

Another week, another top 5! The team has sorted through thousands of papers, and here are the papers that deserve your attention. If you have the head space for ten more fantastic papers check out the Director's Cut. If you would prefer an interactive live journal club, then keep an eye on social media for confirmation of when the next one will be.



The following papers have been split into 3 categories that will allow you to focus on those 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 should change practice

Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients with Severe and Life Threatening COVID-19: A Randomized Clinical Trial by Li et al ¹

Topic: Treatment

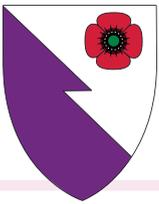
Rating: Head Turner

Scout: Dr Daniel Darbyshire



Based on positive evidence in other illnesses, plasma has been taken from recovered COVID-19 patients and given those who have active disease. This study is an open-labelled RCT from seven centres in Wuhan. Patients were randomised to convalescent plasma or routine care, stratified by severity. The trial was planned to include 200 patients but stopped recruitment at 103 as the outbreak in Wuhan was brought under control. The primary outcome was clinical improvement at 28 days (defined as discharge from hospital or a 2-point improvement on the 6-point disease severity scale). The authors found a difference for those with severe disease, but not life-threatening disease. When taken together there was no significant difference. An accompanying editorial postulates that the effect on those with severe disease might be due to them receiving the treatment earlier than those with life-threatening disease. This may be the case, but it could also be that the treatment is leading to harm in an unmeasured subgroup. The authors should be applauded for the study's endeavour, not reaching sample size because the outbreak was controlled can only be a positive thing overall. However, we are still left unsure what to do about convalescent plasma.





Use of renin-angiotensin-aldosterone system inhibitors and risk of COVID-19 requiring admission to hospital: a case-population study by Abajo et al ²

Topic: Treatment

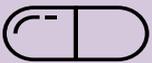
Rating: Head Turner

Scout: Dr Gaby Prager



The role of ACE in SARS-CoV2 infection has been much discussed. There were concerns that the use of ARBs and ACE inhibitors increased susceptibility to SARS-CoV2. Both are widely used and conditions for which they are used very prevalent amongst populations seemingly most susceptible to COVID-19. This case-control study looked to see if exposure to ACEi/ARBs relative to other antihypertensives was higher amongst those admitted with COVID-19. They had 1139 cases and 11390 matched controls.

Abajo et al demonstrated that those taking ACEi and ARBs compared with other antihypertensives did not have a higher risk of being admitted to hospital (OR 0.94, 95% CI 0.77-1.15). This was also the case in less and more 'severe' COVID-19 presentations. The cumulative evidence seriously undermines previous links between these drugs and severity COVID-19. It supports an individualised patient centred approach to their use.



Flattening the Mental Health Curve: COVID-19 Stay-at-Home Orders Are Associated With Alterations in Mental Health Search Behavior in the United States Jacobson et al ³

Topic: Epidemiology

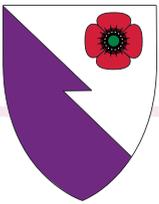
Rating: Head Turner

Scout: Dr Charlie Reynard



Jacobson et al. examine the frequency of searches on google for mental health terminology. In trying to quantify the mental health of the population, they draw an assumption that these searches are linked to the mental health of the people searching them. Blank et al. observe that the period before the lock down was associated with an increased rate of searching for the terms, but that this leveled off once the lock down was imposed. The authors suggest that the anticipation was worse than the event, but the assumption that search numbers are directly proportional to population level mental well health is unproven but does pose important questions. Will mental health issues get worse as the pandemic evolves? Did the decrease in search activity show an improvement, or could it indicate helplessness? This is an interesting look at the topic, and questions the theory that mental health issues have been on a steep upwards trajectory.





Rapid publishing in the era of coronavirus disease 2019 (COVID -19) Lee et al⁴

Topic: Research method

Rating: Worth a peek

Scout: Dr Mina Naguib



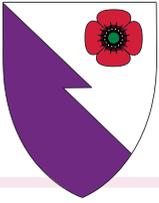
This letter to the editor summarises what the RCEM COVID-19 CPD Team have been feeling – a rapid expansion in the volume of publications related to COVID. They quantify this and the graph looks a lot like exponential growth.

On a number of levels this is excellent; vast volumes of research have been produced on a truly global pandemic with a remarkably rapid turnaround time. The process of peer-review has remained largely intact, though supplemented by a number of notable papers receiving attention at the pre-print stage.

There has, however, also been some particularly poor quality work. Hydroxychloroquine seems to have contributed to particularly high volume of poor quality research; see the Surgisphere debacle with retractions from two high profile journals. A possible association which comes to mind is an endorsement by a controversial world leader. Despite numerous criticisms of certain papers, this is likely proportional to increase in output; perhaps meta-research is required to assess this. Rapid publication around a new disease is essential; for clinical and epidemiologic management of that disease, but also to start reintegrating healthcare for the other health problems which remain

Arguably the bigger issue is the glut of new information and how to make sense of it. This rapid production and translation of knowledge must be met with a critical mind; there is a very serious risk of harm from publishing poor quality research both via distraction and misdirection. Arguably this raises some significant ethical issues. “First, do no harm” must remain central to our work, whether clinically or in writing.





RECOVERY Hydroxychloroquine interim update by Horby & Landray et al ⁵

Topic: Treatment

Rating: Head Turner

Scout: Dr Anisa Jafar



The RECOVERY trial, an RCT with multiple treatment arms for COVID-19, has enrolled over 11,000 patients from 175 UK hospitals. Every 2 weeks, an independent data-monitoring committee has been checking for evidence with enough weight to influence both national and global approaches to COVID-19 management. This week they considered the evidence related to HCQ warranted an interim update (and press release). The HCQ arm had 1542 patients (compared to 3132 in the "usual care" arm) there has been no significant difference in 28-day mortality, hospital stay, illness duration or other outcomes. Follow-up is complete for 80% of enrolled patients, and the lower bound of the confidence interval demonstrates no meaningful benefit. Therefore, with immediate effect, HCQ is being withdrawn from the trial. The press release will be followed by full results. HCQ has had a bumpy ride, and some questionable studies have thrown it into a haze of confusion. If these results hold true, it will signal a robust nail in the coffin for its role in COVID-19.



In summary

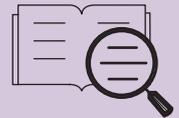
Li et al found mixed results with convalescent plasma

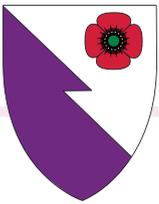
Abajo et al add to the pile of evidence of ACEi and ARB safety

Jacobson et al stress that the mental health may have been worse for the anticipation of lock down

Lee et al shine a light on the flood of research publications

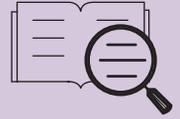
Horby & Landray et al may have hammered the final nail in the coffin of HCQ





References

- 1) Li, L., Zhang, W., Hu, Y., Tong, X., Zheng, S., Yang, J., Kong, Y., Ren, L., Wei, Q., Mei, H. and Hu, C., Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial. JAMA.
- 2) Gombar, S., Chang, M., Hogan, C.A., Zehnder, J., Boyd, S., Pinsky, B.A. and Shah, N.H., 2020. Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19. Journal of Clinical Virology, p.104477.
- 3) Jacobson, N.C., Lekkas, D., Price, G., Heinz, M.V., Song, M., O'Malley, A.J. and Barr, P.J., 2020. Flattening the Mental Health Curve: COVID-19 Stay-at-Home Orders Are Associated With Alterations in Mental Health Search Behavior in the United States. JMIR Mental Health, 7(6), p.e19347.
- 4) Lee, A. and Lin, M.W., 2020. Rapid publishing in the era of coronavirus disease 2019 (COVID-19). The Medical Journal of Australia, 212(11), pp.n-a.
- 5) Horby & Landray, RECOVERY Data Monitoring Committee, 2020. Preliminary Results. [online] Recoverytrial.net. Available at: <<https://www.recoverytrial.net/files/hcq-recovery-statement-050620-final-002.pdf>> [Accessed 7 June 2020].



RCEM CPD COVID-19 team

Dr Charles Reynard, NIHR Doctoral Research Fellow, Editor
Dr Anisa Jafar, NIHR Clinical Lecturer, Associate Editor
Dr Govind Oliver, TERN & RCEM Learning editor, Preston
Dr Mina Naguib, NIHR Academic Clinical Fellow, Manchester
Dr Patricia van den Berg, NIHR Academic Clinical Fellow, Manchester
Dr Gaby Prager, NIHR Academic Clinical Fellow, Bolton
Dr Daniel Darbyshire, NIHR Doctoral Research Fellow, University of Lancaster
Dr Tom Roberts, RCEM Trainee Emergency Research Network Fellow, Bristol
Professor Pamela Vallely, Medical Virologist, University of Manchester
Professor Richard Body, Consultant in EM, University of Manchester
Professor Daniel Horner, Consultant in EM and ICU, Salford
Professor Simon Carley, Consultant in EM, RCEM CPD Lead

