Evidence Update on COVID-19
Clinical trials prioritised by NIHR

This is not a clinical guideline or SOP. This is a summary of the latest evidence available internationally on the management, treatment and science underlying COVID-19 disease.

Interventional drug trials

RECOVERY Trial (clinical trials link)
Randomised Evaluation of COVID-19 Therapy

- Phase II/III trial
- Four treatment arms:
    1. No additional treatment
    2. Lopinavir 400mg - Ritonavir (anti-viral) 100mg by mouth every 12 hours for 10 days
    3. Dexamethasone (corticosteroid) oral or IV 6mg daily for 10 days
    4. Hydroxychloroquine (anti-malarial) by mouth for 10 days (800mg day 1, 400mg thereafter)
    5. Azithromycin (antibiotic) 500mg by mouth or IV one daily for 10 days
- Patient group: Hospitalised >18 years old with confirmed/suspected SARS-CoV2
- Primary outcome: Death or discharge after 28 days
- Location: UK
- Status: Recruiting (Total 2000 patients)

ACTT Trial (clinical trials link)
A multicenter, adaptive, randomised, double blinded, placebo controlled trial to investigate the safety and efficacy of novel therapeutics for the treatment of COVID-19 in hospitalised adults diagnosed with COVID-19

- Phase III
- Treatment:
    - Remdesivir - antiviral adenosine analogue which inserts into viral RNA, terminating them prematurely. Treatment for Ebola.
    - 200mg IV on day 1, then 100mg daily up to 10 days, or placebO
- Patient group: Hospitalised >18 years old with confirmed SARS-CoV2
- Primary outcome: Percentage of subjects reporting severity rating on 8 point scale at day 15 (scale ranges from non-hospitalised to death).
- Location: 54 locations globally including UK
- Status: Recruiting (Total 440 patients)

PRINCIPLE (ISRCTN link)
Platform Randomised trial of Interventions against COVID-19 in older people

- Phase III
- Treatment:
    - Hydroxychloroquine - antimalarial drug
    - 200mg oral tablet or placebo twice daily for 7 days
- Patient groups:
    - 50-64 years old with listed comorbidity
    - ⍰ 65 years old

- Primary outcome: Hospital admission or mortality within 28days
- Location: UK
- Status: Recruiting

REMAP-CAP (clinical trials link)

A randomised, embedded, multifactorial, adaptive platform trial designed to look at multiple treatments for community acquired pneumonia, with a pandemic appendix incorporated in response to COVID-19.

- Phase IV
- COVID domains:
  - Lopinavir 400mg + ritonavir 100mg every 12 hours for up to 14 days (oral or gastric tube)
  - Hydroxychloroquine 400mg every 8 hours (9 doses) then 200mg every 12 hours for 12 days (enterally)
  - Lopinavir/ritonavir and hydroxychloroquine at above doses
  - Interferon β 1a 10µg in 1ml saline, IV bolus daily for 6 days
  - Interleukin 1RA (Anakinra) 300mg daily via central or peripheral line for 6 days
- Patient group: Hospitalised (ICU) >18 years old with COVID-19
- Primary outcome: Days alive and outside ICU at 21 days
- Location: Global including UK
- Staus: Recruiting (Total 6800 patients)

5773 Safety and antiviral activity of remdesivir for severe COVID-9

A Randomised study for severe ventilated (mechanical and non-mechanical) COVID-19 patients

- Phase III
- Treatment:
  - Remdesivir - antiviral adenosine analogue which inserts into viral RNA, terminating them prematurely. Used for Ebola.
  - Not-mechanically ventilated: 200mg on day 1, then 100mg RDV for either days 2 to 5 or days 2 to 10 by IV infusion
  - Mechanically ventilated: 200mg on day 1, then 100mg for days 2 to 10 by IV infusion
- Patient group: Hospitalised >18 years old (or 12-18 years old >40kg) with confirmed SARS-CoV2 and SpO2 $\leq$94% at screening
- Primary outcome: odds ratio of improvement on 7-point ordinal scale on day 14
- Location: Global including UK
- Status: Recruiting (Total 2400 patients)

5774 Safety and antiviral activity of remdesivir for moderate COVID-9

A Randomised study for moderate COVID-19 patients

- Phase III
- Treatment:
  - Remdesivir - antiviral adenosine analogue which inserts into viral RNA, terminating them prematurely. Used for Ebola.
  - 200mg on day 1, then 100mg RDV for either days 2 to 5 or days 2 to 10 by IV infusion
  - Standard care

- Patient group: Hospitalised >18 years old (or 12-18 years old >40kg) with confirmed SARS-CoV-2 and SpO2 >94% at screening
- Primary outcome: odds ratio of improvement on 7-point ordinal scale on day 11
- Location: Global including UK
- Status: Recruiting (Total 1600 patients)

CANCOVID

A multi-center study to assess the efficacy and safety of canakinumab on COVID-19 pneumonia and cytokine release syndrome

- Phase III
- Treatment: Canakinumab - Monoclonal antibody against IL-1 β
- No further information available

COPCOV

Chloroquine prevention of COVID-19 in the healthcare setting; a randomised, placebo controlled prophylaxis study

- Treatment: 3 months
  - Asia - Chloroquine 10mg/kg loading dose, then 250mg daily
  - Europe - Hydroxychloroquine 10mg/kg loading dose then 200mg daily
  - Placebo
- Patient group: Frontline health care workers >16 years old
- Primary outcome: Number of symptomatic COVID-19 infections, severity of COVID-19 symptoms
- Location: Global including UK
- Status: Unknown (Total 40,000 patients)

COVACTA

Randomised, double blind, placebo-controlled, multi centre study for safety and efficacy of tocilizumab (TCZ) in COVID-19

- Phase III
- Treatment:
  - Tocilizumab - anti-IL-6 receptor monoclonal antibody
  - 1 IV dose of TCZ at 8 mg/kg, up to a maximum dose of 800 mg. Up to 1 additional dose may be given if no improvement or symptoms worsen.
  - Placebo dose
- Patient group: Hospitalised >18 years old with confirmed SARS-CoV2 and SPO2 </=93% or PaO2/FiO2 <300 mmHg
- Primary outcome: Clinical status using 7 category ordinal scale at day 28
- Location: Global including UK
- Status: Recruiting (Total 330 patients)

Comparing Efficacy and Safety of Inhaled SNG001 to Placebo

Randomised double blind, placebo controlled trial to determine the safety and efficacy of inhaled Interferon β 1a for the treatment of patients with confirmed COVID-19.

- Phase II
- Treatment:

    - SNG001, nebulised once daily for 14 days
    - Placebo
- Patient group: >18 years old with confirmed SARS-CoV-2 that are hospitalised or in the community if in a risk group: >65-years of age, hypertension, cardiovascular disease, diabetes or a chronic lung condition
- Primary outcome: change in condition measured using the Ordinal Scale for Clinical Improvement during the dosing period
- Location: UK
- Status: Recruiting (Total 400 patients)

RUXCOVID

Multi-centre study to assess the efficacy and safety of ruxolitinib on cytokine release syndrome in patients with COVID-19

- Phase III
- Treatment:
    - Ruxolitinib - Janus kinase (JAK) inhibitor - 10mg twice a day for 14 days, then 5mg twice a day for 2 days, then 5mg once a day for 1 day
- Patient group: >12 years old with COVID-19 infection and need for supplemental oxygen to maintain oxygen saturation above 93%
- Primary outcome: Proportion of patients who become critically ill (require mechanical ventilation and/or FiO2 of 60% or more) in 6 months, and adverse events
- Status: Recruiting (Total 64 patients)

STOP-COVID19

Superiority Trial of Protease inhibition in COVID19

- Treatment:
    - Brensocatib
- Patient group: Unknown
- Primary outcome: Unknown
- Location: UK
- Status: In setup

COV001 vaccine

A phase I/II study to determine the efficacy, safety and immunogenicity of the candidate COVID-19 vaccine ChAdOx1 nCoV-19 in UK healthy adult volunteers.

- Phase I/II
- Treatment:
    - Group 1:
        - Single dose of ChAdOx1 nCoV-19 5x10^10vp
        - Single dose MenACWY vaccine
    - Group 2:
        - Single dose ChAdOx1 nCoV-19 5x10^10vp
        - Single dose MenACWY vaccine
    - Group 3:

        - One dose of ChAdOx1 nCoV-19 5x10^10vp at week 0, then one dose at 2.5x10^10vp on week 4
    - Group 4:
        - Single dose ChAdOx1 nCoV-19 5x10^10vp
        - Single dose MenACWY vaccine
- Patient group: Healthy adults aged 18-55 years
- Primary outcome: Efficacy - number of virologically confirmed COVID-19 cases in 6 months. Safety - occurrence of serious adverse events in 6 months.
- Location: UK
- Status: Recruiting (Total 1112 patients)

REALIST

Repair of ARDS by Stromal Cell administration

- Phase I/II
- Treatment:
    - Transfusion of human umbilical cord derived CD362 enriched mesenchymal stem cells
    - Placebo infusion
- Patient group: Hospitalised with ARDS and confirmed SARS-CoV2 infection, >16 years old and on invasive mechanical ventilation, within 1 week of known insult
- Primary outcome: Oxygenation index and incidence of SAEs
- Location: UK
- Status: Recruiting (Total 75 patients)

Interventional procedural trials

DeVENT

Decision support system to evaluate VENTilation in ARDS - Beacon Caresytem device advices the healthcare worker how to best set the ventilator

- Intervention: Beacon Caresystem device attached to patients ventilator
    - Arm 1 - Beacon device activated
    - Arm 2 - Beacon device deactivated
- Patient group: Hospitalised with ARDS, >18 years old and on invasive mechanical ventilation, within 1 week of known insult, and evidence of pulmonary oedema and hypoxia
- Primary outcome: average driving pressure of mechanical ventilator
- Location: UK, France, Austria
- Status: Recruiting (Total 110 patients,, 50 in the UK and 30 in each of the other 2 sites)

RECOVERY - RS

Recovery Respiratory support: respiratory strategies in COVID-19; CPAP, high-flow and standard care. An adaptive, pragmatic, randomised, controlled, open-label, multicenter effectiveness trial

- Phase III trial
- Three treatment arms:
    1. CPAP according to local practice
    2. High flow nasal oxygen according to local practise
    3. Standard care

- Patient group: Hospitalised >18 years old, critically ill patients with suspected or confirmed COVID-19
- Primary outcome: Intubation rate and mortality up to 30 days
- Location: UK
- Status: Recruiting (Total 4002 patients)

Observational studies - all ages

ISARIC

Clinical characterisation protocol for severe emerging infection with weekly reporting

- Observation:
  - Clinical data reporting
  - Biological samples (blood, nasopharyngeal swab, sputum, urine, stool) for COVID-19 detection
- Patient group: All COVID-19 positive patients
- Location: UK
- Status: Recruiting

DIAMOND SEARCH v1

Diagnosis and management of febrile illness using RNA personalised molecular signature diagnosis - checking genes to diagnose infectious and inflammatory disease

- Observation:
  - Clinical data reporting
  - Biological samples (blood, nasopharyngeal swab, sputum, urine, stool) for COVID-19 detection
- Patient group: All COVID-19 positive patients
- Location: Global (EU funded)
- Status: In setup

FLU-CATs

Evaluation and refinement of pandemic influenza community assessment tools. Real time refinement and validation of criteria and tools used in primary care to aid hospital referral decisions for patients of all ages in the event of a surge during an influenza pandemic.

- Observation: Prospective analysis linking criteria in a GPs assessment of patients with influenza like illness to immediate management decisions and patient outcomes
- Patient group: All ages
- Location: UK
- Status: Recruiting

GenOMICC

Genetics of mortality in critical care - identification of specific genes that cause people to become susceptible to specific infections and consequences of severe injury

- Observation: Blood samples for DNA analysis
- Patient group: All patients with confirmed COVID-19 in critical care
- Location: UK
- Status: Recruiting

PRIEST

Pandemic respiratory infection emergency system triage - aims to optimise triage of people using emergency care system with suspected infection during COVID-19 pandemic, and identify the most accurate triage methods for predicting severe illness.

- Observation: Analyse patient data and evaluate triage methods based on whether they predict serious complications or recommend unnecessary hospital admissions, and modify/develop triage methods to improve this
- Patient group: All patients with confirmed COVID-19 in critical care
- Location: UK
- Status: Recruiting

VIrus Watch

Investigate the extent of the spread of COVID-19 within communities and how social distancing affects the risk of infection

- Observation: Unknown
- Patient group: Unknown
- Location: UK
- Status: In setup (25000 patients)

Observational studies - children and teenagers

Coronavirus infection in primary or secondary immunosuppressed children

Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology

- Observation: Self reporting of experiences and illnesses during COVID-19 pandemic
- Patient group: 16-17 year old immunocompromised children (and their parents)
- Location: UK
- Status: Recruiting

What's the STORY

Serum testing of representative youngsters - sero-epidemiological survey of England.

- Observation: Use serology testing to detect antibodies against COVID-19 in children, adolescents and young adults to determine the proportion that have immunity, and allow modelling of the circulation of SARS-CoV2.
- Patient group: Children aged 0-24 years
- Location: UK
- Status: Recruiting (2300 patients)

Neonatal complications of coronavirus disease

- Observation: Surveillance of neonatal outcomes
- Patient group: Neonates <29 days old with COVID-19 or born to mothers with COVID-19 and needing neonatal care
- Location: UK
- Status: In setup

Observational studies - Pregnant women

UKOSS: Pandemic Influenza in Pregnancy

- Observation: Use the UK Obstetric surveillance system to collect data on pregnancy women with COVID-19 and provide continuous updates on guidance for pregnant women to improve outcomes for women and their babies.
- Patient group: Pregnant women aged 16-45 years admitted to hospital with COVID-19 infection
- Location: UK
- Status: Recruiting

PAN-COVID

Pregnancy and neonatal outcomes in COVID-19

- Observation: Construction of a global database detailing the outcomes for both mother and baby, in women with suspected and confirmed COVID-19. To understand the natural history of SARS-CoV2 and guide treatment and prevention.
- Patient group: Pregnant women with COVID-19 infection
- Location: Global
- Status: In setup

Pre-clinical trials

nCOV: Developing CoV-bnMABs for therapy of highly pathogenic coronaviruses including SARS-CoV2

Develop antibodies to target coronaviruses to provide antibody therapy.

- Location: Unknown
- Status: Unknown

Rapid development of manufacturing processes for future production of adenovirus-vectored COVID-19 vaccine at million-dose scale

- Location: UK
- Status: Unknown

Repurposing FDA-Approved drugs for treatment of 2019 nCoV induced disease

Test library of 100 drugs in vitro to determine if effective against SARS-Cov2 using infected epithelial cells

- Location: UK
- Status: Unknown