COVID-19 Science Report: What’s New
NUS Saw Swee Hock School of Public Health
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What’s New
For regular readers, this section has all the new content across all sections.
References for new content outlined below are located in the main reports.
Some references were from preprints which are preliminary and yet to be peer reviewed, the results should be interpreted with caution.

Clinical Characteristics

Sociodemographic Characteristics
Age. A retrospective cohort study on 305 individuals in the US hypothesized higher risk in adults due to higher ACE2 expression in their nasal epithelium when compared to children.

Clinical Presentation
Initial Presentation. A study reported two COVID-19 positive cases with initial herpes zoster-like lesions.

Symptoms reported over the course of illness. A 32-old-woman COVID-19 positive case in China was reported with a rare case of immune thrombocytopenic purpura nearly two weeks after developing COVID-19 symptoms. Furthermore, A 57-year-old woman presented with erythema nodosum on day 8 of hospital admission.

Progression of Disease. A brain MRI studying brain imaging features on 27 critically ill COVID-19 patients reported 4 patients presenting with leukoencephalopathy, one with microhaemorrhages and 6 with a combination of both.

Recovery. A prospective cohort study of 131 patients discharged after COVID-19 disease reported readmission in 2.29% of cases because of fever or positive SARS-CoV-2 retest. Majority of the cohort patients were self-quarantined and were in the course of recovery.

Laboratory Findings
Viral Load and Seroconversion. In another case report, a patient initially found to be SARS-CoV-2 negative on plasma testing was positive for the virus from lung biopsy samples. This suggests that despite disappearance from other clinical samples, SARS-CoV-2 virus may still persist in lungs. One limitation of this study as stated by authors is the inability to culture the lung biopsy sample and the resultant uncertainty on correlating positive lung sample with infectiousness.

Complications/Morbidity
Heparin resistance. A study found heparin resistance in critically ill patients. Such patients had sub-optimal peak anti-Xa following therapeutic Low molecular weight Heparin (LMWH).

Co-infections have so far not been commonly found in COVID-19 patients. Similar findings were reported in Singapore where rate of co-infection with SARS-CoV-2 was 1.4%. The study conducted at one of the major hospitals in Singapore reported low in-hospital mortality and proportion of patients requiring invasive ventilation (1%) in comparison with community-acquired respiratory virus infections over the same period.

Predictive factors of disease severity. A longitudinal study explored the association of serial viral loads in 308 COVID-19 positive patients that included general patients (n = 70),
The study reported higher viral loads in sputum samples compared to nasal and pharyngeal swab samples. Also, the SARS-CoV-2 viral load was negatively associated with blood parameters and positively associated with cardiovascular system features. The study concluded that resurgence of virus during treatment should be treated as a warning sign of severe illness.

**Mortality**

**Factors affecting Mortality.** A study showed that diabetics on metformin treatment reported reduced in-hospital mortality caused by COVID-19 compared to diabetic patients on non-metformin treatment.

**Diagnostics**

**Appendix A Table 2.1 Upcoming/Available Diagnostics: Molecular tests**
We have updated the table 2.1 for new and existing tests.

**Appendix A Table 2.2 Upcoming/Available Diagnostics: Serological Tests**
We have updated the table 2.2 for new and existing tests.

**Therapeutics**

**Main Therapeutics**

**Remdesivir.** A double-blinded, randomised, placebo-controlled trial on Remdesivir was published in the New England Journal of Medicine on 22 May 2020. It found that a 10 day course of Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalised with COVID-19 and evidence of lower respiratory tract infection.

**Hydroxychloroquine.** An additional study conducted in China also found no significant improvement in clinical outcomes with the use of hydroxychloroquine. In addition, higher frequency of adverse events were observed in the intervention group receiving hydroxychloroquine.

On 25 May 2020, the WHO has suspended drug trials on hydroxychloroquine, citing “safety concerns” as the main reason.

**Hydroxychloroquine and Azithromycin.** In a study analysing data from 671 hospitals across six continents, the efficacy of hydroxychloroquine with or without a macrolide (which includes Azithromycin) was unable to be confirmed. Use of hydroxychloroquine or chloroquine in drug regimens was associated with a lower in-hospital survival and higher frequency of ventricular arrhythmias while being hospitalised.

**Vaccines**

**Vaccines in Development: Coalition for Epidemic Preparedness Innovation funded projects**

**Inovio.** Data regarding preliminary safety and immune responses from the Inovio’s Phase I clinical trial are expected in June. Phase II and III trials are planned to start in July or August and are pending regulatory approval.
Novavax announced on 25 May 2020 that it has started Phase I trials of NVX-CoV2373, and have enrolled the trial’s first participants. They expect preliminary immunogenicity and safety results in July. Phase II is expected to be conducted in multiple countries including the United States, and would access a broader age range of participants.

Vaccines in Development: Other Vaccine Collaborations

**CanSino Biologics.** A study of the CanSino Ad5 vectored COVID-19 Vaccine was published in the Lancet on 22 May 2020. In this study, 108 participants aged 18 to 60 years old were given either a low, moderate or high dose of the vaccine. ELISA antibodies and neutralising antibodies increased significantly at day 14 and peaked 28 days after inoculation. Specific T cell response peaked at 14 days post vaccination. The most common adverse reactions were fever, fatigue, headache and muscle pain, with the highest incidence in the high dose group.

Containment Measures

**Detection/Contact Tracing**

**Use of natural language processing (NLP) and artificial intelligence (AI) based methods.** The Medical University of South Carolina Health system used NLP and AI methods with unstructured patient data to predict and prioritise testing appointment scheduling. Text analytics revealed that concepts such as “smell” and “taste” were more prevalent than expected in patients testing positive and screening algorithms were adapted to include these symptoms. The model categorised patients into High, Medium and Low risk categories, which proved to be acceptably accurate when verified against actual testing. This helped to prioritise testing appointment scheduling. (Page 20)

Hospital Infection Control and Protection of Healthcare Personnel

**HCW stress and burnout.** A cross sectional survey on 2,707 HCWs revealed that 51% reported burnout, with various reasons including work impacting household activities, feeling pushed beyond training, COVID-19 patient exposure and having to make life prioritisation decisions. It was noted that PPE was protective against burnout. The study also pointed out that HCWs should be well supported to ensure good healthcare quality during the pandemic. (Page 27)

**HCW protection IC practices.** In a study where a DNA oligonucleotide surrogate for contaminated bodily fluid based on the Cauliflower Mosaic Virus was inoculated into a bed rail in an isolation room, swabs taken found that the virus transferred to 41% of all surfaces in the ward within 24 hours, peaked at 52% on Day 3, and persisted throughout the 5 day sampling period. This implied a combination of poor cleaning, patients and carers not adhering to hand hygiene protocols, and highlighted the importance of these measures. (Page 28)

**IC control measures in a radiotherapy department in Zhongnan hospital in Wuhan.** IC control measures included scheduled treatment times to reduce waiting room density, daily staff temperature check, donning of biosafety level 3 protection for high risks procedures, strict following of hand hygiene/decontamination measures and patients having to wear surgical masks at all times. 153 patients with 1,752 visits underwent radiotherapy from 28 Jan to 10 Mar. 39 staff were tested for COVID-19 and none were tested positive. (Page 30)

**Reporting system in a university hospital in Italy.** The reporting system, where HCWs are assessed according to their transmission risk levels (based on degree of contact with
confirmed cases, whether they were with/without PPE and swab test results) and are either suspended from work temporarily for 7 days, allowed to return to work early, or allowed to continue working with self-monitoring over a 14-day period. The system contributed to good transmission control in the hospital: the hospital received 1,065 COVID-19 positive patients, 1,303 swabs were done among HCWs, and only 23 tested positive. (Page 34)

**On respirators.** A review study pointed out the following key points on respirator use for HCWs. Organisations can consider flexible policies providing more than one respirator model type (or reusable respirators which a substantial proportion of HCWs preferred over disposable designs):

- Respirator performance standards are applicable across industries and repurposing respirators to healthcare from other industries is appropriate.
- Proper fit testing is required for safe use.
- Some clinical procedures (such as chest compression) may impact fit even with fit testing.
- All respirator types compromise user comfort and ease in communication. (Page 35)

Another study pointed to the current worldwide shortage situation with COVID-19 (especially for FFP2 respirators) and how the untraceable origin of respirators supplied to hospitals meant the need for quality check of supplies. A protocol at a hospital Netherlands tested a minimum Total Inward Leak (TIL) of 8% for FFP2 respirators (based on EN149+ A1:2009 standard) and only 33% of tested respirators met the requirements. (Page 36)

**On aerosol transmission.** A study sought to identify the escape of small particle aerosols from patients’ airways through simulating breathing conditions with 0.28µ aerosols and a fixed cadaver head and different masking arrangements. Virtually no aerosolised particles were detected with a novel Negative Airway Pressure Respirator (NAPR) System made via an Ambu mask fitted with suction tubing attached to a HEPA filtration system, vis-à-vis other arrangements (no mask, surgical mask, and modified Ambu anesthesia mask). Local negative-pressure environment around the patient’s nose and mouth is critical to minimise the risk to HCWs associated with procedures of upper and lower airways. (Page 36)

**Community Hygiene**

**Population behaviour and compliance.** An online questionnaire study which evaluated and scored Vietnamese adults on personal preventive measures (eg. wearing masks outdoors, coughing/sneezing etiquette etc) and personal community preventive measures (eg. avoiding gatherings/public transport, usage of individual spoons/plates etc) found the scores high, especially for personal preventive measures. The strong preventive behaviour of the Vietnamese population could be the reason for the low number of COVID-19 infections and nil mortality up to first week of May 2020. (Page 42)

**Decreasing Social Mixing/Increasing Social Distance**

**Contact patterns in schools.** A study based on survey data on Wuhan and Shanghai found that the largest number of contacts were recorded in school settings, and school closures eliminated contacts between school-aged individuals. The study also suggested that despite lower susceptibility to infection among school-aged individuals, school closures can significantly reduce overall transmission and disease burden and reduce peak incidence by 64%, although as an intervention by itself, it cannot reduce Rt<1. (Page 49 and 51)
Workplace and School Closures

Safe reopening after closure. A review article pointed out that the uncertainty of whether most children evade infection or are largely asymptomatic when infected requires caution when reopening schools. Considerations to guide safe reopening include:

- Exploration of surveillance methods
- Privacy considerations with viral surveillance and contact tracing efforts.
- Consideration of children with chronic conditions, vulnerability to COVID-19 or conditions that often present with COVID-19 symptoms (eg asthma), who may face barriers to school re-entry.
- Benefits of after-school activities and physical education, and innovative ways to safely conduct rather than defer/abandon them. (Page 52)

China and Lockdowns

A study evaluated the impact of social distancing measures on contact patterns in Wuhan and Shanghai before and during the outbreak. Average daily number of contacts per participant reduced from 14.6 to 2.0 in Wuhan and 20.6 to 2.3 in Shanghai. Impact of social distancing measures was modelled to drastically reduce Rt. (Page 70)

Exit Strategies

Level of transmission and transmission dynamics

The dispersion factor (k) is a measure of variability in empirically observed cluster sizes. A low dispersion results in a steadier growth of the epidemic, while a larger dispersion may imply that some cases account for a disproportionate number of secondary cases with individual-level variation in the risk of secondary transmission. The estimated k values for Hong Kong, Japan and Singapore are estimated to be 2.3, 0.51 and 1.78 respectively. With a hypothetical seeding of 50 infections, the probabilities of an SSE with cluster size of 30 or more are 0.114, 0.0411, and 0.412 respectively.

Health system capacity

Healthcare workers and support staff should be protected, including those working in the community, and in residential and care homes. PPE guidelines should be communicated, supported and adopted by staff.

Surveillance

The Pandemic Recovery Acceleration Model (PRAM) analytic tool was developed and implemented in Nebraska. It consists of 3 disease specific values, namely daily new cases, newly reported deaths and percentage positive tests per day, and 3 health care resource specific values, namely daily percentage total of acute care hospital beds, ICU beds and ventilator capacity used by COVID-19 positive patients. For each measure/value, rolling averages over past 1-3 days (5-7 day averages have also been proposed; reflective of current position) and 8-14 days (reflective of past position), along with the ratio of the two rolling means (trend index reflective of velocity of change) are tabulated. The Recovery Composite Index indicates the rate of acceleration or deceleration of pandemic recovery, while the Recovery Ratio Index indicates the velocity of the impact on health care resources relative to the velocity of the pandemic spread.
**Herd immunity**

A preprint study in Japan noted that at $R_0$ of 2 or more, herd immunity approaches are unlikely to be socially acceptable (based on an upper bound of overall mortality) assuming current infection fatality rates are not overestimated.

**Gradual easing**

Individuals living in care institutions should be protected. A score-based risk classification may also be considered in the classification of vulnerable subgroups.

Other recommendations in schools include donning of PPE by teachers and adults, phasing the reopening of schools, rapid detection and response to localised outbreaks in school with adequate testing and tracing infrastructure, and gathering feedback from schools and key stakeholders.

Options proposed beyond post arrival quarantine include risk-based approaches of lifting restrictions between countries with low transmission rates, good surveillance and transparent reporting, and a proof of immunity from travellers under the International Health Regulation.

A preprint modelling study in Australia suggested that a staged relaxation of social distancing in a low transmission setting by increasing school attendance (to 60%), then lowering community-wide contact reductions and increasing workforce attendance (to 80%), with continued increased case isolation, may not result in a severe spike in cases. However, containment measures should be held longer before being eased if widespread community transmission was present.

A preprint study suggested that a second wave is commonly noted in modelling scenarios (with a peak that tends to be higher than the first peak if $R_0$ is less than 2.4), and a third wave is possible when 1/inverse of the average duration of infectiousness is between 5-7 days, and the transmission rate is up to 0.4 per day. An increase in the level of adaptation of the population to containment measures (novel social behaviour) increases the number of waves (from 2 to 6/7); no second wave occurs in the event of slow adaptation such that the first wave confers herd immunity.

**Mass testing**

With a recent rise in cases in Wuhan, China embarked on an ambitious exercise of testing all 11 million people in the city. In just under two weeks, about 6.68 million have been newly tested, with 200 found to be actively infected but not currently with symptoms. This massive effort relied on pooling of 10 samples into a batch to be tested, which optimised the number of tests needed and time taken. Results were then made available to individuals after 3 days via popularly social media platform app WeChat. This exercise is estimated to have cost at least 1 billion yuan (USD $140 million).

**Contact tracing**

A report in UK suggested that a containment strategy with app-based tracing is effective with an uptake rate of 80% among smartphone users, or 56% of the entire population. Given low smartphone use among the elderly, it was recommended that shielding (partial lockdown) be continued.

A preprint study noted that contact tracing of contacts-of-contacts reduces the size of outbreaks beyond that that results from tracing of contacts only. However, a large proportion of the population may have to be quarantined at any one time. This may be reduced by
combining contact tracing with testing and releasing of quarantined cases, or physical distancing to reduce the number of links.

**Country Journeys**

This week’s update includes Singapore and high-level information on demographics and wider impacts of the pandemic.

Most countries are continuing to move forward with gradual reopening.

Areas that allowed church services and reopening of clubs and bars have reported clusters.

High-risk industries common across countries include meat processing / packing, distribution centres, call centres. This may be due to susceptibility of the environment and ability to social distance or due to them being essential services and therefore open.

Countries that reopened sectors earlier are developing more nuanced and flexible policies, such as targeted closures in response to cases, and more developed masking policies (eg allowing schools to opt in/out of mask wearing depending on the case numbers of an area).