How research nurses and midwives are supporting Covid-19 clinical trials

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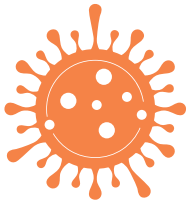
In this article...

- The research taking place into possible treatments for Covid-19
- How the pandemic has affected standard research delivery practices
- How research staff have adapted to overcome the challenges Covid-19 poses

How research nurses and midwives are supporting Covid-19 clinical trials



Key points

Research is a key part of the government's response to the pandemic; trusts were encouraged to support and run studies endorsed by the four chief medical officers

Most existing studies were suspended and research teams redeployed into clinical practice Covid-19 research

Many Covid-19 studies are identifying and testing drugs that may help treat symptoms or reduce the disease's impact

Standard research practices have required changes due to severely ill patients, absent family members and infection control

The pandemic has highlighted the importance of research and the vital role of clinical research nurses and midwives

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Abstract In response to the coronavirus pandemic, many clinical trials have tested existing drugs that may help treat Covid-19. NHS trusts have been encouraged to prioritise studies approved by the four chief medical officers, and clinical research nurses and midwives have been crucial to the delivery of these studies. Adaptations to standard research practices have been required – the consent process has been changed to reflect patients' loss of capacity and the absence of family members, while the collection of biological samples and other patient data has required research nurses and midwives to find solutions to being in an isolation environment. Results of early studies have identified some initial treatment options for patients; many other studies are ongoing.

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Clinical research has been a key part of the government's response to the coronavirus pandemic and its plan to contain, delay, research and mitigate (Scally et al, 2020). To date, Covid-19 research has mainly focused on clinical trials to:

- Identify and plot the course of the disease to better understand it;
- Identify and test existing drugs that may help treat symptoms or reduce the impact of the virus;
- Test a vaccine.

Clinical research nurses and midwives have been central to the rapid implementation of these clinical trials (Jones et al, 2020). Nurses and midwives working on wards and in clinical departments during the pandemic may also have supported or seen research staff collecting patients' consent and data; these are the most visible elements of delivering clinical trials. There is less knowledge and awareness of the huge 'behind-the-scenes' effort and organisation required to enable patients across the UK to contribute, through research, to understanding and treating the virus.

This article illustrates how research delivery, along with the work of clinical research nurses and midwives, has been crucial in underpinning the research effort during the coronavirus pandemic. In particular, it focuses on the challenges of, and adaptations to, informed consent, data collection and drug delivery in the high-risk context of Covid-19 care in hospitals, and includes specific examples. It also highlights the varied practices and innovations applied by research nurses and midwives across organisations.

AUKLRN

Covid-19 research studies

Developing drugs to treat new diseases is often a long, involved process that takes 10-15 years. In response to the emergence of SARS-Cov-2, the novel coronavirus responsible for the current pandemic, research became key. To identify potential treatments in a timely manner, researchers and pharmaceutical companies focused on drugs that had already been tested and licensed to treat inflammatory diseases (such as rheumatoid arthritis) or viral pathogens (such as Ebola and HIV) in the hope that they would effectively treat Covid-19, the disease caused by SARS-Cov-2.

Tocilizumab is one such drug: this biological anti-inflammatory therapy licensed for the treatment of rheumatoid arthritis is being trialled to investigate whether it ameliorates the cytokine cascade (whole-body acute inflammatory response) seen in severe cases of Covid-19 and, thus, improves outcomes.

One drug already shown to be beneficial is remdesivir, a broad-spectrum anti-viral medication developed to treat Ebola. Progress has been swift and early results show it reduces hospitalised patients' recovery time by 30%; the drug is now available for the treatment of adults and children with severe Covid-19 (Beigel et al, 2020).

Data from the RECOVERY trial (Box 1) has reported that treating patients on respiratory support with dexamethasone reduces mortality by 36% for those who are ventilated and 18% for those on oxygen (RECOVERY Collaborative Group, 2020).

These are just a few examples from the vast amount of ongoing research; by mid-May 2020, more than 1,000 Covid-19 clinical trials involving >150 treatments were running globally (Bit.ly/ABPIPharmCovid).

Clinical research is a routine aspect of most acute trusts' workload. Research teams can be found across many key areas, such as oncology, haematology, cardiovascular disease and musculoskeletal disease. Most acute trusts develop a bespoke portfolio of recruiting studies based on their clinical specialties and some develop their own specialist research teams in rare disease areas. At the onset of the coronavirus pandemic, however, a more centralised system of research trials was developed.

To maximise patient recruitment and swiftly identify beneficial therapeutic options that could be developed into treatment pathways, trusts were encouraged to prioritise studies approved by the UK's four chief medical officers (CMOs). Many of these studies use an adaptive platform design, in which a single master protocol enables multiple drugs to be evaluated simultaneously. This design means a study can adapt to include or discontinue treatment arms as new information emerges, to ensure the most up-to-date treatment options are available (Saville and Berry, 2016). As such, research nurses and midwives have needed to learn quickly about such trials and the drug treatments used.

Box 1 illustrates some of the CMO-endorsed studies that research nurses and midwives have been supporting.

Box 1. UK prioritised, CMO-endorsed Covid-19 research trials

RECOVERY trial

This is a randomised trial of adults, maternity patients and children hospitalised for confirmed Covid-19. Eligible participants are randomly allocated to one of several treatment arms, each of which offers an intervention given in addition to the usual standard of care. The main aim of the study is to review the effect of each treatment on in-hospital death, discharge and need for ventilation. Current treatment arms include:

- Lopinavir-ritonavir (commonly used to treat HIV) – initial treatment arm; now discontinued as no benefit found
- Low-dose dexamethasone (a steroid used for a range of conditions, typically to reduce inflammation) – now only recruiting children, already licensed for use in adults
- Azithromycin (a commonly used antibiotic)
- Tocilizumab (an anti-inflammatory treatment given by injection)
- Convalescent plasma (collected from donors who have recovered from Covid-19; contains antibodies against the SARS-Cov-2 virus)

Read more at Bit.ly/RECOVERYtrial

REMAP-CAP trial

This trial aims to determine the best range of treatments for patients who become severely ill and are admitted to intensive care units due to Covid-19. It is evaluating:

- Different antiviral drugs
- Steroids to reduce inflammation
- Treatments that act on the immune system and are often used to treat other conditions, such as rheumatoid arthritis (interferon-ß1a, anakinra, tocilizumab and sarilumab)

The trial will investigate how these drugs work in combination, with additional treatments added over time.

Read more at Bit.ly/REMAP-CAPtrial

RECOVERY-RS trial

This is a respiratory support trial. People who have been intubated and ventilated are excluded. Eligible patients are randomised to receive one of three treatment options:

- High-flow nasal oxygen (HFNO)
- Continuous positive airway pressure (CPAP)
- Standard care for patients diagnosed with Covid-19

The study aims to determine whether HFNO or CPAP is clinically effective compared with standard care.

Read more at Bit.ly/RECOVERY-RStrial

CMO = chief medical officer

Challenges for research nurses and midwives

Clinical research nurses and midwives have been pivotal in the early set-up and implementation of CMO-endorsed Covid-19 research trials; this has, ultimately, enabled treatment options to be offered to patients for a disease that has no known cure. At the start of the pandemic, most existing research studies were suspended; only those essential to patient safety continued, supported by a skeleton research workforce. Some research teams were redeployed clinically to support areas such as intensive care, while others quickly adapted to infectious disease research.

Standard research procedures include identifying potential participants, supporting the informed-consent process, collecting biological samples, collecting clinical and demographic data, and delivering novel trial drugs. Supporting participants and their families during the clinical and trial procedures is also a key part of a research nurse or midwife's role. For Covid-19 trials, it has been necessary to

adapt and innovate so these procedures can be delivered within a context of severely ill patients, absent family and the required isolation and infection control procedures.

Informed consent

Gaining informed consent has been a notable challenge. In normal circumstances, potential trial participants receive verbal and written information and time to consider the particular study, with discussions often involving their family or GP. They must show they fully comprehend the study and its personal impact and have the capacity to give their consent (Biros, 2018). However, many patients admitted to hospital with Covid-19 are too unwell to fully engage with the standard practices of taking informed consent and demonstrating capacity. In these situations:

- Clinical research doctors and nurses try to explain the study to potential participants and receive verbal consent;
- An independent doctor or nurse from the clinical team is present to verify that the study is in the patient's best interests, the patient receives an explanation of what is involved and verbally agrees to participate;
- A witness consent form is signed by the independent clinician, not the patient.

Obtaining consent from patients who are so unwell they have lost capacity has presented different challenges. Ordinarily, in this situation, the next of kin is consulted and asked to give consent on the patient's behalf; however, during the pandemic, relatives have been unable to visit patients, so this has not been possible. Instead, a clinician responsible for the patient's care, but independent of the trial, acts as a legal representative and gives consent on the patient's behalf, confirming participation is in their best interest. Whenever possible, this has been preceded by a telephone discussion with the patient's relatives to ensure they are informed.

The logistics of complying with infection prevention and control (IPC) measures has also posed challenges. It is a regulatory requirement to take three copies of the signed consent form: one is for the patient, one remains in patient's notes, and the other is filed in the research study folder. In line with IPC guidance, items from the room or bed area of a patient who is Covid-19 positive must be quarantined for 5-14 days (depending on local policy) before they can be fully accessed. Usual practices have, therefore, needed to be reviewed to ensure compliance.

Teams have developed various solutions to navigate this issue, including:

- Photographing the consent form through a bay or side room internal window, then uploading the photo using the secure application Pando;
- Taking consent from a witness who can sign the consent form away from the Covid-19-positive area so the usual governance processes can be followed.

QUICK FACT

190,000
UK patients who have participated in Covid-19 research

Data collection

Additional hurdles exist around data collection, as this usually involves use of paper-based documents to record procedures and clinical and demographic data. Restrictions on removing paperwork from a Covid-19-positive environment have meant research data must be added to a patient's electronic care record via a PC or tablet; data extraction and entry into specific trial databases is then required at a later date.

As there have been so many patients with Covid-19 in ward areas, much data has been collected by research nurses and practitioners. Research nurses shielding at home also made a significant contribution by supporting this remotely. A huge benefit has been the ability to upload data in real time – as an example, live information from the national database for the International Severe Acute Respiratory and Emerging Infection Consortium's coronavirus clinical characterisation consortium was shared with the government to help guide decisions and policies around the UK's response to the pandemic.

Sample collection

The collection and processing of blood and other biological samples have also been complicated by IPC measures. To reduce the number of staff exposed to Covid-19 and conserve personal protective equipment, research staff collaborated closely with clinical nurses and phlebotomists, combining the collection of routine and research samples to reduce both teams' workloads.

Samples placed into a high-risk biological sample bag in a Covid-19 area are transferred at the door of the isolation bay or room into a clean sample bag, which is held by a nurse or researcher on the 'clean' side of the door. As the samples are infected, laboratory processing requires a specialist class 2 hood for air extraction. When sample processing was at its busiest, class 2 hoods were not always available; this necessitated support from external laboratories and volunteer laboratory staff with the required specialist skills.

Drug delivery

The administration of clinical trial drugs also poses challenges. Dispensing and administering trial drugs follows standard procedures, but patients are randomised to receive either the active drug or a placebo. This, along with the fact that the labelling and handling of clinical trial drugs is often different to (and more complicated) that of regular medicines, has put extra pressure on pharmacy departments that are already stretched.

When drugs are on a ward, IPC measures and documenting trial drugs also add to the complexity of administration.

Conclusion

The pandemic has taught us that we need to be 'research ready' for public health emergencies and that emergency plans need to include careful consideration of the research workforce. Flexibility and contingency planning must be built into research protocols so they are practical and feasible to implement in a pandemic. Solutions must be found to enable all patients affected by infectious diseases to participate in research if they so wish.

Clinical research nurses, midwives and practitioners have enabled >130,000 UK patients to participate in Covid-19 research, classified as "urgent public-health research", over a very short period of time (National Institute for Health Research, 2020). Their adaptability, skill and commitment to finding viable treatments and vaccines highlight the need to recognise, train and retain this crucial group. **NT**

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