

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 an interactive live journal club captures your interest then checkout the webinar Tuesdays at 11:00, [click here to register](#).



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

### Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility by Arons et al <sup>1</sup>

Topic: Epidemiology

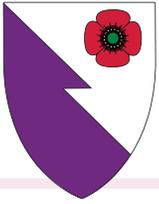
Rating: Head Turner

Scout: Dr Govind Oliver

The risk of nosocomial spread of COVID-19 is very real. Understanding this aspect of transmission is particularly important as we simultaneously deliver care to patients in COVID and non-COVID areas. This study presented findings of serial point-prevalence testing in a skilled nursing facility. From the first positive test within the home, within 23 days 57 of 89 residents (64%) tested positive. At the point of publication 15 (26%) had died and 11 were

hospitalised. 48 of 67 (63%) of residents who participated in serial point-prevalence surveys tested positive; 27 (56%) were asymptomatic. Rapid and widespread transmission was demonstrated and more than half of those testing positive were asymptomatic. It is very apparent that infection control precautions need to be vigilantly adhered to in order to prevent transmission amongst members of the team and to our patients.





**Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial by Wang et al <sup>2</sup>**

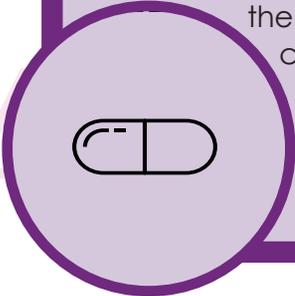
Topic: Treatment

Rating: Worth a peek

Scout: Professor Simon Carley



Remdesivir has been shown to be effective against Sars CoV2 in animal and lab models, with many clinicians hoping that this drug is most likely to be effective in humans. This is the first placebo controlled RCT of Remdesivir in humans and if you read the press or just follow social media you might think that it is a magic bullet. This study has been touted as showing a real effect, but does it really? If you read the paper you will realise that there was no benefit in the primary outcome (Hazard ratio 1.23 (CI 0.87-1.75)). The primary clinical endpoint was time to clinical improvement within 28 days after randomisation. Clinical improvement was defined as a two-point reduction in patients' admission status on a six-point ordinal scale, or live discharge from the hospital, whichever came first. Similarly, there were no statistically significant changes in the secondary outcomes, and crucially there was no difference in viral load. This is important as decreasing viral load is the purported mechanism of Remdesivir. Sadly this is another study that fails to demonstrate a significant effect on Sars CoV2 in humans. Other studies of this drug are in progress and we should wait until then before advocating for this medication.



**Clinical impact of renin-angiotensin system inhibitors on in-hospital mortality of patients with hypertension hospitalized for COVID-19 by Tedeschi et al <sup>3</sup>**

Topic: Epidemiology

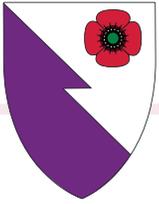
Rating: Head Turner

Scout: Professor Rick Body



Previous work has shown that hypertension, diabetes and cardiovascular disease are predictors of adverse prognosis in patients with COVID-19. We also know that SARS-CoV-2 enters cells via the ACE-2 receptor. This has led many to question whether ACE inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) may be harmful in these patients. However we still have no evidence in this regard. Meanwhile, we must decide whether to continue treatment with ACEIs and ARBs for patients on chronic therapy with those agents who develop COVID-19. In this study from ten Italian hospitals, the authors selected 311 patients with hypertension from a cohort of patients with proven COVID-19. They ran a multivariate Cox regression analysis to identify which predictors independently identified patients at higher risk of death. Age, gender, presence of cardiovascular comorbidities and COPD were considered along with ACEI/ARB therapy. After accounting for those other factors, ACEI/ARB therapy did not predict in-hospital mortality (adjusted hazard ratio 0.97, 95% CI 0.68-1.39; p=0.88). This is relatively low-level evidence. However, because there is no signal to suggest harmful effects of ACEI/ARB therapy, this lends support to the practice of continuing chronic ACEI/ARB therapy while further evidence is awaited.





### Convalescent Plasma Transfusion for the Treatment of COVID-19: Systematic Review by Rajendran et al<sup>4</sup>

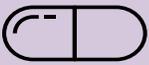
Topic: Treatment

Rating: Head Turner

Scout: Dr Charles Reynard



Can we use the blood of the recovered to treat the infected? The use of convalescent plasma has been considered for the treatment of infectious diseases for over a hundred years. It has been widely muted to be of potential benefit in COVID-19 but there is little hard evidence. This systematic review by Rajendran et al underlines the paucity of evidence. They identified five studies including only 27 patients, with no randomisation and no control arms. Amongst heterogeneous outcomes there may be a signal here that this is a treatment strategy worth pursuing. This is far from conclusive and larger randomised trials are needed to prove safety and efficacy.

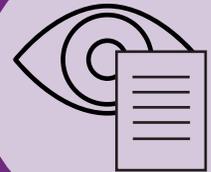


### Cytokine release syndrome in severe COVID-19 by Moore et al<sup>5</sup>

Topic: Epidemiology

Rating: Worth a peek

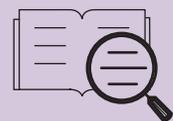
Scout: Professor Simon Carley



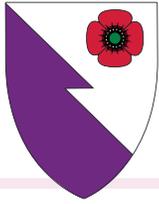
We are still learning how and why Covid-19 results in critical illness in a proportion of patients. For those who suffer cardiovascular collapse in critical care there are similarities between what we see in Covid-19 and in other cytokine release syndromes such as those seen after CAR(T) therapies and in patients with severe SARS and MERS infections. This paper explains the pathophysiology of cytokine release syndrome and the importance of IL-6 in the inflammatory process. This purported mechanism also explains many of the features we see in severe disease such as lymphopenia and raised ferritin levels. This also explains why drugs such as Tocilizumab might help patients with severe disease. This drug is now being tested in the UK as part of the RECOVERY randomised controlled trial.



### In summary



Arons et al warn us of the damage COVID-19 can do in a care home<sup>1</sup>  
Wang et al deal another blow to the antiviral treatments<sup>2</sup>  
Tedeschi et al reinforce the positive ACEi narrative<sup>3</sup>  
Rajendran et al revived an old therapy from within ourselves<sup>4</sup>  
Moore et al mapped a path through the cytokine storm<sup>5</sup>



## References



- 1) Arons, M.M., Hatfield, K.M., Reddy, S.C., Kimball, A., James, A., Jacobs, J.R., Taylor, J., Spicer, K., Bardossy, A.C., Oakley, L.P. and Tanwar, S., 2020. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *New England Journal of Medicine*.
- 2) Wang, Y., Zhang, D., Du, G., Du, R., Zhao, J., Jin, Y., Fu, S., Gao, L., Cheng, Z., Lu, Q. and Hu, Y., 2020. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *The Lancet*.
- 3) Tedeschi, S., Giannella, M., Bartoletti, M., Trapani, F., Tadolini, M., Borghi, C. and Viale, P., 2020. Clinical impact of renin-angiotensin system inhibitors on in-hospital mortality of patients with hypertension hospitalized for COVID-19. *Clinical Infectious Diseases*.
- 4) Rajendran, K., Narayanasamy, K., Rangarajan, J., Rathinam, J., Natarajan, M. and Ramachandran, A. (2020), Convalescent plasma transfusion for the treatment of COVID-19: Systematic review. *J Med Virol*. Accepted Author Manuscript. doi:10.1002/jmv.25961
- 5) Moore, B.J.B. and June, C.H., 2020. Cytokine release syndrome in severe COVID-19. *Science* (New York, NY).

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