outcomes collected at earliest of death, discharge or 28 days



Antiviral 1

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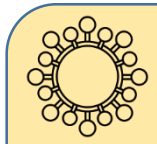
Protocol V21.1



Antiviral

K — Molnupi[illegible] [illegible]sual care alone

OUTCOMES

Current for pregnant adults with COVID-19

RECOVERY
Randomised Evaluation of COVID-19 Therapy

ELIGIBLE PATIENTS

High-dose corticosteroids (hypoxic)

E — High dose steroids *or* Usual care alone

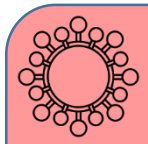
SGLT-2i comparison

F — Empagli[illegible] Usual care alone

Baseline data collected
Participants enter ≥1 comparisons

R

Outcomes collected at earliest of death, discharge or 28 days



Antiviral 1

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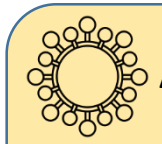
Protocol V21.1



Antiviral

K — Molnupi[illegible] [illegible]sual care alone

OUTCOMES

High dose steroids – pregnancy and postpartum

RECOVERY
Randomised Evaluation of COVID-19 Therapy

Pregnant women should receive **either**

- prednisolone (130 mg) orally **or**
- hydrocortisone (540 mg in divided doses) intravenously **or**
- methylprednisolone (100 mg) intravenously for five days

- followed by **either**
  - prednisolone (65 mg) orally **or**
  - hydrocortisone (270 mg in divided doses) intravenously **or**
  - methylprednisolone (50 mg) intravenously for five days.

Postpartum women – as above **or**

- Dexamethasone may also be considered as per the adult regimen (including if breastfeeding or expressing)
  - dexamethasone 20 mg (base) once daily by mouth, nasogastric tube or intravenous infusion for 5 days followed by dexamethasone 10 mg (base) once daily by mouth, nasogastric tube or intravenous infusion for 5 days

Current for pregnant adults with COVID-19

RECOVERY
Randomised Evaluation of COVID-19 Therapy

ELIGIBLE PATIENTS

High-dose corticosteroids (hypoxic)

E — High dose steroids *or* Usual care alone

SGLT-2i [illegible]

F — Empagli[illegible] Usual care alone

Baseline data collected
Participants enter ≥1 comparisons

R

Outcomes collected at earliest of death, discharge or 28 days

Antiviral 1

J — Sotrovimab *or* Usual care alone

Protocol V21.1

Antiviral [illegible]

K — Molnupi[illegible] [illegible]sual care alone

OUTCOMES

Sotrovimab in pregnancy and postpartum

RECOVERY
Randomised Evaluation of COVID-19 Therapy

- As the binding target for sotrovimab is unique to COVID-19 viral proteins, it is not expected that the administration of sotrovimab in pregnancy will affect fetal development
- No binding to human embryofetal proteins in a cross-reactive binding assay
- Therefore appropriate to offer sotrovimab to pregnant women with COVID-19 in a clinical trial setting as:
  - Potential for significant maternal and fetal benefit
  - No perceived fetal risks to treatment

We will be continuing to examine pregnancy outcomes using UKOSS

RECOVERY for pregnant women

RECOVERY
Randomised Evaluation of COVID-19 Therapy

Site teams

This page contains additional information for RECOVERY site team members. Follow these links for guidance on randomisation and how to collect follow-up data.

RECOVERY Privacy Notice for Trial Staff

INTERVENTION INFORMATION

RECOVERY intervention sheet - empagliflozin

RECOVERY intervention sheet - baricitinib

RECOVERY intervention sheet - tocilizumab

RECOVERY intervention sheet - dimethyl fumarate

RECOVERY position statement on baricitinib and tocilizumab

Measurement of additional early phase assessment outcomes SOP v1.3

GUIDES FOR SPECIFIC PATIENT GROUPS

RECOVERY for paediatric patients

RECOVERY for patients with chronic kidney disease

RECOVERY for pregnant and breastfeeding women

RECOVERY and remdesivir

COLLABORATORS' MEETINGS SLIDES

We apologise if you were unable to join the meetings.

26 April 2021	27 April 2021
22 February 2021	23 February 2021
25 January 2021	26 January 2021
4 January 2021	5 January 2021
7 December 2020	8 December 2020
16 November 2020	17 November 2020

Pregnancy information document

RECOVERY
Randomised Evaluation of COVID-19 Therapy

RANDOMISED EVALUATION OF COVID-19 THERAPY (RECOVERY)

for pregnant and breastfeeding women

Pregnancy lead: Prof Marian Knight

With support of UK Teratology Information Service (Dr Ken Hodson, Medical Director)

	RECOVERY trial protocol	Adaption for pregnancy
Eligibility	Patients are eligible if all of the following are true: i. Hospitalised ii. Confirmed SARS-CoV-2 iii. No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if they were to participate in the trial	Same eligibility
Interventions	**First randomisation part E** • High-dose corticosteroids **First randomisation part F** • Empagliflozin **First randomisation part J** • Sotrovimab **First randomisation part K** • Molnupiravir	Interventions for pregnant women • Substitution of corticosteroid (part E) iv hydrocortisone/iv methylprednisolone/ oral prednisolone (in place of dexamethasone) • Sotrovimab *Not recommended in pregnancy* • *Empagliflozin* • *Molnupiravir*
Follow-up/ outcomes	Ascertained at the time of death or discharge or at 28 days after randomisation (whichever is sooner): ➢ Vital status (alive/ dead, with date and presumed cause of death, if appropriate) ➢ Hospitalisation status (inpatient/ discharged, with date of discharge, if appropriate) ➢ Use of ventilation (none/ previous/ ongoing, with days of use and type, if appropriate) ➢ Use of renal dialysis or haemofiltration (none/ previous/ ongoing)	Same follow-up and outcomes, with **addition of UKOSS COVID-19 case number** (for pregnancy and baby information) to allow later data linkage
		Adaptions for breastfeeding
		Dexamethasone may be considered, otherwise the same interventions as in pregnancy should be used. UKOSS case number added if available.

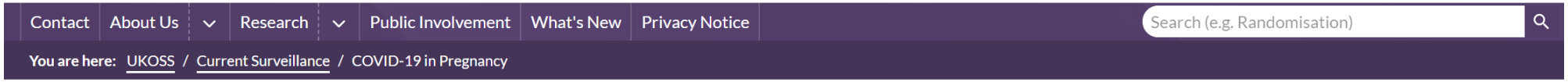
Follow-up = the same, + linkage

RECOVERY
Randomised Evaluation of COVID-19 Therapy

NPEU

Nuffield Department of
POPULATION HEALTH

UNIVERSITY OF OXFORD



COVID-19 in Pregnancy

UKOSS
UK Obstetric Surveillance System

Key points

- Covid-19 is an infectious disease caused by a new strain of coronavirus.
- Covid-19 had not been detected in humans before the outbreak in December 2019.
- As the virus is new, little is known about its effect on certain groups of people, including pregnant women.

Surveillance period

1st March 2020 – 31st March 2021

Background

On this page

Update on progress

RECOVERY
Randomised Evaluation of COVID-19 Therapy

- 160 pregnancy leads identified, supported by research midwives
- Midwife champions on board

- 134 pregnant or postpartum women recruited*
  - *4 with pregnancy/postpartum status to be confirmed

- 4 recruited in the most recent wave

Thank you

RECOVERY
Randomised Evaluation of COVID-19 Therapy

Ashford and St Peter's Hospitals NHS Foundation Trust	Leeds Teaching Hospitals NHS Trust	Oxford University Hospitals NHS Foundation Trust
Barts Health NHS Trust	Liverpool University Hospitals NHS Foundation Trust	Pennine Acute Hospitals NHS Trust
Bolton NHS Foundation Trust	Liverpool Women's NHS Foundation Trust	Royal Berkshire NHS Foundation Trust
Bradford Teaching Hospitals NHS Foundation Trust	Luton and Dunstable University Hospital NHS Foundation Trust	Royal Free London NHS Foundation Trust
Cambridge University Hospitals NHS Foundation Trust	Manchester University NHS Foundation Trust	Sheffield Teaching Hospitals NHS Foundation Trust
Chelsea and Westminster Hospital NHS Foundation Trust	Medway NHS Foundation Trust	Sherwood Forest Hospitals NHS Foundation Trust
Chesterfield Royal Hospital NHS Foundation Trust	Milton Keynes University Hospital NHS Foundation Trust	Shrewsbury and Telford Hospital NHS Trust
Croydon Health Services NHS Trust	NHS Greater Glasgow and Clyde: Glasgow Royal Infirmary	St George's University Hospitals NHS Foundation Trust
Epsom and St Helier University Hospitals NHS Trust	NHS Greater Glasgow and Clyde: Queen Elizabeth University Hospital	The Newcastle Upon Tyne Hospitals NHS Foundation Trust
Frimley Health NHS Foundation Trust	NHS Lothian: Royal Infirmary of Edinburgh	United Lincolnshire Hospitals NHS Trust
Guy's and St Thomas' NHS Foundation Trust	North Cumbria Integrated Care NHS Foundation Trust	University College London Hospitals NHS Foundation Trust
Imperial College Healthcare NHS Trust	North Tees and Hartlepool NHS Foundation Trust	University Hospitals Of Leicester NHS Trust
James Paget University Hospitals NHS Foundation Trust	North West Anglia NHS Foundation Trust	Western Sussex Hospitals NHS Foundation Trust
Kettering General Hospital NHS Foundation Trust	Northampton General Hospital NHS Trust	Worcestershire Acute Hospitals NHS Trust
King's College Hospital NHS Foundation Trust	Northumbria Healthcare NHS Foundation Trust	Wye Valley NHS Trust
Kingston Hospital NHS Foundation Trust	Nottingham University Hospitals NHS Trust	

Q&A

RECOVERY
Randomised Evaluation of COVID-19 Therapy