EMJ COVID-19 monthly top five (June 2021)

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Rajesh Chatha, Matthew Reed, Harriet Jennings, Aaron McClatchey, Abdelrahman Shahin, Camilla Williamson, Brian McGowan, Govind Oliver

Edited by Govind Oliver on behalf of the Royal College of Emergency Medicine (RCEM) COVID-19 CPD team

Following from the successful 'RCEM weekly top five' series starting in April 2020, this is the eighth of a monthly format for *Emergency Medicine Journal* (EMJ) readers. We have undertaken a focused search of the PubMed literature using a standardised COVID-19 search string. Our search between 1 and 31 May 2021 returned 2654 papers limited to human subjects and English language. We also searched high-impact journals for papers of interest.

Our team have narrowed down the most interesting, relevant and important of the papers and provided a critical snapshot of five of those we felt most deserved EMJ readers' attention. Importantly, we have highlighted not only the main findings from the papers but also key limitations and considerations for EM clinicians when interpreting the work. In doing so, we have created an accessible window into pertinent research findings for our busy colleagues during this fast-paced and ever-changing COVID-19 landscape.

The papers are ranked in one of three categories, allowing you to focus on the papers that are most vital to your practice:

- Worth a peek—interesting, but not yet ready for prime time.
- Head turner—new concepts.
- Game changer—this paper could/should change practice.

This month's searches were undertaken by the Emergency Medicine Research Group Edinburgh based at Royal Infirmary of Edinburgh. We look forward to next month's instalment from the team back in Manchester with a change in direction for the Journal Update as we expand to include studies beyond COVID-19.

COVID-19 vaccine coverage in healthcare workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (siren): a prospective, multicentre, cohort study

Topic: prevention

Rating: game changer

Vaccine platform efficacy remains at the core of public health policy with figures ranging between 62.1% and 95% in large-scale phase III trials, depending on the vaccine and population.[1–7]

The SIREN study, a UK healthcare worker cohort study, assessed the early effectiveness of vaccination against infection over the initial 8-week period following vaccination. Participants underwent fortnightly COVID-19 PCR testing and 4 weekly antibody testing. The primary outcomes were the number of people vaccinated and the number of SARS-CoV-2 infections.

The study included 23 324 participants, of which 89% had received one vaccine dose and 8% had received their second dose. Of those vaccinated, 94% received the BNT162b2 (Pfizer) vaccine. Groups which were less likely to be vaccinated included women, individuals aged under 35, minority ethnic groups, individuals living in areas of higher deprivation and individuals with certain jobs, such as porters.

The BNT162b2 vaccine was 70% effective at 21 days after initial dose, and 85% effective at 7 days after second dose. It was found to be effective against the B.1.1.7 (WHO Alpha/Kent) variant of concern. Interestingly, vaccinated individuals were less likely to display typical COVID-19 symptoms and more likely to be asymptomatic compared with those in the cohort that had not been vaccinated.

This is less than the 95% efficacy quoted in the original phase III trial,[2] which may result in study population differences. It may also result from the BNT162b2 vaccine not being effective against the new variants.

Bottom line: The BNT162b2 vaccine is effective in reducing COVID-19 infection rates in healthcare workers but does not eliminate risk completely. Continued testing and personal protective equipment remain essential.

Arterial events, venous thromboembolism, thrombocytopenia and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study

Topic: vaccine complications

Outcome rating: head turner

Concerns regarding vaccine side effects have been prominent in the press.[8] This population-based cohort study was undertaken to assess rates of cardiovascular and haemostatic events in the first 28 days after the first dose of ChAdOx1-S vaccination in Denmark and Norway.

The study included 281 264 people aged 18–65 who were vaccinated over a 6-week period; 73.6% of these had full 28-day follow-up. The excess events per 100 000 vaccinations were statistically significant with respect to venous thromboembolic events (11, 95% CI 5.6 to 17.0) and cerebral venous thrombosis (2.5, 95% CI 0.9 to 5.2). No increase in intracerebral haemorrhage, thrombocytopenia or bleeding was observed. Fewer arterial events (83 vs 86 expected) and deaths (15 vs 44 expected) were observed in the vaccinated cohort compared with the expected event rate in the general population.

Despite the increased rate of venous thromboembolism, it is rare (estimated at a rate of 13.6 per million following first dose in the UK),[9] which may explain why it was missed in the original phase III trial.[3] These events are thought to result from the ChAdOx1 vaccine constituents causing the formation of antiplatelet factor 4 antibodies.[10]

A weakness of the study was the event capture was dependent on the accuracy of coding by clinicians, which may have led to under-reporting. Furthermore, at the time of the study, the ChAdOx1-S vaccine was mainly being given to healthcare workers. The population therefore may not be representative of the wider population and limit the generalisability of findings.

Bottom line: This study demonstrates an increased rate of venous thromboembolism in those who received the ChAdOx1-S vaccine; however, when compared with risk of thromboembolism with COVID-19, which is estimated as 42.8 per million in a US cohort, the risk is small.[9]

Characteristics of COVID-19 patients with bacterial coinfection admitted to the hospital from the emergency department in a large regional healthcare system

Topic: treatment

Rating: worth a peek

As many patients with COVID-19 present with fever and respiratory symptoms, it is not unreasonable to consider empirical antibiotic treatment.[11 12] Some national guidelines recommended antimicrobial prescription to cover for coinfection or atypical pneumonias.

This retrospective study sought to describe the rate of bacteraemia associated with COVID-19. It reviewed all adult patients admitted to 14 hospitals' emergency departments, across the state of Indiana, with PCR-confirmed COVID-19 infection over a 6-week period. The primary outcome was the rate of bacteraemia. The secondary outcomes were clinical and laboratory features that may indicate bacteraemia. Of 542 patients admitted with confirmed COVID-19 infection, 395 had blood cultures performed on admission, with six (1.1%) true-positive results. An additional 14 (2.6%) patients had positive respiratory cultures treated as true pathogens in the first 72 hours. Independent predictors for bacteraemia were low blood pressure and elevated white blood cell count, neutrophil count, blood urea and lactate.

A study limitation is the inclusion of only patients with PCR-confirmed COVID-19. The overall rate of bacteraemia or bacterial infection may be different in patients with 'suspected COVID-19', and since COVID-19 PCR results may not be available early in the patient admission, this evidence does not inform our initial decision on empirical antibiotics.

Once a patient is confirmed to have COVID-19, the study findings suggest that the rate of concurrent bacterial infection is likely quite low, and therefore it may be safe at this point to stop antibiotic treatment.

Bottom line: This study found low rates of bacteraemia in patients admitted with COVID-19 infection, and in haemodynamically stable patients, antibiotics may not be indicated.

Frontline interdisciplinary clinician perspectives on caring for patients with COVID-19: a qualitative study

Topic: well-being

Outcome rating: worth a peek

How to support frontline workers remains a topic of focus.[13] This study aimed to evaluate factors contributing to clinician distress and motivation during the COVID-19 pandemic. Semistructured interviews were conducted with 50 (32 women and 18 men) frontline healthcare workers and thematically analysed. Volunteers were purposively sampled to allow for representation from a variety of professional backgrounds (physicians, nurses, paramedics and advanced practitioners).

The key themes identified as factors in clinician distress were (1) depersonalisation and barriers to care; (2) powerlessness in uncertainty; and (3) physical, emotional and mental exhaustion, whereas supportive factors included (1) being driven by moral duty and (2) activities bolstering morale and confidence.

Using their identified key themes, the authors formed a list of suggestions for healthcare organisations to help address some of the issues raised. These include visible leadership, clear communication of guidelines and policies, childcare for healthcare workers, transparency, peer support and clinical updates.

A particularly poignant finding was the increased distress among clinicians bearing witness to healthcare inequalities such as vulnerable patient groups having disproportionately higher rates of COVID-19. Addressing these inequalities was strongly advocated.

The study is single centre and non-UK based, which limits the generalisability of these findings. It was also conducted quite early in the pandemic, and the temporal changes in perspectives on these same issues over the pandemic also need to be considered.

Bottom line: Psychological distress faced by clinicians during the COVID-19 pandemic is multifactorial. Healthcare organisations may wish to consider targeted approaches that reduce the emotional burden on frontline staff.

Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised controlled, open-label, platform trial

Topic: Treatment

Rating: head turner

Convalescent plasma has been used for over a century as passive immunotherapy for influenza pneumonia, but whether it has a role in COVID-19 is not understood.[14]

The randomised, controlled, open-label, platform trial (Randomised Evaluation of COVID-19 Therapy) is assessing several possible treatments in patients hospitalised with COVID-19 in the UK. It is underway at 177 NHS hospitals. This part of the study aimed to evaluate the efficacy and safety of convalescent plasma in patients hospitalised with COVID-19. Of 16 287 enrolled patients, 11 558 (71%) were eligible to receive convalescent plasma and were assigned to either the convalescent plasma group or usual care. There was no significant difference in 28-day mortality between the two groups: 1399 (24%) of 5795 patients in the convalescent plasma group and 1408 (24%) of 5763 patients in the usual care group died within 28 days (rate ratio 1.00, 95% CI 0.93 to 1.07; p=0.95). This study had nearly eight times as many patients as previous studies combined. The authors performed a meta-analysis combining this trial's data and those of previous studies. This also showed no significant improvement in mortality with a combined mortality rate ratio of 0.98 (95% CI 0.91 to 1.06, p=0.63).

The are some important limitations. These findings are for late-stage severe COVID-19, where viral replication may not be the main driver of illness severity and factors such as immune-mediated response have more of a role. The clinical efficacy of convalescent plasma may also rely on the variant the donor and recipient were exposed to matching.

Bottom line: In patients hospitalised with COVID-19, high-titre convalescent plasma does not improve survival.

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