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Increasing recruitment into covid-19 trials

An urgent priority for the NHS

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Since March 2020, UK researchers have established over 70 urgent public health studies to investigate potential treatments, vaccines, and diagnostic tests for covid-19. NHS hospitals have had a vital role in delivering these studies at pace and scale, despite working under extreme pressure. The results are now informing practice worldwide.

In June 2020, the Recovery trial found that dexamethasone, a widely available corticosteroid, improved survival among covid-19 patients on ventilation by 36% (28 day mortality rate ratio 0.64; 95% confidence interval 0.51 to 0.81).[1] The NHS immediately made it the standard of care, and it is estimated to have averted 12 000 deaths in the UK up to the end of 2020 and 650 000 worldwide.[2]

Trials save lives. They cannot do so, however, without the participants on which they depend. Recruitment of patients with covid-19 to UK clinical trials must now be prioritised. Although vaccines against SARS-CoV-2 are a cause for optimism, they do not mean that the virus will be eradicated. The pandemic remains a national and international emergency, and it is imperative efforts continue to find new, safe, and effective treatments to lessen its severity and impact, in the UK and globally.

Enrolment into Recovery, which passed 20 000 patients in December, has varied between 7% and 10% of hospital admissions for covid-19. This achievement has been possible only because everyone within the NHS has risen collectively to the challenge.[3]

Recruitment rates vary substantially across the NHS, however, leaving plenty of opportunity to improve participation. While some hospitals (such as trusts in Leicester and Hartlepool) have recruited 25-50% of patients admitted with covid-19, others have recruited less than 5% of admissions, and some less than 2%.

Recovery continues to evaluate convalescent plasma, monoclonal neutralising antibodies (REGN-COV2), aspirin, and colchicine. In the case of convalescent plasma and REGN-COV2, it is important not to miss benefits that might be confined to patients with early disease or those unable to mount a good antibody response themselves. Doubling the rate of recruitment would halve the time taken to get clear answers to important questions about these treatments.

The Remap-Cap trial,[4] based in intensive care units and designed to evaluate treatments for the sickest patients, has shown that the corticosteroid hydrocortisone has similar effects on mortality to dexamethasone. The trial recruits around 20% of all patients in UK intensive care units but also has variation among hospitals and therefore scope for further improvement.

The largest community based covid-19 trial in the UK, Principle,[5 6] evaluates treatments to prevent hospital admission or transmission, including doxycycline and inhaled budesonide. Recruitment has been slow because of the disruption of primary care during the first wave, reaching 2000 participants in December. To aid recruitment Principle now allows patients to participate remotely regardless of the location of their registered general practitioner.

Integrating research into routine care

Although we acknowledge the extreme pressure currently felt throughout the NHS, all hospitals, clinics, and general practices should do all they can to make trial recruitment a priority, advancing efforts to improve survival and recovery from covid-19. Senior leadership that valued research and encouraged its integration into routine clinical care was a key factor in hospitals with good recruitment during the first wave. Everyone should be involved, both doctors and nurses, senior and junior.

All eligible patients should be offered the opportunity to take part in a clinical trial, whenever feasible, and research should become part of the clinical pathway for patients with covid-19 in the NHS. In this national emergency, we should all explore options for boosting research and enrolment resources, including staff that can be made available “out of hours” or over weekends.

Individual trusts throughout the UK and academic university partners could support recruitment into trials in several ways. These include online and digitally enabled (smart phone) messaging of trial requirements and locations to patients, clear signposting to further information, access to trial recruitment advice for clinicians and patients, and local clinical and research champions who could coordinate trial participation.

This crisis provides an opportunity to embed large scale randomised trials at the heart of NHS care. Such an approach could transform the way the NHS evaluates and deploys treatments for common chronic diseases and emergencies, including heart disease, diabetes, degenerative musculoskeletal disorders, cancers, and seasonal influenza. All have a major effect on patients’ lives and place a substantial burden on the health service.

The Recovery trial has shown that such approaches can be tailored to understand better the role of existing drugs (dexamethasone, hydroxychloroquine) as well as novel treatments (REGN-COV2). Delivering

similar trials across the whole country would increase participation of both patients and frontline NHS staff in critical research, and improve the robustness and generalisability of the results. Engagement from all NHS hospitals is vital in achieving this goal.

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