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.

COVID-19 mRNA vaccination and myocarditis or pericarditis

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In April, 2021, international news media first reported rare cases of young men in Israel who had developed myocarditis shortly after vaccination with the Pfizer-BioNTech mRNA vaccine against SARS-CoV-2.[1] Since then, many observational studies from Asia,[2] Europe,[3–5] the Middle East,[6,7] and North America[8,9] have found COVID-19 mRNA vaccination to be associated with a short-term increased risk of myocarditis. Furthermore, this association has been established using multiple types of analysis, including comparisons of observed-to-expected rates,[6,8,9] case-control studies,[2] self-controlled cases series,[3,4] and cohort studies.[4,5,7]

In *The Lancet*, Hui-Lee Wong and colleagues[10] robustly replicate the previous findings using large-scale US health plan claims data. Notably, the new study uses data from four health plan databases, covering more than 100 million individuals. Of these, 15 148 369 were aged 18–64 years and registered to have received a COVID-19 mRNA vaccine (53·1% male and 13·0% aged 18–25 years). Similar to previous studies, Wong and colleagues[10] observed higher than expected rates of myocarditis (and pericarditis, a closely related clinical presentation), specifically in individuals younger than 35 years, with the highest risk among men aged 18–25 years after their second COVID-19 mRNA vaccine dose. The absolute risk of myocarditis or pericarditis, calculated as the incidence rate within 1–7 days of vaccination, for men aged 18–25 years after a second vaccination dose was 2·17 (95% CI 1·55–3·04) cases per 100 000 person-days for the Moderna vaccine, mRNA-1273, and 1·71 (1·31–2·23) cases per 100 000 person-days for the Pfizer-BioNTech vaccine, BNT162b2. Furthermore, the study supports the previous finding that the association is principally short term. The data indicate that this adverse event primarily occurs within 1–7 days of vaccination, because a longer duration of follow-up attenuated the association. Although not significantly different, the study found a tendency towards a higher risk of myocarditis after vaccination with mRNA-1273 in a head-to-head comparison with BNT162b2 (with an adjusted incidence rate ratio of 1·43 [95% CI 0·88–2·34] among men aged 18–25 years). Similar findings of a more pronounced risk of myocarditis after mRNA-1273 in comparison with BNT162b2 have been observed in other large observational studies.[3–5,9]

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Despite being both stringent and relevant, the study by Wong and colleagues has some limitations. First, the use of historical comparators, in this case from the year 2019, is potentially problematic. Historical shifts in hospital use (and thereby in disease incidence rates), which is probable during a pandemic, could skew the magnitude of the association. Second, increased awareness about myocarditis and pericarditis in the population could have lowered barriers to health-care-seeking behaviour and hospital admission, possibly contributing to surveillance bias. Third, the use of claims databases as the source of study material provides little specification of the demographic composition of the study population, with no information on the race, ethnicity, or socioeconomic background of the individuals studied. Fourth, the study includes only individuals with health-care insurance, restricting its generalisability. Nevertheless, the findings by Wong and colleagues[10] are analogous to the other major observational studies on this topic, supporting the overall validity of their approach.

There are still two major unanswered research questions: firstly, are there any long-term consequences of vaccine-associated myocarditis; and secondly, what is the biological mechanism linking COVID-19 mRNA vaccination to these rare cases of acute myocarditis and pericarditis?

Although the long-term outcomes of vaccine-associated myocarditis and pericarditis are unclear,

the current knowledge on the short-term clinical trajectories are reassuring. The clinical presentations of myocarditis after COVID-19 mRNA vaccination have been predominantly mild and few patients have required intensive treatment.[9] However, one case-series, published in 2022, of adolescent patients found a persistence of radiographic abnormalities at follow-up examinations, which could be cause for concern.[11] However, the patients followed up had excellent clinical outcomes, suggesting minimal chronic morbidity attributable to vaccine-associated myocarditis. Nevertheless, the continuous surveillance of this patient group for any increased frequency of heart failure, sudden death, or related cardiac comorbidities is necessary.

With regard to the underlying disease mechanism, it is necessary to note that myocarditis and pericarditis are not novel side-effects of vaccination. Other vaccinations, especially smallpox vaccination, have previously been associated with a similar increased risk of myocarditis.[12] These findings suggest that the disease mechanism is specific neither to the newly developed mRNA vaccines nor to exposure to the SARS-CoV-2 spike protein. Other mechanisms have been suggested, yet hard evidence explaining the association is absent. Future mechanistic studies into potential mechanisms are therefore warranted and could provide valuable insight, leading to even safer COVID-19 mRNA vaccines.

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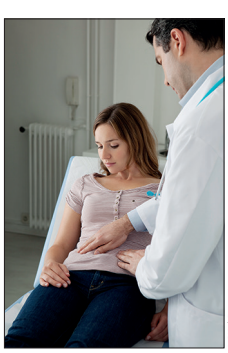
Head-to-head biologic therapy in Crohn's disease

The therapeutic armamentarium for the chronic inflammatory bowel diseases—Crohn's disease and ulcerative colitis—is rapidly expanding, yet treatment failure remains common, with substantial impact upon patients' quality of life and health-care costs, including hospitalisation and surgery.[1] There is increasing emphasis on the attainment of deep remission with mucosal healing in the hope of improving outcomes,[2] leading to a shift in treatment paradigm towards top-down therapy, with early use of biologic therapy increasingly favoured over conventional therapy (corticosteroids and immunomodulators). Three classes of biologic therapy are currently widely used in Crohn's disease, all targeting distinct inflammatory pathways: the tumour necrosis factor (TNF) antagonist therapies infliximab and adalimumab; the interleukin-12/23 inhibitor ustekinumab; and the integrin inhibitor vedolizumab, which have variable efficacy and safety profiles. Although the optimal positioning of these therapies is of great importance, head-to-head trials are scarce and there has been reliance on retrospective studies and indirect comparisons through network meta-analyses.

In *The Lancet*, Bruce Sands and colleagues[3] report the findings of a multicentre, randomised, controlled trial (SEAVUE) that compared the efficacy and safety of ustekinumab and adalimumab in 386 biologic-naive patients (mean age 37·2 years [SD 13·1]; 201 (52%)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