World view

By Nicole Mather

How we accelerated clinical trials in the age of COVID-19

The United Kingdom's RECOVERY trial shows a way to benefit patients faster.

In March, as the tsunami of COVID-19 hit Europe, it became obvious that the virus could overwhelm the United Kingdom's National Health Service (NHS). To address this issue, colleagues and I repurposed infrastructure so that clinical trials could safely get data about more treatments from more patients more quickly.

This allowed the NHS to run the biggest randomized COVID-19 clinical trial in the world – and to identify a treatment, amid the heat of the epidemic, without bypassing regulatory processes. It built on investment in programmes and infrastructure established in 2017 as government strategy, when I was director of the Office for Life Sciences.

We worked nights and weekends to pivot NHS DigiTrials services – which had been set up in 2019 for planning large clinical trials – towards providing more kinds of information, including patient results, and applied the new services to the ambitious RECOVERY trial. This trial, based at the University of Oxford, aims to rapidly test a range of potential treatments for people ill with COVID-19. If any such treatments work, moving faster could save more lives.

On 16 June , RECOVERY announced that dexamethasone, a commonly available steroid, could reduce mortality by one-third in people with severe respiratory complications owing to COVID-19. Remarkably, this study encompassed 12,000 patients and 176 sites over a 3-month period. Looking back, I see ideas that could be broadly applied to accelerate trials around the world.

The RECOVERY trial had five key features that distinguish it from a standard approach. It had a short, flexible protocol – just 20 pages long – that laid out the design and data and regulatory requirements, and allowed trial arms to be halted or added. It received ethical and regulatory approval in just 9 days, compared with the standard 30–60 days. Its recruitment procedures were straightforward, with only a two-page consent form and a one-page bedside form to be completed by clinicians. It accelerated data collection and processing through NHS DigiTrials. And it quickly made results public – the announcement was followed by a preprint on the medRxiv server and journal publication within a month (The RECOVERY Collaborative Group. *N. Engl. J. Med.* http://doi.org/gg5c8p; 2020).

What lessons can be applied to trials in the future? How can we revamp procedures and leverage technology to accelerate findings, and do so without sacrificing transparency, patient involvement and peer review?

First, streamline bureaucracy. We've gone so far towards managing risk that we've created layers of bureaucracy that absorb time and money, and, paradoxically, increase the risk that beneficial treatments are not tested – or worse, that ineffective treatments are used widely in the rush to 'do something'. Clinical-trial protocols, ethical-consent forms and patient-information leaflets can run to thousands of words. Review processes can take months, requiring different data sets and sequential approvals.

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There is no excuse – we must pare down to the key questions to accelerate the process. Some early lessons came during the West Africa Ebola outbreak. During Ebola, and again during COVID-19, the UK Medicines and Healthcare Products Regulatory Agency (MHRA) prioritized and processed clinical-trial applications within a week. During COVID-19, the Health Research Authority (HRA) reduced the average ethical-review cycle from 60 to 10 days.

In the longer term, any approach to prioritization needs careful consideration and consultation, but coordinating regulatory functions can accelerate the process. For example, the Combined Ways of Working pilot programme, launched in 2018, allows clinical-trial applications to be submitted for concurrent review by the MHRA and HRA.

Second, leverage data systems. The RECOVERY trial benefited from UK investments in NHS health-data systems. That includes the work of our NHS DigiTrials team – a consortium of NHS Digital, my team at IBM, the University of Oxford and Microsoft. These data systems meant that only minimal demographic and consent data had to be collected at a patient's bedside and were then integrated with routine NHS information on treatment, diagnosis, COVID-19 tests, clinical results and survival.

Third, enable trust. Accelerating research during COVID-19 meant less opportunity to engage patients in the design and delivery of trials. As trials restart, we must broaden efforts to involve patients and the public. To engender trust in the use of health data for research, and to explain its potential to transform care, we need to work with institutions in which the public has confidence, such as charities or non-governmental organizations.

Fourth, maintain transparency. RECOVERY aimed to balance rapid sharing and expert review. The full protocol and core documents are available on a public website. Key results were made available through public statements, and fuller details were published as preprints simultaneously with submission to a peer-reviewed journal. Results were shared with major international groups such as the World Health Organization. NHS hospitals were urged to adopt the use of dexamethasone within hours of the public announcement.

All these lessons are broadly applicable to many countries. As we turn our attention back to other major causes of illness and death – such as cancer, and cardiovascular and neurodegenerative diseases – we should apply the lessons from COVID-19 to streamline clinical trials and deliver effective treatments.

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