Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

systolic blood pressure levels from less than 120 mm Hg to more than 170 mm Hg, extending observations from epidemiological studies.[1] In agreement with previous reports,[3,4] antihypertensive treatment appears to reduce incident stroke and heart failure by a greater extent than ischaemic heart disease. However, the reported benefit at low entry systolic blood pressure in patients with a high proportion (75%) of ischaemic heart disease suggests that the risk of blood pressure lowering in this group of patients (ie, a J-curve for risk) might not be a problem in most patients.

Of note, this systematic review could not include all eligible trials, which is an inherent limitation of all individual participant data meta-analyses. However, the investigators assessed the risk of acquisition bias, and also did sensitivity analyses excluding trials, without important effects on their findings. The findings might not be generalisable to patient groups with concomitant conditions not studied in these analyses (eg, heart failure).

The similar relative benefits of treatment in primary and secondary prevention presented in the study by the BPLTTC[9] indicate that the cardiovascular risk of an individual will be a major determinant of the absolute benefit of treatment, confirming the importance of risk assessment in individual patients.[10] These findings have important implications for clinical practice, and suggest that antihypertensive treatment might be considered for any person for whom the absolute risk for a future cardiovascular event is sufficiently high. This suggestion calls for simple, reliable multivariable risk prediction tools made readily available in the electronic health record systems used by health-care providers. The use of patient self-reported computerised medical history taking could facilitate such development.[11] Taken together, decisions about offering people antihypertensive treatment are all about cardiovascular risk reduction.

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Tocilizumab in COVID-19: some clarity amid controversy

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Hyperactivation of the immune response, including release of pro-inflammatory cytokines such as interleukin-6 (IL-6), might play a key role in the pathophysiology of severe illness from COVID-19.[1] Consistent with this notion, one of the few therapies that reduces mortality in hospitalised patients with COVID-19 is the corticosteroid, dexamethasone.[2] Accordingly, there has been great interest in examining whether treatment with additional, more targeted anti-inflammatory agents beyond steroids could provide further benefit.

Tocilizumab is a recombinant humanised monoclonal antibody that inhibits binding of IL-6 to both membrane and soluble IL-6 receptors. Early observations from

Tempura/Getty Images

China suggested improved outcomes in hospitalised patients with COVID-19 who received tocilizumab.[3] These preliminary reports were followed by large observational studies in critically ill patients with COVID-19, which suggested a mortality benefit with tocilizumab.[4] Subsequent randomised clinical trials examining tocilizumab reported conflicting results, but these trials differed considerably in size, study design, and illness severity of the patients enrolled. For instance, several initial trials[5–7] failed to show a mortality benefit for tocilizumab, but these trials enrolled fewer than 300 patients each and were thus underpowered to detect differences in death between groups.[8] Additional limitations of early trials were exclusion of critically ill patients[5,7] and imbalances in the use of steroids between tocilizumab-treated and tocilizumab-untreated patients.[9] The Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) study published in 2021 was, until now, the largest trial (n=803) to examine tocilizumab in COVID-19, and showed a survival benefit.[10] However, as REMAP-CAP was limited to critically ill patients, the role of tocilizumab for hospitalised but non-critically ill patients with COVID-19 remained unclear.

In *The Lancet*, the Randomised Evaluation of COVID-19 Therapy (RECOVERY) Collaborative Group reports its findings from the largest trial of tocilizumab to date.[11] Particularly in light of the conflicting findings from the heterogeneous and generally underpowered studies described in the foregoing, the importance of the findings from the RECOVERY trial cannot be overstated. RECOVERY is a multicentre, randomised, controlled, open-label, platform trial that was designed to examine the role of several treatments in patients hospitalised with COVID-19 in the UK. In a herculean effort, the investigators recruited more than 27 000 hospitalised adults with clinically suspected or confirmed SARS-CoV-2 infection from 177 sites in the UK between April 14, 2020, and Jan 24, 2021, randomly assigning them to one of several treatment groups. Patients were eligible for random assignment to tocilizumab versus usual care if they had hypoxia (oxygen saturation <92% on room air or requirement for supplemental oxygen), systemic inflammation (C-reactive protein ≥75 mg/L), and no clear evidence of an active infection other than SARS-CoV-2.

In total, 4116 adults were randomly assigned to tocilizumab (n=2022) or usual care (n=2094), several times more patients than in all previous randomised trials of tocilizumab combined. The mean age was 63·6 years (SD 13·6), 2774 patients (67%) were male, and 3018 (73%) were White. The median time from hospitalisation to random assignment was 2 days (IQR 1–5 days), and 562 patients (14%) were receiving invasive mechanical ventilation at the time of random assignment. Most patients (82% in both groups) were receiving systemic corticosteroids at the time of random assignment, in contrast to some earlier tocilizumab trials. The primary outcome, all-cause mortality within 28 days of random assignment, occurred in 35% of patients allocated to usual care and 31% of patients allocated to tocilizumab (rate ratio 0·85; 95% CI, 0·76–0·95; p=0·0028). Patients in the tocilizumab group were also more likely to be discharged from the hospital within 28 days than patients in the usual care group.

The RECOVERY trial investigators should be commended for this substantial investigation, the results of which will undoubtedly have major implications for the treatment of hospitalised patients with COVID-19. However, several limitations should be mentioned. First, the study was open label, and thus participants and local study staff were unmasked to the treatment allocation. Second, one of the concerns surrounding tocilizumab use in patients with COVID-19 is the risk of secondary infection, and although tocilizumab did not result in any deaths from secondary infection, the investigators did not collect data on non-fatal infections or other adverse events. Third, important physiological data regarding hypoxaemia, such as longitudinal assessment of the partial pressure of arterial oxygen to the fraction of inspired oxygen, were not collected. Fourth, only 1837 (91%) of 2022 patients in the tocilizumab group and 1918 (92%) of 2094 patients in the usual care group had data available on study drug receipt. Fifth, among the 1837 patients assigned to tocilizumab with data available on study drug receipt, only 1534 (84%) actually received the drug. However, the net effect of this crossover in an intention-to-treat analysis would be to bias the results toward the null, and thus the reported results are probably an underestimate of the true benefit of tocilizumab in reducing death. Finally, given that patients with COVID-19 often have a prolonged hospital course, it is unclear whether a reduction in 28-day mortality will

translate into longer-term mortality benefit, and we look forward to the preplanned analyses at 6 months.

In summary, the RECOVERY trial provides the most definitive evidence thus far to address the controversy over whether tocilizumab should be added to our armamentarium of treatments for severely ill patients with COVID-19. The answer is yes. Questions remain about tocilizumab's efficacy and safety in other settings, such as those with C-reactive protein concentrations of less than 75 mg/L and among paediatric patients (the RECOVERY group is doing a separate trial in children, which is ongoing), and among more gender and racially diverse populations. Importantly, the 28-day mortality rate of 31% in the tocilizumab group, although lower than the placebo group, remains unacceptably high, and thus additional therapies are urgently needed to further reduce mortality in severely ill patients with COVID-19. Several treatments, including other immunomodulators and antibodies against the spike protein of SARS-CoV-2, are under investigation.[12]

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Hospital admissions due to COVID-19 in Scotland after one dose of vaccine

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The BNT162b2 mRNA vaccine from Pfizer–BioNTech[1] and the ChAdOx1 nCoV-19 vaccine from Oxford–AstraZeneca[2] were the first two products deployed in the UK's COVID-19 vaccination programme. In accordance with the strategy set by the nation's Joint Committee on Vaccination and Immunisation (JCVI), vaccines were initially prioritised for care home residents and staff, individuals older than 80 years, and front-line health-care and social care workers. In December, 2020, in response to surging transmission of SARS-CoV-2, JCVI advised delaying the second dose of these vaccines to achieve broader population coverage with the first dose.[3]

In *The Lancet*, Eleftheria Vasileiou and colleagues[4] report the interim findings following COVID-19 mass vaccination with a first dose in Scotland. The analysis includes 1 331 993 individuals vaccinated between Dec 8, 2020, and Feb 22, 2021. The authors constructed this comprehensive cohort by linking vaccination, primary care, laboratory testing, hospital admission, and mortality datasets covering 5·4 million people in Scotland. By Feb 22, 2021, an impressive 78·6% of adults aged 80 years and older, 85·9% of adults aged 65–79 years, and 13·9% of adults aged 18–64 years had received at least one dose of the vaccine. Uptake was higher in women than in men, with 35·1% of women and 25·0% of men vaccinated by this date.

Randomised vaccine trials of these products reported only small numbers of severe COVID-19 cases and hospital admissions. In contrast, the real-world data from Scotland captured 723 hospital admissions due to COVID-19 among