The Science and Business of COVID-19 Webinar Series

Webinar Highlights

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Contents

Introduction

A joint effort of the SingHealth Duke-NUS Global Health Institute (SDGHI), Saw Swee Hock School of Public Health (SSHSPH) and the American Chamber of Commerce (AmCham) in Singapore, The Science and Business of COVID-19 Webinar Series draws on expertise located across these organizations and brings together other international experts to provide a rich multidisciplinary discussion across the public and private sectors. Through this Series, the connection between medicine and science to economic and business interests will be explored – where possible, strategies that can be adopted by businesses to be better prepared will be outlined.

This first session aimed to provide an overview of the basic concepts of infectious disease epidemiology and helped us understand and change the epidemic curve. Various challenges and outcomes of infection prevention and control strategies such as healthcare professional protection, contact tracing, isolation, quarantine, travel restrictions and entry screening were explored. In addition, the speakers discussed the impact of the COVID-19 outbreak on business operations and shared their on-the-ground experience from their respective fields.

You can access the recording of the webinar here.

Clinical and Epidemiological Aspects of COVID-19

The current COVID-19 pandemic is caused by SARS-CoV-2, one of a series of two other zoonotic coronaviruses which have caused epidemics in the past – SARS (2003) and MERS (2012 to present).

From a clinical aspect, what separates SARS-CoV-2 from SARS and MERS is that COVID-19 has a much broader spectrum of disease manifestations, from mildly symptomatic to severe illness, to even asymptomatic presentation.

- Contrast to MERS, which generally has been centred around the Middle-East and still closely associated with its reservoir, the camel.
- Contrast to SARS, where illness patterns were very distinct and transmission was thought (at that time) to occur predominantly when people were symptomatic.

This is probably the main factor which has driven community-based outbreaks and the rapidity of spread across the world. Despite the mortality rates which are quoted to be lower than SARS in 2003, the absolute number of cases and deaths, and the current pandemic's ability to overwhelm medical systems is completely unprecedented.

Clinical manifestations: insights from the National Centre for Infectious Diseases (NCID)

- About 50% of patients have pneumonia on presentation; the rest have a mild form of the disease which is quite indistinguishable from the common cold.
- Of those who have pneumonia, about 20% have a more severe form of pneumonia. There are about 5% of patients who will be critically ill and in need of ICU care.
- Patients who fall into the last category tend to be older with comorbidities, lower lymphocyte counts and/ or raised inflammatory markers (CRP, lactate dehydrogenase).

Treatment: worldwide rush to look for therapeutic agents and vaccines with multiple trials ongoing, but efforts limited by lack of robust data, extensive length of time needed especially for human trialling. The earliest forecast would be about 1 to 1.5 years before anything can be put onto the market, but even that is an optimistic prediction.

Therefore, in the meantime, public health measures that are being taken by governments remain very important to curb the virus' spread.

Screening: PCR Test, Antigen Tests, Antibody Serology Testing

Primary method of COVID-19 diagnosis – a molecular Polymerase Chain Reaction (PCR) test is used to test for the presence or absence of the virus in someone who is actively being infected by looking for the SARS-CoV-2 gene.

- A fairly complex test and needs to be done in the lab, but it's highly accurate.
- The test looks for gene sequences, so finding it does not necessarily mean that the virus is alive or viable; but at least we know that the virus RNA is there.

Currently, Singapore does not have any licensed antigen tests and is not really looking to use it due to lack of good data and caveats from previous experiences – for example, low performance characteristics of influenza antigen tests newly introduced in 2009, only 50% sensitivity.

A serology test tries to find out if an exposed person has been infected in the past by looking for antibodies IGM and IGG (looking for immunity). It takes about 14 days after the onset of illness for the antibodies to show up – a significant time lag which reduces the test's usefulness.

Immunity passports: concept that individuals who carry SARS-Cov-2 antibodies are automatically assumed to be immune to reinfections, proven by serology testing

- Problem – currently unknown how long this immunity lasts for.
- Insights from SARS and MERS – for SARS, we have some data that immunity can last for about 2 to 3 years. Limited studies for MERS have shown that 80% of MERS patients might have immunity up to 18 months, but this means that 20% don't, and the immunity seems to be correlated with the severity of illness as well.
- Therefore, from what we know of other respiratory and coronaviruses, it is unlikely that a recovered COVID-19 patient will get infected straightaway if re-exposed to the virus, but no strong data to support or rebut this.

More science and research will have to go into this area for us to develop a conclusive view on this.

Vitamin Supplements and Immunity-Boosting Therapies, Specifically Vitamin C, Vitamin D and Zinc – Does It Work? Any Recommendations?

In multiple randomised control trials, there is data for Zinc and Vitamin C in decreasing the number of acute respiratory infections as they are important micronutrients that function as cofactors and enzymes in fighting infections.

Of course, the data here is pertaining to common cold viruses, but extrapolating from that, it still makes sense that against COVID-19 and respiratory infections in general, having a diet replete in nutrients will be helpful.

If there are concerns, especially in certain higher-risk subpopulations with mineral or vitamin deficiencies — then yes, it might make sense to recommend vitamins for those people.

But if a person has a nutritionally balanced diet that is replete in vitamins, he/ she will not be as high-risk and in need of supplementation as compared to those with unbalanced diets.

In a sentence: no data specific to COVID-19, but no harm taking supplements as well.

Role of Chloroquine and Hydroxychloroquine From Both the Treatment and Prophylactic Perspectives

In-vitro, we know that chloroquine and hydroxychloroquine, along with other drugs such as Kalethra and Remdesivir have activity against SARS Co-V-2. But what happens in a petri dish and what happens in the human body can be quite different. Current in-vivo trial data are contradictory at best, leaving a lot of questions and concerns to be addressed.

Various toxicities have been reported from use of chloroquine, hence, the NCID national guidance does advise against use of chloroquine, with a caveat that hydroxychloroquine can be considered for certain groups of patients.

However, therapies will need to be tried while we are awaiting good trial data because it is sometimes unfeasible to wait for all the randomised control trials and good quality data to be released before acting, especially in the face of large patient loads.

In these kinds of situations (where we are lacking in data), doctors will have to extrapolate from existing data, draw from their available clinical experience and hold nuanced discussions with patients and their caregivers to see where the possible benefits may outweigh the risks.

The treatment of Covid-19 is still an evolving field, hence there is a need for more evidence before proper recommendations can be put forward.

Modelling to Estimate Progression of the Pandemic, Responses, Etc.

In general, all models simplify reality, and they do so to draw our focus to some sections of that reality.

Many transmissions models that stimulate the spread of COVID-19 are similar in the sense that they are formulated around how individuals in a population move from one place to another, and how quickly they move. Susceptible individuals may acquire the infection, and eventually die or recover.

The most basic models assume that everyone have the same chance of acquiring an infection from an infected person; they also assume even interactions and that individuals with the disease are equally infectious. More advance models account for age, sex, their health status and social behaviours like mixing patterns — who meets whom, when, and in which places.

Many governments across the world are relying on such mathematical projections to help guide decisions in this pandemic. These models can be useful tools for those for us to see how and where the pandemic is heading.

One of the challenges we face in modelling outbreaks is that we don't typically observe the transmission events themselves. Instead, we just observe people becoming ill and needing hospitalisation. So, when modelling how the pandemic is likely to progress, it is essential to account for the time lag between onset of symptoms and the daily reported number of new cases.

Strategies: 'Flattening the Curve' Versus Achieving Herd Immunity

Transmission models: not just modelling the number of people affected, but equally, the number of ICU beds, the number of ventilators – the availability of essential core resources in the healthcare system for epidemic management.

Related to this is the idea of flattening the curve, reducing the number of people coming into the health system at any given point in time to ensure that the health system does not collapse freely. It helps us to keep the number of new infections each day at a low enough level such that health systems can cope; and buys us time to get ourselves prepared.

Herd immunity: For

- Flattening the curve through measures such as having multiple lockdowns in the interim risks stretching the economic winter for a substantial period of time. Whereas if we let nature take its course and allow for COVID-19 parties (very much like pox parties), the population may strive towards herd immunity within six to nine months. There will be tremendous health consequences – many people may die. But, economically, it seems to be a reasonable strategy.

Herd immunity: Against

- Problems with letting nature take its course, striving for herd immunity – we do not actually know how long the immunity can last in recently-recovered patients. Some evidence even suggests that people could be easily re-infected.
- Overall, we do not know enough about the current pandemic for us to be able to say that herd immunity is a definite solution. It is too risky to make that claim. Therefore, it makes it more important for us to think of measures that can flatten the curve to better contain this pandemic.

Economic Impact of COVID-19 and How Countries Have Responded to the Pandemic

We've seen some flavour of lockdown in pretty much every country in this region and around the world. Whether we call it lockdowns, circuit breakers, social distancing or quarantine, these are typically to safeguard populations, to flatten that curve so that healthcare systems won't be overwhelmed.

And within these lockdowns, we are seeing attempts by some governments to at least safeguard the essential businesses — healthcare delivery, the manufacturing and other key sectors in the economy; highlighting the need to balance public health safety with economical concerns.

Nevertheless, the economic impact of this pandemic is monumental, and unfortunately this is going to be disproportionately impacting the poor in both developing and developed countries.

A piece of research from the Australian National University in King's College London estimated that over half a billion people may fall into poverty because of COVID-19 and its lockdown restrictions. That's between 6-8% of the global economy. It can set our fight against poverty by a decade or as much as thirty years in regions such as Sub-Saharan Africa and the Middle East.

Is the Cure Worse Than the Disease?

Bill Gates gave a stark rebuttal to this line of thinking: “There really is no middle ground, and it’s very tough to say to people, ‘Hey, keep going to restaurants, go buy new houses, ignore that pile of bodies over in the corner. We want you to keep spending because there’s maybe a politician who thinks GDP growth is all that counts.”

That said, as the pandemic progresses, we will eventually have to make difficult choices about when to open the economy knowing that some may die and yet, at the same time, bearing in mind that many will also die from the impact of prolonged unemployment and poverty. This is especially so in developing countries with no government social safety net.

The “Quality Adjusted Life Year” concept in health economics uses the cost-per-QALY to make difficult decisions about funding healthcare. The cost-per QALY helps us, to put it in a grim way, put a dollar amount on life. A similar concept will be required for decisions around balancing COVID-19 and the economy because every decision is a trade-off, those trade-offs should be explicit rather than implicit.

This is a “grim calculus” that requires input from clinicians, economists, and ethicists – multidisciplinary action.

Should Countries 'Unlock'?

Control measures, such as travel and lockdown restrictions, isolation of cases and other physical distancing interventions seem to have been effective in reducing the effective reproduction number of the virus. However, they cannot last indefinitely as they come at high societal and economic cost.

Moreover, the strain of COVID-19 on health systems comes in different forms — suspended vaccination programs for other diseases is an example of how there may be other long term consequences.

The questions now are — how do we know what measures to lift; how much can these interventions be relaxed?

- It is very difficult to discern precisely which measures are most effective, but we should aim to keep the interventions that are less disruptive to our livelihoods, but more effective at mitigating the spread. Some researchers suggest that we may need to consider intermittent physical distancing for the period of several months or years even.

There is no model answer for a 'best response' to such a complex pandemic. The timely implementation of control measures is key to success and it must strike a balance between early-enough application to reduce the peak of the epidemic and ensuring that it can be feasibly maintained for an appropriate period of time.

How Should Countries 'Unlock'? Can Mathematical Models Really Provide Some Guidance?

Mathematical projections can guide interventions real-time, for sure, but these models require really good data to provide useful inputs for informing policies.

Unlocking should be gradual and well-planned. Countries should not go from complete locked-down status to full reintroduction overnight.

- Need to ensure that appropriate infrastructure is in place before 'unlocking' safely – namely strong testing and contact tracing capabilities.
- Current recommendation is to reintroduce sub-groups of populations in a phase-like manner. These efforts should be rigorously studied as it is likely for hotspots of infection to flare up post-unlocking, and will require targeted lockdowns periodically.
- New tools such as serology tests to measure exposure to the virus and immunity will help us get back to work with confidence. New practices we've learned during lockdown such as not going to work sick, paid sick leave, increased telecommuting, and handwashing should remain.

It will be important to study the changes in people's social behavior during this whole outbreak period – the way they interact with others during lockdowns or other types of regulations – as it will directly affect the inputs into mathematical projections.

Even when the unlocking does happen, it will be a while before the world can resume the full level of economic freedom we enjoyed pre-COVID 19. However, we cannot wait for the pandemic to be completely over before starting to recover our economy.

The economy is going to have to recover in new ways. We'll probably see the global economies recovering sector by sector; schools and travel opening up before large concerts.

We'll also have to look at new ways of doing business, from online models to fashion labels thinking about sustainability, to just-in-time production models. A lot of creativity is needed to help us get back to business sooner.