

The only thing coming close to stretching emergency medicine clinicians as much as the cases of COVID-19 is the volume of information about it. This flash update gives clinicians the weekly top 5 research papers, and the findings that can influence your practice on the front-line.

We are also incredibly lucky to have Professor Richard Body to guide us through the key papers, with an online interactive journal club on Tuesday 14 April 2020 at 11:00. [Click here to register!](#)

These have been split into 3 categories that will allow 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

Clinical Characteristics of Coronavirus Disease 2019 in China by Guan et al ¹

Topic: Epidemiology

Rating: Head-turner

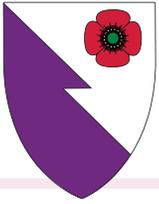
Scout: Dr Charlie Reynard



The Chinese experience must inform our own practice, and this retrospective observational study of just over a thousand patients does just that. They examined PCR confirmed inpatients and captured data for 14% (1099) of all hospitalised infections over 552 sites (7736 at time of publication). The take home messages are:

- Median incubation period was 4 days (inoculation to symptoms).
- In total, 86.2% of patients had abnormalities on chest CT, compared to 59.1% who had abnormalities on chest x-ray. The majority of non-severe cases also had CT or radiographic abnormalities (84.5% and 54.2% respectively).
- Lymphopenia was present in 83.2% of patients at admission.
- A number of routine laboratory tests were found to have prognostic value. These included CRP, D-dimer, AST, ALT, LHD, procalcitonin, creatinine and creatine kinase.
- Median duration of hospital stay was 12 days. During admission, 91.1% of patients were diagnosed with pneumonia, whereas only 3.4% were diagnosed with ARDS and only 1.1% had a diagnosis of shock.
- The most common symptoms were cough, fatigue, sputum production, shortness of breath, myalgia, headache, sore throat and chills. However other symptoms also occurred (e.g. nausea or vomiting in 5%; diarrhoea in 3.8%).
- Shortness of breath and (interestingly) diarrhoea were more common in patients who died or required admission to intensive care.





The Italian coronavirus disease 2019 outbreak: recommendations from clinical practice by Sorbello et al ²

Topic: Treatment

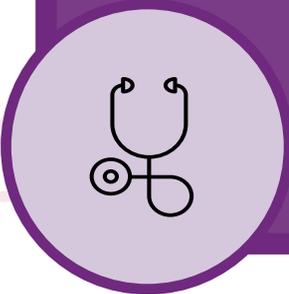
Rating: Worth a peek

Scout: Professor Simon Carley



Italy was one of the first European countries to be hit by the coronavirus, and as they learnt from the Chinese experience we would be wise to learn from them. Sorbello et al have drawn together impressive expertise in this article reviewing the Italian experience of airway management. For us the most interesting messages were:

- **Minimise** exposure during intubation by reducing staff in the room, and assigning an independent observer.
 - **Maximise** chances of success by using video-laryngoscopy, using the most experienced intubator, and generally no cricoid force should be performed (unless indicated otherwise).
 - We couldn't put it better ourselves so here are the author's own words "Delaying avoidable tracheal intubation may be beneficial but delaying unavoidable tracheal intubation is a significant concern."



A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19 by Cao et al ³

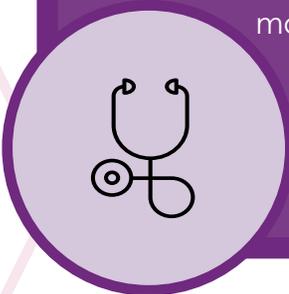
Topic: Treatment

Rating: Worth a peek

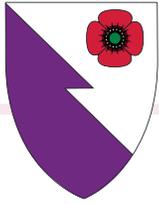
Scout: Dr Charlie Reynard



To be so early in a pandemic and already have a randomised control trial is remarkable. Cao et al examined the anti-viral medications lopinavir-ritonavir in 199 patients with confirmed COVID-19. The primary endpoint was clinical improvement and there was no significant difference between intervention and control groups. It did not work. However this was a small trial that may have included a sicker cohort of patients.



A lot of us would have been looking for positive signals from this small rough-and-ready RCT but unfortunately if this result is replicated these antivirals are unlikely to be of benefit.



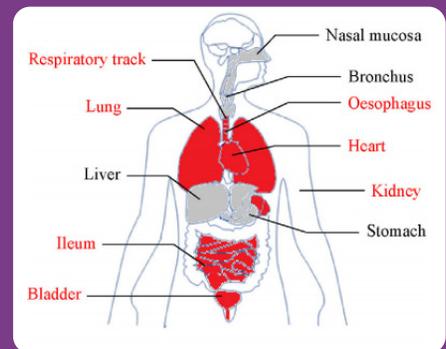
Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection by Zou et al ⁴

Topic: Pathophysiology
Rating: Head-turner
Scout: Dr Blair Graham



It is sometimes easy to forget that this disease is barely 16 weeks old, but the pathophysiology shifting under our feet will remind us. This article highlights potential organs that could be affected by COVID-19. Zou et al used pre-existing datasets to examine the expression of ACE2, a SARS-CoV-2's binding site, around the body. They generated a risk map of organs with the potential to be affected. This seems to make perfect sense when matched against the symptoms reported by Guan et al, including sore throat, cough, shortness of breath, nausea and vomiting, diarrhoea and derangements of liver and renal function. It also matches with anecdotal reports of myocarditis and dysuria.

Figure from Zou et al³ - 2019-nCoV infection-related vulnerable organs with high risk are highlighted in red; low-risk organs are indicated in gray. This figure from is recreated under the creative commons attribution 4.0 international license, which is available here.



Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial by Gautret et al ⁵

Topic: Treatment
Rating: Head-turner for all the wrong reasons
Scout: Dr Charlie Reynard



The use of hydroxychloroquine in the treatment of COVID-19 has not been proven.

This trial by Gautret et al has been lauded by some as proof that hydroxychloroquine has a clinical effect. There are significant methodological issues, which mean that the results are far from conclusive. It is an open label **non-randomised** trial of hydroxychloroquine and azithromycin. It included 42 patients from an ongoing study. The primary outcome of negative nasopharyngeal swabs were not patient centred and might not be reliable or clinically relevant. On day six 100% in the intervention arm had no virus detectable on PCR of a nasal sample compared to 57.1% in the control arm. This is a weak (and potentially flawed) signal that hydroxychloroquine might work.





In summary



Guan et al ¹ warned us from China to watch out for a multitude of symptoms. Sorbello et al ² shared the Italian experience for us to thoroughly plan intubation procedures.

Cao et al ³, in a small rough and ready RCT, showed no effect for Lopinavir-Ritonavir.

Zou et al ⁴ mapped at risk body systems and reminded us that there is a lot we don't know.

Gautret et al ⁵ demonstrated the need for good randomised control trials.

Talking of large multi-centre randomised control trials...

RECOVERY is a UK based RCT examining lopinavir-ritonavir, hydroxychloroquine, dexamethasone and beta interferon. After being open just over two weeks, an astronomical 2000 patients have been recruited with 147 active sites. It is off to an extraordinary start, and is going to be a WHOPA of a trial.

References



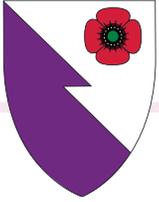
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