



FEATURE

MEDICAL RESEARCH

RECOVERY trial: the UK covid-19 study resetting expectations for clinical trials

Emma Wilkinson talks to the researchers who recruited 7000 NHS patients in a few weeks

Emma Wilkinson

Sheffield

In a short space of time, doctors and researchers have learnt a lot about how covid-19 progresses in the people infected. There's even a handful of potential treatments—but no good evidence on whether they work or do harm.

Yet, as soon as this coming June, the RECOVERY trial may be able to provide clinicians with some answers. With 7586 NHS patients signed up from 172 sites around the UK (as of 24 April; live figures are available at www.recoverytrial.net/for-site-staff), the stunning pace of this recruitment is in keeping with a trial that went from concept to first patient in less than a fortnight.

Martin Landray, professor of medicine and epidemiology at the University of Oxford, and his colleagues knew that delays in setting up clinical trials had hampered efforts in treating Ebola. By the time everything was in place the outbreak had passed, and, when the next wave hit, clinicians were back to square one. So, at the start of March, while watching the pandemic unfold in Italy, Landray and colleagues realised that they had a window to prepare—and to do it at a speed completely unheard of in clinical trials. “On Tuesday we wrote the protocol and on Friday submitted it [for ethics approval],” he says. “Nine days after we wrote the protocol the first patient was enrolled.”

Dynamic design

RECOVERY aims to evaluate drugs with the potential to help patients admitted to hospital with confirmed covid-19. The team took the pragmatic approach that to include a drug would require a reason to believe that it might work, a known safety profile, and enough of a supply for a large trial. The design is dynamic, with the expectation that drugs will be added and removed as the evidence changes or as new candidates are developed.

Patients are being randomly assigned to usual care or to one of four treatments: lopinavir-ritonavir, low dose dexamethasone, hydroxychloroquine, or azithromycin. The team has also just gained additional approval for patients who meet specific criteria to be randomly allocated a second time, to a tocilizumab arm.

The main outcomes are death, discharge, need for ventilation, and need for renal replacement therapy at 28 days.

This is the largest trial being conducted for covid-19 anywhere, the researchers say. Peter Horby, trial co-leader and professor of emerging infectious diseases and global health, says that its size is critical. He explains, “I've been involved in fairly small scale trials, and what you often find is that you don't see a significant effect, and that leads to a drug being ditched because they are not powered to identify modest but important findings. “With this kind of acute severe viral pneumonia it is going to be very challenging to find something that will have a dramatic effect, and we should be designing trials accordingly.”

United (Kingdom) effort

Anthony Kerry, consultant respiratory physician at the Great Western Hospitals NHS Trust in Wiltshire, says that his hospital has recruited 57 patients in 20 days thanks to a large team of clinicians, research nurses, and pharmacists who have worked to make this happen. “People have been ignited to take part, and it's really very well spread across large parts of the UK,” he says—“and that gives us quality in terms of numbers but also a range across the UK population.”

A few factors make the UK well placed to get this kind of study ready so quickly. A nation united in its support for the NHS is one key aspect, says Kerry, who believes that the unique nature of the NHS as an “idea” that people can really get behind has helped the speed of recruitment. Landray also highlights key advantages in terms of regulation and ethics, a good NHS trials platform, central funding, and control over drug supplies, as well as having the chief medical officers write to every trust to urge them to take part.

Yet the investigators knew that they would need to scrap much of the usual bureaucracy whereby trials of this size usually take months, if not years, to set up. “For all of us, that was quite refreshing,” says Landray. “We had this opportunity to focus

on what really needs to be done and not be distracted by the minutiae.”

Everything was streamlined, with all documents freely available online, including the protocol and approval. “What we are seeing is what happens when people are empowered and motivated,” Landray adds.

Obstacles remain, most notably in getting timely data from primary and secondary care, which will be especially important in the long term. And only 10% of potential patients are currently signed up, suggesting that there is scope to do more.

So far, recruitment has surpassed expectations—but it will, of course, be results that matter. “If we knew the answer we would

have been doing that all along,” says Landray. “There are a number of people who think these drugs are wonderful and some who think the drugs are terrible, but none of them can prove that they’re right.”

Correction: On 29 April we amended Martin Landray’s quote in the fourth paragraph to remove an incorrect statement.

Competing interests: I have read and understood BMJ policy on declaration of interests and have no relevant interests to declare.

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