

Voice of the Expert

Professor Roman Jaeschke is the Professor of Medicine and Department of Health Research Method, Evidence and Impact at the McMaster University in Canada. He is actively involved in Critical Care Medicine and is the lead author of the world-famous McMaster Textbook of Medicine. On behalf of JIMA, Dr Rudrajit Paul and Dr TanukaMandal conducted an *online interview* with Dr Jaeschke about the current coronavirus pandemic in the first week of May, 2020.

Dr Roman, welcome to JIMA, the oldest medical journal in India. On behalf of this journal, we will be asking you a few questions on COVID-19 pandemic. We thank you for your valuable time.

Dr.Roman, we were going through the online McMaster perspective series. It is certainly useful. But there are a few more queries which we would like to discuss with you.

(1) In Belgium, it has been reported that doctors are sometimes doing retrospective diagnosis. For example, if a patient has already died and the doctor is told that he/she had fever and dyspnoea, the case is categorized as coronavirus. Is this approach correct? Or will it falsely increase the mortality figures?

(a) The mortality rate from COVID-19 is not clear. The 'right' percentage requires that both numerator and denominator are known and accurate. Yet without widespread testing or serological examination, the number of people who went through the infection is unclear. Same for cause of death: it is likely that some of the deaths categorized in Belgium as 'COVID-19 related' were in fact not due to this virus, thus increasing perceived mortality. But, requiring more for diagnosis would miscategorise and miss some of the real cases of COVID-19. Both ways have problems, and both may be manipulated. There are obviously possibilities of geographically different either virus mutation or genetic predisposition. Time will show.

(2) You have said that Remdesivir has very little benefit compared to the cost. So are you using it for your patients? If so, are the insurance people covering its cost?

(a) It was the person I was interviewing who said so. The cost-benefit ratio is in the eyes of person obtaining benefit and incurring cost. Let's assume the cost of drug is really 4,500 US \$ per treatment. Let's assume that the mortality reduction is in the 'reported' range (around 4%). That means that we would need to treat 25 patients to

prevent one from dying. This will translate into about 110,000 US \$ per averted death. In the world where some of the diabetic or heart failure medication cost 10,000 \$ per year, and some biologic drugs cost 20,000-40,000 \$ per year, cost of 110,000\$ per life (say, with 1-5-10-20 more years to live) does not seem out of range. I suspect this one-time cost will be widely accepted if scale of benefit is confirmed.



Professor Roman Jaeschke

(3) Smokers are protected from COVID. This is just an observational data. Should smokers be less concerned during the epidemic? If this is so, why is female mortality less than male? Females are usually less likely to be smokers (at least in India). Also is this observation true only for smoking or for any form of tobacco?

(a) I would not pay much attention to this finding. Certainly not enough to start smoking! I understand some trials of nicotine replacement therapy (patches) are being conducted. In the meantime anything else I say is a speculation. Except: smoking kills.

(b) The reason for gender differences is not clear. Possibly related to estrogen level.

(4) Have you any experience with auto proning of patients?

(a) No. We are starting an RCT of doing so. Plenty of experience with proning, which became a norm looking at major gains in oxygenation. As of today (May12) I have seen a report from New York about self proning in emergency department with striking improvement in oxygenation. Something to at least start thinking about, if not doing.

Editor's note : Physicians managing Covid-19 should be trained in prone ventilation.

(5) Someone mentioned vasoplegia as a pathophysiology of COVID illness. Can you please elaborate?

(a) The lungs are usually very efficient in matching ventilation and perfusion. If part of the lung is not ventilated, vessels auto-regulate (constrict) and blood is diverted away from that region. In COVID-19 it appears this is not the case, and blood continues to circulate through non-ventilated areas resulting in refractory hypoxia.

(6) There were no drugs in the recent two corona epidemics. Will there be anything this time? What does the trend suggest?

(a) Predicting the future is notoriously difficult. Yes, there will be treatment – the obvious question is when, and how effective it will be (pneumococcus pneumonia kills despite great antibiotics, after all). The rest is still guessing - If I had a free rein, I would like to have an option to use remdesivir and convalescent plasma. I would be happy to use them still in clinical trial. I would prefer platform trial, where my patient would likely get 'something'.

(7) Hydroxychloroquine Sulfate study in Brazil was stopped due to cardiac side effects. What is the status of other similar trials?

(a) Over 100 trials of HCQS are registered. We need to wait, probably another 4-8 weeks. In the meantime, we are not using antimalarials. Need data convincing of benefit.

(8) How common is sepsis in COVID patients? Is sepsis the main cause of death?

(a) My limited experience tells me that sepsis (as defined currently) occurs in minority of patients. In our hospital about 10% of patients admitted with COVID-19 require life support. Those who survive have prolonged and refractory hypoxia with complications of long term ventilation.

Editorial note : Indiscriminate use of antibiotics in Covid-19 patients is not needed.

(9) You have said that false hope generated by the media is often causing the relatives to pressure physicians into using doubtful remedies like steroids. How are you overcoming this situation in your hospital?

(a) We are in the centre which for years prides itself with rational approach. As health care professional we

support each other and have quite clear pattern of practice. Being on one page with your colleagues is crucial. Being convinced that you would do the same for your relative or want for yourself is helpful. In the end, if you spend enough time explaining that we do all what seems reasonable, people will almost always accept it. It is difficult, though – it is much easier to give 'something'. But please keep in mind that giving oxygen and fluids and antipyretics is already 'something'.

(10) How many health care persons are affected in your set up?

(a) We had less than 10 cases in our hospital. That, taking into account that we have 2,000 workers, is not likely excessive. But, we are quite lucky – our hospital has relatively few COVID-19 patients. I have just seen a data which showed that 1 metre physical distancing decreases odds of being infected 5 folds, and adding another meter cuts it in half. Good eye protection is very effective (fold odds decrease) and so are masks.

(11) What is effect of Heparin in COVID? What is Prophylactic or therapeutic dose and duration of use of Heparin?

(a) This is clearly evolving and moving towards higher doses. People are looking for reasons to give more. RCTs awaiting. Some anticoagulate fully if D-Dimer is (markedly) elevated. Personally I am 'migrating' towards increasing prophylactic anticoagulation dose by 50%; some of my colleagues advice to double it. Unfortunately, this is still opinion based. But, data will be coming soon.

Editor's note : In CCU, the care pathway of Covid-19 patients should include heparin prophylactically.

(12) What is the use of CT pulmonary angiogram in COVID-19?

(a) We are really trying to limit transfer of patients. I would send person to CT almost exclusively to rule out large PE. But, if hypoxia is resistant, I may anticoagulate anyway. This is clearly opinion based. Transfer only if whatever I see will change management.

Editor's note: Transfer of Covid-19 patients for investigations increases the chance of spread of the infection. So, such investigations should be minimized.

(13) What are the pros and cons of use of Mechanical ventilation vs High flow nasal cannula?

(a) This is evolving. Original advice was to intubate early. Survival was so low after intubation, that I see people moving away from it. No clear data, so it is frequently institution based pattern of practice. HFNC and possibly CPAP will be my choice if there is no need for immediate intubation.

(14) What is the Role of D-dimer in COVID-19? How much you are using it?

(a) Time will show. I suspect we will measure and follow it in all patients, and anticoagulate (unless strong contraindication) all with elevation. How much elevation? Twice / three times upper limit of normal? Five times? The higher the D-dimer, more likely to require anticoagulation. At least until data show this is wrong (hopefully right).

Editor's note: In hospitals managing Covid-19 patients, D-dimer testing should be available.

(15) What is the Treatment policy for asymptomatic patients?

a. Essentially no treatment. Self isolation.

(16) How much is Lockdown acceptable to people?

(a) It depends on the people. And the country. And the culture. And the politics. And if you had older relatives. And if somebody in your family takes immunosuppressant. Or is pregnant. Or is about to lose the job. Or has no means to survive without work.

(17) How are you using the Risk stratification or prognostication tools in COVID-19?

(a) I assume you are asking for predictions of death. As a biostatistician I have very healthy respect for determining the population risk – by that I mean that I can predict that from 100 people ‘scoring something’ 25 will die. As a clinician I know, however, that I am not sure which 25. So, as of now, I rely on clinical acumen which simply says – ‘the sicker you are, the less likely you are to survive’ and ‘it is better to be young and otherwise healthy than old and already unwell before’. Mind you, all scores are doing essentially the same, adding points for age, diabetes, CV disease, limited mobility, malfunctioning kidneys or liver, etc.

If those prognostications tool are to be ever used to decide arbitrarily on treatment versus palliation, they have to be applied equally and uniformly. This would require same criteria applied by the same people (?group of people) to all patients. I hope this will not be needed; neither in Canada, nor in India.

Dr Roman, thank you for your time.

We are sure our readers will be delighted to know your viewpoint. As you said, the Covid situation is now evolving and we will have a lot more alterations in the management protocol in the coming days. Hopefully, we will be talking with you again in the future.