

# Medicine

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# DEAN'S MESSAGE

Dear Reader,

On December 21 last year, a cruise ship set sail from Hamburg, Germany, on what was supposed to be a 140-day journey. On board were uninvited and unseen stowaways. One hundred and seventy days later, the MV Artania finally docked at the German port of Bremerhaven after an epic, six-month odyssey. Of the more than 1,000 passengers, only eight were left on board along with a skeleton crew. More than 800 passengers had disembarked along the way to catch flights home, while another 200 or so were evacuated to hospitals. En route home, the ship made numerous diversions to drop off crew members, before returning to a world vastly changed from the one it left in December.

The voyage of the MV Artania may be seen as a metaphor for all countries struggling to cope with an infectious disease that has crept up on our unsuspecting world. We assumed 2020 would be like the years before—breezy, smooth sailing, business as usual. Then came news of an infectious outbreak in China, followed by the first cases here just before the Lunar New Year. Healthcare systems around the world were engulfed by the sudden flood of patients, all presenting flu-like symptoms with an alarming number deteriorating into respiratory failure. The cases spiked, economies ground to a halt as worried governments enacted population lockdowns and freezes on travel, discouraged and even banned interactions between people as scientists struggled to understand this frightening, mysterious virus that was making so many people around the world fall ill, and killing some along the way.

Collectively, the nations of the world found they had entered a new, bewildering and uncertain time. People lost jobs as economies lost steam and companies shed staff. Holiday trips abroad were abandoned, family reunions were postponed indefinitely, shopping trips meant just grocery runs and food takeaways. Masks became compulsory facial accessories. A global race was launched to produce vaccines and antiviral medications to halt the spread of COVID-19. Here on the Yong Loo Lin School of Medicine campus, all other research was suspended while our virologists and molecular biologists joined with colleagues from DSO, A\*STAR, and other biomedical institutions in the search for a solution.

Eight months on, we know so much more about the silent, killing virus that has taken more than 608,000 lives and incapacitated more than 14 million people worldwide\*. Our confidence in the human race's ability to corral and outsmart the virus is gradually returning, boosted by the plateauing of infection rates here and among various countries. But while much remains to be discovered about COVID-19, we have uncovered much about ourselves. We have learned that we are able to adapt, after the initial shock, hiccups and some discomfort, to a new way of living and working. We have found that what was, need not be going forward.



Viruses mutate, allowing them to survive better. We too must change and adapt to meet the challenges life throws at us. To a certain extent, the challenge of the virus is also a question about who we are, individually and as a community. My colleagues and I have embarked on an irreversible path to re-examine assumptions about our work and the way we go about it here at the School, from the way we teach our students, to the processes that guide and inform our functions and daily operations. We will ride the tsunami of inevitable changes that are being brought about by COVID-19, to identify opportunities that will allow us to transform and work more effectively and productively. We are investing heavily in digital systems and infrastructure and we will be deploying and using these even more extensively in a post-COVID world, so that we are able to continue to operate successfully and safely.

It is into this greatly changed world that the graduating Medicine and Nursing Classes of 2020 is entering. We have taught and trained them well and are confident that the knowledge and skills they have acquired in the years here at the School have prepared them to meet the tests and challenges that await them in the wards, clinics and wherever they find themselves working. In this regard, we have not changed. The NUS medical school continues to carry out the mission she was established to do more than 115 years ago—prepare young men and women to care for the health and healthcare needs of Singapore and beyond.

Stay healthy, sail boldly, surmount together.

Yours sincerely,

*Yap Seng*

Chong Yap Seng  
Lien Ying Chow Professor in Medicine  
Dean, NUS Yong Loo Lin School of Medicine

\*as of 21 July 2020, Johns Hopkins Coronavirus Resource Centre

# ISOLATION, LONELINESS & RE-CONNECTING IN THE TIME OF COVID-19

by Dr Noreen Chan

Head & Senior Consultant, Division of Palliative Care, National University Cancer Institute, Singapore

The COVID-19 situation has hit some harder than others, but everyone has been affected by the rapidly changing circumstances and the need to self-isolate. At the start of the year, phrases like #socialdistancing, #flattenthecurve and #circuitbreaker had not entered our lexicon, we could not imagine what it would be like to stay at home all the time, not to be able to see friends and family, and to wear a mask when outside.

The infection control requirements have imposed an unprecedented level of isolation on all levels of society, exposed fault lines and inequalities, and turned long-cherished customs and beliefs on their heads. For example, when Work from Home (WFH) and Home-based Learning (HBL) became mandatory, it became evident that being forced to stay together at home was not only uncomfortable and inconvenient for those in cramped accommodation, but even harmful for victims of domestic violence.

Social conventions and practices have been drastically altered. We have been told not to shake hands, children are asked to stay away from seniors, grandparents are unable to cuddle their grandchildren. Palliative care and social work professionals who pride themselves as “low tech, high touch” now find that they cannot touch, and other ways must be found to connect. Suddenly we are all forced to stand apart, to embrace solitude.

This is so different from 17 years ago, during SARS. It was a different disease, a different time, a different world. Yes, we were all in PPE in the hospital isolation wards, but outside it felt much like normal. No one wore masks, you could go shopping or to the cinema, it was not taboo to meet your friends. In fact, hanging out with friends and families was a vital form of respite for us healthcare workers, who were



Dr Noreen Chan (second from right) and her colleagues in their Personal Protective Equipment (PPE) during the 2003 SARS outbreak.

grappling with an unknown disease that was killing our colleagues.

I was actually handed a HQO or Home Quarantine Order—one of my patients had developed SARS—and in order to ensure that I obeyed the rules, a CISCO officer came to my house to install a webcam, which was the height of IT sophistication at the time. The internet was not a new thing, but there wasn't even “1G”, only dial-up internet access, so the webcam had to be connected to the telephone line. Every day at a random time, someone would ring the house phone and I would be told to go and sit in front of the webcam for 5 minutes.

All of us healthcare workers felt that people did not generally understand what we were going through, but we supported one another and we knew we had to keep going, because it was the right thing to do. So although there was a sense of isolation, I do not think we ever felt lonely or disconnected.

Yes, there is a difference between isolation (being alone) and feeling lonely. Susan Pinker, psychologist and author of “The Village Effect” calls loneliness “a subjective feeling of being alone against your will” ... “a feeling of being excluded and of existential angst”. All over the world, people have been reporting increasing stress and anxiety as a result of COVID-19, and part of that distress comes from the enforced isolation. Humans are a social species, we use cooperation and connection to survive and thrive, so when we cannot do what we are hardwired to do, this makes it even more difficult to deal with the existential challenges of the pandemic.

And the challenges are enormous, especially for two groups of patients: the thousands of migrant workers affected by COVID-19 and isolated in hospitals and community facilities, away from their support networks; and patients at the end of life, whose loved ones cannot be with them for a variety of reasons.



## Times Like These

by The Foo Fighters  
(David Grohl, Taylor Hawkins,  
Nate Mendel, Chris Shiflett)

I, I'm a one way motorway  
I'm the one that drives away  
Then follows you back home

I, I'm a street light shining  
I'm a wild light blinding bright  
Burning off alone

It's times like these you learn to live again  
It's times like these you give and give again  
It's times like these you learn to love again  
It's times like these time and time again

I, I'm a new day rising  
I'm a brand new sky  
To hang the stars upon tonight

I am a little divided  
Do I stay or run away  
And leave it all behind?

It's times like these you learn to live again  
It's times like these you give and give again  
It's times like these you learn to love again  
It's times like these time and time again

It's times like these you learn to live again  
It's times like these you give and give again  
It's times like these you learn to love again  
It's times like these time and time again

It's times like these you learn to live again  
It's times like these you give and give again  
It's times like these you learn to love again  
It's times like these time and time again

It's times like these you learn to live again  
It's times like these you give and give again  
It's times like these you learn to love again  
It's times like these time and time again



For the terminally ill patients, measures such as lockdowns have resulted in family members being “stuck” overseas, unable to travel back. Or visitor restrictions in hospitals that allow one or two visitors at a time for patients who are critically ill. Ironically, this has had a positive outcome of increased usage of community hospice services, as patients and families choose to avoid going to the hospital.<sup>1</sup>

Within the Isolation or COVID wards however, no visitors are allowed, not even if the person is dying. As a result, healthcare staff are the ones to ensure that the patient does not die alone, and that their families know that. Even after death, the grieving families have to deal with restrictions—on which funeral directors they can use, what the funeral wake can be like, how many mourners can be present.

While we can treat physical symptoms like breathlessness or pain, the psychological, emotional and spiritual distress of isolation can be harder to deal with. International and regional palliative care bodies have recognised the pandemic as causing significant problems for isolated palliative patients and families.<sup>2</sup>

Healthcare professionals have turned to technology to allow patients the comfort of seeing and speaking to their loved ones, and innovations such as robots or virtual/augmented reality may allow isolated patients to “experience” the outside world more vividly. Some might say it is cold comfort, but in times like these, even the smallest comfort has value.

What about the healthcare professionals, the frontline workers putting their own health and wellbeing on the line for others? We have had to continue to go to work, and many serving in high-risk areas have isolated themselves from their families. The media has reported that hundreds of healthcare staff from all over the world have died as a result of COVID-19—including at least one doctor by suicide—and many more will be infected and affected in one way or another. How do you run a marathon when you do not know where the finish line is? How can we prevail through these dark days?

Maybe we should learn something from the Stockdale Paradox. This term was coined by author James Collins in his book “Good to Great”, following his interview with Admiral James Stockdale, on how he survived seven brutal years in a Vietnamese POW camp. Stockdale had said, “This is a very important lesson. You must never confuse faith that you will prevail in the

end—which you can never afford to lose—with the discipline to confront the most brutal facts of your current reality, whatever they might be.”

This apparently contradictory—hence the term paradox—ability to balance optimism and reality, what some would call a “hope for the best, prepare for the worst” mentality, is what I see in some of my patients. They hope for more time, but they also accept the reality that they might not have that time. So they speak of miracles and also make practical preparations; they plan for future holidays (that likely won't happen) yet do not forget to cherish the present.

What lessons can we take from COVID-19 and the enforced isolation, and how do we re-connect in new and meaningful ways? Technology can help, but we have to find ways of bringing ourselves to the interaction as authentically as possible. Even if our patients and families cannot see our faces, nor even hear us clearly behind the masks, they can still see our eyes, they can hear what is in our voices, and they can feel what our presence, intention and empathy bring to the conversation. Even separated by distance and time zones, we can be together in our shared humanity.

The former USA surgeon general, Dr Vivek Murthy, has written a book (soon to be published) called “Together: The Healing Power of Human Connection in a Sometimes Lonely World,” and to him, “Relationships are what make our lives worth living.” Our relationships are being challenged and re-defined by the pandemic, which is not a bad thing if you have been taking your relationships for granted, including your relationship with yourself.

Healing is not about curing. Healing is about restoring, making whole. When the worst of the pandemic is over, the new “whole” that we as individuals, communities and humanity co-create, will be different from what we had before, what we had thought was important and worthwhile. The healing actually has to begin now, because amongst the hurt are the seeds of tomorrow's wholeness. We need to help ourselves, and one another, to reconnect and restore.

<sup>1</sup> <https://www.straitstimes.com/singapore/more-terminally-ill-patients-staying-at-home-or-in-hospice-not-hospitals>

<sup>2</sup> <http://globalpalliativecare.org/covid-19/uploads/briefing-notes/briefing-note-the-psychological-and-social-implications-of-physical-isolation-for-patients-and-families-during-the-coronavirus-pandemic.pdf>

# COVID-19: UPDATES FROM SINGAPORE WEBINAR SERIES

The ongoing health, economic and social impact brought about by the onslaught of the COVID-19 pandemic, together with potentially long-lasting behavioural, lifestyle and psychological changes in people all around the world, tell us that the novel coronavirus has a further reach than the disease it brings. The COVID-19: Updates from Singapore webinar series has seen a range of perspectives from leading experts in disciplines such as medicine, public health, economics, policy making and science that have shed light on the risks, unknowns and opportunities in this unprecedented time.



**Professor Dale Fisher**

Chair of the Global Outbreak Alert and Response Network (GOARN) at the World Health Organisation (WHO)



**Associate Professor David Allen**

Senior Consultant in the Division of Infectious Diseases at University Medical Cluster, NUH



**Professor Paul Ananth Tambyah**



**Professor Wang Linfa**



**Mr Kishore Mahbubani**



**Associate Professor Alex Cook**



**Professor Leo Yee Sin**



**Associate Professor Graeme McLaren**



**Associate Professor Audrey Chia**



**Professor Heidi Larson**

COVID-19 and its far-reaching impacts have become topics of interest in academic discussions and conversations since the emergence of the novel coronavirus in January. The “COVID-19: Updates from Singapore” webinar series was set up to educate and contribute to the discourse surrounding COVID-19, when people were hungry for more information about this mysterious disease. As Asia’s leading medical school, the Yong Loo Lin School of Medicine takes pride and enthusiasm in advancing the knowledge of medicine and science.

The hour-long webinar session has been running since 9 April, every Thursday at 7pm, moderated and hosted by Dr David Allen, Senior Consultant in the Division of Infectious Diseases at University Medical Cluster, NUH.

Professor Dale Fisher, Chair of the Global Outbreak Alert and Response Network (GOARN) at the World Health Organisation (WHO), who is also a Professor at the NUS Yong Loo Lin School of Medicine, provides weekly updates guided by epidemiology charts and dashboards that show the infection numbers and death toll of countries and regions. Overviews of the virus progression in each region are presented systematically, with Prof Fisher giving his expert opinion on particular peaks and troughs observed in the curve and the methods that each region and country were adopting to contain the spread.

A guest speaker follows with a talk or presentation for the topic of the week, after which Dr Allen moderates a discussion with questions from the floor. Each webinar session since has seen an average of 5,000 registrations, with an audience tuning in from 73 different countries. Viewers surveyed for feedback have included hospital administrators and clinical staff, as well as people from outside the medical industry.

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...no one particular demographic is immune to the novel pathogen and its disease. Rather than pin all hopes on a vaccine, it would be more productive if we could learn to adapt, live and manage the virus spread.

## UNDERSTANDING THE PANDEMIC OF THE 21<sup>ST</sup> CENTURY

The tricky nature of the coronavirus and the intensity of its spread has given it a reputation: 'the pandemic of the 21st Century'. With regard to its origins, impact on health and accompanying medical treatments, viewers heard from infectious diseases experts who were in the thick of research and clinical action alike, since COVID-19 begun its rampant spread. As the first speaker of the series, Prof Paul Tambyah shared the clinical findings from patients who contracted COVID-19, outlined the symptoms observed throughout the infection period and subsequent clinical management interventions that were introduced to contain its highly infectious spread. Prof Leo Yee Sin, Executive Director of the National Centre for Infectious Diseases (NCID), echoed similar sentiments when she spoke about the virus's unique transmission patterns and multiple hurdles faced while combatting this tricky virus. Prof Leo, who coordinates the national outbreak response in this crisis, also works at the frontline. She gave a cautionary warning that no one particular demographic is immune to the novel pathogen and its disease. Rather than pin all hopes on a vaccine, it would be more productive if we could learn to adapt, live and manage the virus spread.

Professor Wang Linfa, Director of the Programme in Emerging Infectious Diseases at Duke-NUS Medical School, Singapore, posited that though wildlife like bats and pangolins had possible roles to play in the origins of this novel coronavirus, it was very likely that a rise in human activities such as wildlife trading and farming aggravated the virus' transmission. He also outlined how the genetic mutations of the SARS-CoV-2 virus is distinctly different from identified viruses like SARS-CoV and the Ebola virus. This gave rise to differences in the symptoms presented and produced cohorts who do not exhibit symptoms.

In one of the sessions, Associate Professor Graeme Maclaren, an intensive care physician from the National University Heart Centre in Singapore, spoke about the hierarchy of life support techniques that could be used to resuscitate critical COVID-19 patients in order to gain more control over the patient's physiology.

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It is important to keep in mind that the extent of the global outbreak in the following months will depend on many key factors that can be shaped.

## COVID-19 BEYOND MEDICINE

It takes a public health crisis to witness the beauty of many disciplines coming together to tackle the rapidly-evolving disease. Professor Alex Cook, Vice-Dean of Research and Domain Leader of Biostatistics and Modelling at the NUS Saw Swee Hock School of Public Health, shed some light on how mathematical epidemiology methods, such as disease modelling in statistics, have come in handy in predicting the course of the pandemic and its transmission patterns. Mathematics has also been key in mapping out the possible scenarios that could take place depending on the kinds of policy adopted, while moving towards the recovery phase.

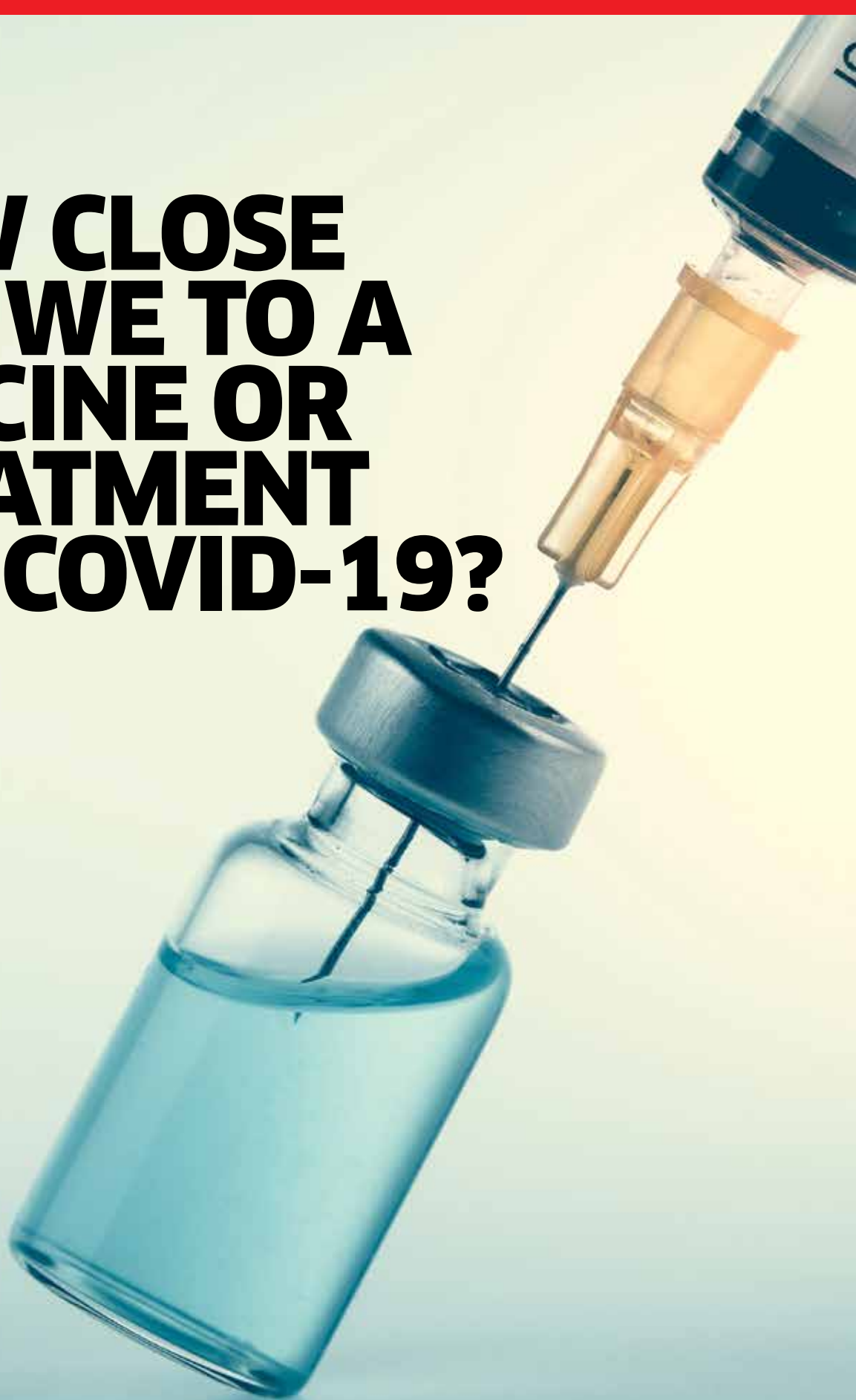
Aside from health, the emergence of COVID-19 has cast a spotlight on the intricacies in geopolitical relationships and cooperation among countries. Singaporean academic and former diplomat, Mr Kishore Mububani, provided a fascinating account of how effective and deliberate management of geopolitical competition between two of the world's leading superpowers can define the world's progress during and in a post-COVID-19 era. In times like this, nations were urged not to turn inwards, but look towards good leaders who are advocates of global cohesion and cooperation to drive solutions to cope with the aftermath of COVID-19. Associate Professor Audrey Chia, Director of the

Leadership Development Programme from the NUS Business School, emphasised that good leadership matters in crises, especially in health systems, where good leadership has immediate impact on health responsiveness, risk protection and improved efficiency, if used strategically.

In a post-COVID-19 world that envisions a COVID-19 vaccine, one of the many issues leaders have to contend with is the volatility of public trust and perceptions around new and existing vaccines. Professor Heidi Larson, Founding Director of the Vaccine Confidence Project in the London School of Hygiene and Tropical Medicine, deduced that it would take the collective efforts of governments to actively communicate the benefits of vaccines to increase public willingness to receive them for the sake of preserving citizen health.

The world has clearly not seen the end of COVID-19. With so much more to learn and understand about the virus and its disease, the initial run of 12 webinar sessions has been extended to 24 sessions. Subsequent sessions will cover softer issues such as preserving mental health in a pandemic, and the costs and ethics surrounding the search for a globally-viable vaccine.

# HOW CLOSE ARE WE TO A VACCINE OR TREATMENT FOR COVID-19?





**Many different vaccines and drugs are being developed and tested at a record-busting pace, thanks to an unprecedented level of worldwide collaboration. However, it will likely take months to a year before we have a vaccine or drug.**

by Dr Khor Ing Wei  
Dean's Office

**S**adly, COVID-19 and the virus that causes it, SARS-CoV-2, need no introduction. Suffice to say, this has been a devastating pandemic like no other, redefining life and death in ways we have never seen before. What is more alarming, it may not be the last or even the worst pandemic to come our way. As the world slowly emerges out of lockdown and braces for a new normal, resumption of full commercial and social activities will depend on us having an effective COVID-19 vaccine and treatments for people who are already infected. So, how close are we to finding a vaccine and antiviral treatments?

To think about which treatments will work for COVID-19, we first need to understand how the disease progresses. In the earlier phase of COVID-19, the virus is reproducing rapidly and infecting host cells. Effective treatments in this phase will likely be those that prevent the virus from replicating itself or infecting cells. If the patient's immune system is strong enough to clear the virus on its own, the disease stops there. This happens in 81% of COVID-19 cases.<sup>1</sup> However, in 19% of cases, patients progress to a more severe phase of the disease, experiencing respiratory distress within 10 to 14 days after they first feel sick.<sup>1</sup> In 5% of these cases, inflammation becomes the main problem, causing respiratory failure, sepsis, multiple organ failure and even death.<sup>2,3</sup> Thus, different therapies that address inflammation are needed at this point.

When a candidate vaccine or antiviral drug is available, they must be tested in clinical trials with human subjects before they can be approved for use in humans. Typically, a candidate therapeutic is tested in a relatively small number (<100) of healthy people to determine its safety (side effects and toxicity), sometimes in several dosages. This is called a Phase 1 clinical trial.<sup>4</sup> If a therapeutic proves safe, it is then tested for efficacy and side effects in up to several hundred people with the targeted disease, and sometimes with a control group that receives placebo or the standard of care. This is called a Phase 2 clinical trial. If Phase 2 results are promising and severe side effects are absent or present in a relatively small number of patients, the next phase (Phase 3) testing involves many more patients (several hundreds to thousands) who may be at multiple testing sites. Phase 3 often includes a control group.

In the face of the devastating sickness and upheaval caused by the COVID-19 pandemic, scientists and clinicians have responded with an unprecedented level of collaboration, sharing data more openly than in any other time in recent memory. For example, in January 2020, Chinese scientists publically shared the genetic sequence of the SARS-CoV-2 virus. Equally important, government and non-profit organisations are providing large amounts of funding to pharmaceutical companies and research institutes, and collaborating across many countries, to accelerate development, clinical testing and production of the most promising vaccine and drug candidates.<sup>5</sup> In some cases, candidates have been developed and clinical trials begun within a few months, compared with years or decades before the pandemic.

## VACCINES



The world will not be able to fully open up again until we have an effective vaccine (or vaccines) that protects us against COVID-19, produced in large enough amounts to immunise large numbers of people.

As of July 2020, more than 120 candidate vaccines are under development, with the possibility of even more that have not been widely reported.<sup>6</sup> Some of these vaccine candidates are currently being tested in clinical trials, while others are scheduled to start clinical testing later in 2020 (Table 1). Other candidate vaccines are at an earlier stage of preclinical development and are not discussed in this article.

Most of the vaccines currently in use are either whole virus vaccines, subunit vaccines or viral vector vaccines. Whole virus vaccines include the intact virus that is inactivated in some way (eg, by heat or chemicals) to make it less likely to replicate and cause disease. Subunit vaccines include a portion of the virus, usually a key protein or proteins. Viral vector vaccines incorporate a viral protein in another, more harmless virus which serves as a vehicle to stimulate the immune response. The spike (S) protein of SARS-CoV-2, which fuses with the host cell membrane and enables the virus to get into cells, is the obvious starting point for subunit vaccines. Scientists made an important finding that the pre-fusion form of the S protein is much more likely to provoke a strong neutralising antibody response than the post-fusion form.<sup>7</sup>

The “new kids on the block” are the DNA vaccines and mRNA vaccines. Large-scale production may be quicker and less expensive for these vaccines because they are less complex than virus, subunit or viral vector vaccines. However, the current batch of clinical trials represent the first time they are being tested in humans.

The various vaccines are also projected to have different effects on the immune system. Some vaccines aim to induce neutralising antibodies (traditionally the holy grail of vaccine response), while others aim to induce both neutralising antibodies and T cells (potentially a more effective dual response). As opposed to “regular” antibodies, neutralising antibodies are those that bind to the virus and prevent it from infecting cells. However, we will have to wait for results from the clinical trials to know for sure how the human immune system will respond to each of these vaccines.

After a safe and effective vaccine is identified, large amounts of it will need to be produced. Usually, a promising vaccine candidate would be identified after clinical trials, and only at that point would it be manufactured at scale. However, the urgent needs caused by the pandemic means that this stage has to be accelerated as well. Some pharmaceutical companies have manufactured or are planning to manufacture large amounts of their vaccine candidates, while they are still undergoing clinical trials. This way, if the candidate proves to be a safe and effective vaccine, it would already be produced in large quantities and can be quickly used to vaccinate populations.

Moderna, the company developing the mRNA vaccine that has shown promising results in Phase 1 trials, has received almost half a billion USD from the U.S. government to ramp up efforts and produce large quantities of its vaccine if its later trial results are also promising. The Coalition for Epidemic Preparedness Innovations (CEPI) (which is funded by several European countries, Canada, Saudi Arabia and the Bill and Melinda Gates Foundation) has contributed hundreds of millions of dollars to accelerate clinical trial testing and manufacturing of several promising vaccine candidates.

Table 1.

Some of the vaccine candidates currently being developed<sup>8,9</sup>

### Whole virus vaccines

Vaccine Candidate	
<b>Whole virus vaccine candidate</b>	
Developed By <b>Sinovac Biotech</b> (China)	
How It Works Whole SARS-CoV-2 virus that has been inactivated so it does not replicate in the body.	Stage of Development and Early Results Phase I/II clinical trial started in April 2020. More than 90% of participants showed a neutralising antibody response. A Phase 3 trial is expected to start soon.
Vaccine Candidate	
<b>Whole virus vaccine candidate</b>	
Developed By <b>University of Queensland</b> (Australia), <b>Peter Doherty Institute for Infection and Immunity</b> (Australia), <b>Viroclinics Xplore</b> (Netherlands), <b>CEPI</b>	
How It Works Whole, live SARS-CoV-2 virus with the S protein locked in a 3-D shape that can induce neutralising antibodies.	Stage of Development and Early Results Phase 1 trial of 120 healthy people started on 13 July, 2020.

### Subunit vaccines

Vaccine Candidate	
<b>WNVX-CoV2373</b>	
Developed By <b>Novavax</b> (U.S.), <b>The Coalition for Epidemic Preparedness Innovations (CEPI)</b> , <b>the European Commission</b> , and the <b>Paul Ehrlich Institute</b> (Germany)	
How It Works Pre-fusion S protein linked to a nanoparticle (Novavax's proprietary technology), injected together with Novavax's Matrix-M adjuvant. <sup>10</sup> Goal is to cause immune cells called antigen-presenting cells to move to injection site, stimulating neutralising antibody and T cell responses against the virus.	
Stage of Development and Early Results Phase I/II started late May 2020. CEPI has committed USD388M towards clinical trials and manufacturing.	
Vaccine Candidate	
<b>SCB-2019</b> (S-Trimer)	
Developed By <b>Clover Biopharma-ceuticals</b> (China)	
How It Works Native (probably pre-fusion) S protein of SARS-CoV-2, administered together with Dynavax's FDA-approved CpG1018 adjuvant (used in an approved vaccine for Hepatitis B virus). <sup>11</sup> By injecting this in the muscle, the goal is to induce neutralising antibodies against the virus.	
Stage of Development and Early Results Phase 1 trial started in late June 2020 to evaluate the safety and ability to provoke an immune response of various doses of SCB-2019.	

## Viral vector vaccines

<b>Vaccine Candidate</b> <b>Ad5-nCoV</b>	
<b>Developed By</b> <b>CanSino Biological</b> (China) and the <b>Academy of Military Medical Sciences' Institute of Biotechnology, China</b>	
<b>How It Works</b> Entire spike protein in an adenovirus type 5 (Ad5) vector. By injecting this in the muscle, the goal is to induce neutralising antibodies against the virus.	<b>Stage of Development and Early Results</b> Results of Phase I trial, evaluating safety and ability to provoke an antibody response of 3 different vaccine doses, showed increases in neutralising antibodies and T cells, with peaks at 28 days and 14 days, respectively. <sup>12</sup> Similar proportions of people in the low-, medium- and high-dose groups experienced adverse events, such as pain at injection site, fever, fatigue, headache and muscle pain, with a few participants in high-dose group reporting more severe fever, fatigue and/or muscle pain. High pre-existing levels of antibodies against adenovirus (a common virus) reduced the neutralising antibody response to the vaccine. Based on results of Phase 1, Phase 2 will evaluate safety and immunogenicity of low and medium doses of vaccine vs placebo in 500 subjects. Phase 2 started recruiting in April 2020.

<b>Vaccine Candidate</b> <b>AZD1222</b> (previously known as ChAdOx1 nCoV-19)	
<b>Developed By</b> <b>Jenner Institute, University of Oxford</b> (U.K.) and <b>AstraZeneca</b> (U.K.). <b>AstraZeneca</b> to manufacture and distribute vaccine.	
<b>How It Works</b> S protein in a chimpanzee adenoviral vector that does not replicate in the body. Goal is to inject into the muscle and stimulate production of neutralising antibodies and T cells against the virus.	<b>Stage of Development and Early Results</b> Phase 1/2 trial testing safety and immunogenicity in 510 subjects started end April 2020, expected to complete in May 2021. Phase 2/3 trial started end May 2020. The same team previously used this technology for MERS and obtained strong immune responses in clinical trials. U.K. government has committed £65.5M towards clinical trials.

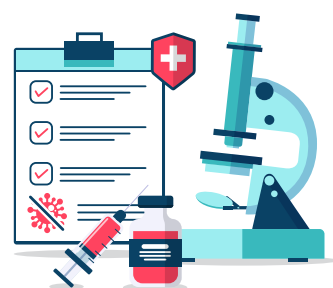
<b>Vaccine Candidate</b> <b>Ad26.COV2-S, recombinant</b>	
<b>Developed By</b> <b>Johnson &amp; Johnson</b> and <b>Biomedical Advanced Research and Development Authority (BARDA)</b> (U.S. government)	
<b>How It Works</b> Ad26.CoV2-S, recombinant consists of proteins from SARS-CoV-2 incorporated in a viral vector that does not replicate.	<b>Stage of Development and Early Results</b> Clinical trials started in late July 2020. First batches of vaccine could be available for Emergency Use Authorisation (FDA's rush approval for urgent use) in early 2021. <sup>22</sup> Johnson & Johnson and BARDA have committed a total of USD1 billion to this effort.

## mRNA vaccines

<b>Vaccine Candidate</b> <b>mRNA 1273</b>	
<b>Developed By</b> <b>Moderna</b> (U.S.), and <b>U.S. National Institute of Allergy and Infectious Disease (NIAID)</b> (U.S. government)	
<b>How It Works</b> mRNA encoding the entire pre-fusion S protein of SARS-CoV-2, wrapped in a lipid nanoparticle. Goal is to inject into the muscle and stimulate a neutralising antibody response against the virus. <sup>13</sup>	<b>Stage of Development and Early Results</b> Phase 1 trial with 45 healthy subjects, evaluating safety, side effects and ability to provoke an immune response to 3 different vaccine doses, started in March 2020. An interim report published on 14 July described strong immune responses (similar or better than those in patients who recovered from COVID-19) in all participants, with no severe side effects at low and medium doses. <sup>13</sup> The high dose produced severe side effects in 3 participants. Phase 2, evaluating safety, side effects and ability to provoke an immune response in 600 healthy subjects, started end May. Includes only the low and medium doses. Phase 3 is slated for end July. U.S. government has committed ~USD500M towards clinical trials and manufacturing.

<b>Vaccine Candidate</b> <b>COVAC1</b> (Self-replicating RNA vaccine)	
<b>Developed By</b> <b>Imperial College</b> (U.K.) and the <b>U.K. government</b>	
<b>How It Works</b> The RNA vaccine is injected into a muscle, where it is translated into the S protein, which will then stimulate an immune response against the virus. <sup>14</sup>	<b>Stage of Development and Early Results</b> Phase I trial started in late June 2020, and will evaluate safety and ability of 2 vaccine doses to provoke a neutralising antibody response in 300 healthy people. A larger trial of 6,000 people is planned for October 2020. <sup>15</sup> The U.K. government has committed £41M towards the effort.

<b>Vaccine Candidate</b> <b>Several mRNA molecules</b>	
<b>Developed By</b> <b>BioNTech</b> (Germany) and <b>Pfizer</b> (U.S.)	
<b>How It Works</b> mRNA molecules that code for proteins that bind to the SARS-CoV-2 receptor (likely the S protein).	<b>Stage of Development and Early Results</b> Phase 1 trials of mRNA vaccine BNT162 in several hundred healthy people are ongoing. <sup>16</sup> Preliminary results showed that BNT162 could induce neutralising antibody responses similar to those in people recovering from COVID-19. Phase 2 in end July will include more people (thousands), including some who are at higher risk of COVID-19.



## DNA vaccines

<b>Vaccine Candidate</b> <b>INO-4800</b>	
<b>Developed By</b> <b>Inovio Pharmaceuticals (U.S.) and CEPI</b>	
<b>How It Works</b> DNA vaccine that matches the DNA sequence of the virus. Injected through the skin, followed by electroporation. <sup>17</sup> Goal is for the DNA to go into the cells, and cause virus-specific antibodies and T cells to be produced.	<b>Stage of Development and Early Results</b> Early results of Phase 1 trial showed antibody and T cell responses in 94% of subjects and no serious side effects 8 weeks after receiving the vaccine. <sup>18</sup> Phase 2 efficacy trial planned in summer 2020.

## Repurposed vaccines

<b>Vaccine Candidate</b> <b>Repurposed Bacillus Calmette-Guerin (BCG) vaccine, currently used for TB in some countries</b>	
<b>How It Works</b> The BCG vaccine may stimulate the innate immune system, the body's first line of defense against invaders, which could help to prevent the SARS-CoV-2 virus from infecting cells and reproducing. Still need more evidence that it works against SARS-CoV-2.	
<b>Stage of Development and Early Results</b> Large trials in the U.S., Australia and the Netherlands are ongoing to evaluate the efficacy of BCG vaccine for respiratory illnesses, including COVID-19.	

## Will be tested in upcoming clinical trials in 2020

<b>Vaccine Candidate</b> <b>LUNAR-COV19</b> (self-replicating mRNA vaccine)	
<b>Developed By</b> <b>Acturus Therapeutics (U.S.), Duke-NUS Medical School (Singapore), Catalent (U.S.) and the Singapore government.</b> Catalent will perform large-scale manufacturing of the vaccine (up to 100s of millions of doses).	
<b>How It Works</b> The mRNA likely encodes the S protein of SARS-CoV-2, combined with a lipid-mediated delivery system. Goal is for a single injection of low-dose mRNA vaccine to enter cells and produce viral proteins, which will stimulate neutralising antibody and T cell responses against the virus. <sup>19</sup>	
<b>Stage of Development and Early Results</b> A clinical trial of 76 healthy adults is projected to start in Singapore in August 2020.	
<b>Singapore's Involvement</b> The Singapore government has provided \$10M funding towards the vaccine's development, and will own the rights within Singapore. <sup>19</sup> Duke-NUS researchers performed preclinical testing, showing that the vaccine induced strong neutralising antibody and T cell responses.	

## Will be tested in upcoming clinical trials in 2020

<b>Vaccine Candidate</b> <b>Viral vector vaccines</b>	
<b>Developed By</b> <b>BioNTech (Germany) and Pfizer (U.S.)</b>	
<b>How It Works</b> 1. S protein incorporated into a measles virus vector that is weakened to minimise risk of causing measles. <sup>20</sup> 2. S protein of SARS-CoV-2 incorporated into a vesicular stomatitis virus (VSV) vector (carrier). This vector was used in Merck's Ebola vaccine. <sup>20</sup>	
<b>Stage of Development and Early Results</b> Clinical trials of the first vaccine candidate projected to start in the coming months, while trials of the 2nd candidate could start later in 2020. <sup>20</sup>	
<b>Vaccine Candidate</b> <b>CVnCoV (mRNA vaccine)</b>	
<b>Developed By</b> <b>CureVac (Germany) and CEPI</b>	
<b>How It Works</b> mRNA coding for a part of the S protein of SARS-CoV-2. <sup>21</sup>	
<b>Stage of Development and Early Results</b> Phase 1 started end June 2020, and will evaluate safety, side effects and ability to provoke an immune response of several vaccine doses in 168 healthy subjects. Phase 2 (with several thousands of subjects) expected to start in Autumn 2020. CureVac has extensive experience working with mRNA therapies and is planning to build a new production facility in the next 2 years. Together with its present facilities, this would enable it to manufacture several billion vaccine doses per year. <sup>21</sup> The European Commission has offered up to €80M towards development and manufacturing.	
<b>Vaccine Candidate</b> <b>DNA vaccine</b>	
<b>Developed By</b> <b>Sanofi Pasteur (France) and GlaxoSmithKline (GSK) (U.K.)</b>	
<b>How It Works</b> DNA vaccine that codes for a protein (antigen) that will stimulate an immune response against SARS-CoV-2, administered together with GSK's adjuvant. <sup>23</sup>	
<b>Stage of Development and Early Results</b> Clinical trials expected to start in Q3 or Q4 2020 and available by Q3 or Q4 2021. <sup>23</sup>	





## ANTIVIRALS



While vaccines are typically used to protect healthy people from getting sick with COVID-19, antiviral drugs can also be used to treat people who already have the disease. Some antiviral drugs prevent the virus from infecting cells, which is the first step in establishing an infection. Other antivirals work by binding to virus particles already present in a person, targeting the virus for destruction by the immune system. Yet other antiviral drugs suppress the inflammatory response and are mainly effective in more severe COVID-19 infections, in which inflammation is a major problem. Most of the antivirals that are currently being tested or that are scheduled for testing in 2020 are antibodies or small molecules, a class of chemical compounds (Table 2).

One small molecule, remdesivir, was originally developed to treat Ebola virus infection. It has since emerged as one of the most promising antiviral candidates, speeding up recovery in hospitalised COVID-19 patients in an early report (Table 2). Singapore is playing an important role in the development of remdesivir as a COVID-19 treatment, with COVID-19 patients here involved in three clinical trials of the drug. Using an innovative AI tool, NUS researchers have also predicted that remdesivir, together with lopinavir and ritonavir (an HIV drug combination) may just be the deadly cocktail that takes down SARS-CoV-2.

Antibodies isolated from the blood of patients who have recovered from COVID-19 can be potent antiviral agents, useful for protecting people against infection and treating the disease in COVID-19 patients. One such antibody, AOD01, was identified from screening B cells (the cells that produce antibodies) as part of a Singapore whole-of-government effort, involving scientists at the DSO National Laboratories and the NUS Yong Loo Lin School of Medicine, as well as collaborators at the Ministry of Defence, Ministry of Health and the Economic Development Board. AOD01 had one of the highest neutralising activities against SARS-CoV-2 reported to date in cell culture (the ability to block the virus from infecting cells). A clinical trial of AOD01 is planned in the coming months.

Another candidate, APN01, is neither an antibody or a small molecule. Instead, it is a protein that mimics the receptor used by SARS-CoV-2 to enter cells in the body. The hope is that APN01 will bind to the virus, thus preventing the virus from binding to its receptor and infecting cells.

## REPURPOSING DRUGS AS ANTIVIRALS



One way to speed up the process of obtaining drugs that can be used in humans is to repurpose existing drugs, which have already been tested in clinical trials and approved by regulatory authorities for other diseases. Several of the antivirals that are being tested in COVID-19 clinical trials are repurposed antibodies or small molecules that were originally developed for diseases such as HIV, Ebola and inflammatory arthritis (Table 2).

Table 2.

Some of the antiviral drug candidates currently being developed

### Mimic of virus receptor

Antiviral Drug Candidate

**APN01**

Developed By

**Apeiron Biologics** (Austria)

How It Works

Mimic of the human angiotensin converting enzyme 2 (rhACE2), the protein receptor that the virus uses to get into cells.<sup>24</sup> Goal is for rhACE2 to bind to the virus, preventing it from binding to the ACE2 receptor on cells. APN01 also reduces harmful inflammation in lungs and prevents acute respiratory distress syndrome.

Stage of Development and Early Results

Phase 2 testing of APN01 vs placebo in 200 patients is ongoing. Skipped Phase 1 and went directly into Phase 2 testing after regulatory approval in April.<sup>24</sup>

### Antibodies

Antiviral Drug Candidate

**Actemra®/ Roactemra®** (toxilizumab)

(Original indication: rheumatoid arthritis; cytokine storm side effect of CAR-T therapy)

Developed By

**Roche** (Switzerland) and **BARDA** (U.S. government)

How It Works

Inhibits function of interleukin-6 (IL-6), an important protein in the inflammatory response. Goal is to reduce excess inflammation in severe COVID-19.<sup>25</sup>

Stage of Development and Early Results

A clinical trial in France showed a reduction in deaths or life support interventions, vs a control group.<sup>25</sup> Safety and efficacy of the drug plus standard of care being tested in a Phase 3 trial (COVACTA), vs placebo plus standard of care, in patients hospitalised with severe COVID-19. Outcomes measured: clinical status, mortality, clinical improvement, length of time on supplemental oxygen, need for mechanical ventilation and viral load.<sup>26</sup> Another Phase 3 trial (REMDACTA) testing the efficacy and safety of the drug plus remdesivir (see below) vs placebo plus remdesivir in patients hospitalised with severe COVID-19 started on May 28.<sup>27</sup>

Antiviral Drug Candidate

**REGN-COV2**

**NEW**

Developed By

**Regeneron Pharmaceuticals**

How It Works

Cocktail of 2 antibodies that bind to the S protein of SARS-CoV-2.

Stage of Development and Early Results

Results from a Phase 1 trial showed that REGN-COV2 is likely safe. Currently being tested in a Phase 2/3 trial in hospitalised and non-hospitalised COVID-19 patients, and in a Phase 3 trial to evaluate its ability to prevent infection in people exposed to a COVID-19 patient.

## Antibodies

Antiviral Drug Candidate **NEW**  
**LY3819253**, human monoclonal antibody specific for SARS-CoV-2

Developed By  
**AbCellera Biologics (Canada), Eli Lilly (U.S.), and the Vaccine Research Center, NIAID (U.S.)**

**How It Works**  
 Starting with 500 antibodies obtained from the blood of one patient who had recovered from COVID-19, AbCellera used its platform to select a few top antibody candidates and is now testing one (LY3819253).

**Stage of Development and Early Results**  
 Phase 2 clinical trial of patients with mild or moderate COVID-19 and Phase 1 trial of patients hospitalised with severe COVID-19 are ongoing.<sup>31</sup>  
 In May, AbCellera received \$175.6 million in support from the Government of Canada towards developing antibody therapies against COVID-19.

Antiviral Drug Candidate **NEW**  
**IFX-1** (InflaRx)

Developed By  
**InflaRx (Germany)**

**How It Works**  
 Antibody specific for C5a, a component of the complement system that is involved in inflammation. This may be useful in treating more severe COVID-19 disease.<sup>32</sup>

**Stage of Development and Early Results**  
 A Phase 2/3 trial in COVID-19 patients with severe pneumonia is ongoing.<sup>32</sup>  
 Early results showed that IFX-1-treated patients had a lower death rate than patients who did not get IFX-1.

## Chemical compounds (small molecules)

Antiviral Drug Candidate  
**Remdesivir**  
 (Original indication: Ebola virus infection)

Developed By  
**Gilead Sciences (U.S.) and NIAID (U.S. government)**

**How It Works**  
 RNA polymerase inhibitor (blocks RNA polymerase enzyme that virus needs to replicate). Shown to inhibit SARS-CoV-2 in cell culture; case studies have also reported some improvement in patients with severe COVID-19.<sup>33</sup>

**Stage of Development and Early Results**  
 Gilead is conducting two Phase 3 "SIMPLE" trials (1 for severe and 1 for moderate COVID-19), of 5-day and 10-day remdesivir treatment regimens plus standard of care, vs standard of care alone.  
 Early results from 1st SIMPLE trial in severe COVID-19 patients showed similar time to clinical improvement for patients on the 5-day and 10-day treatments (>50% recovered by Day 14). Most patients did not have severe side effects.<sup>34</sup>

Results from 2nd SIMPLE trial in moderate COVID-19 showed that 5-day treatment plus standard of care led to 65% higher rate of clinical improvement at Day 11 vs standard of care alone.<sup>35</sup>

A large Phase 2 trial (conducted by NIAID) is studying remdesivir vs placebo in 1059 patients hospitalised with COVID-19. Early results showed that patients on remdesivir recovered more quickly than those on placebo (11 vs 15 days).<sup>36</sup> The full report is expected soon.

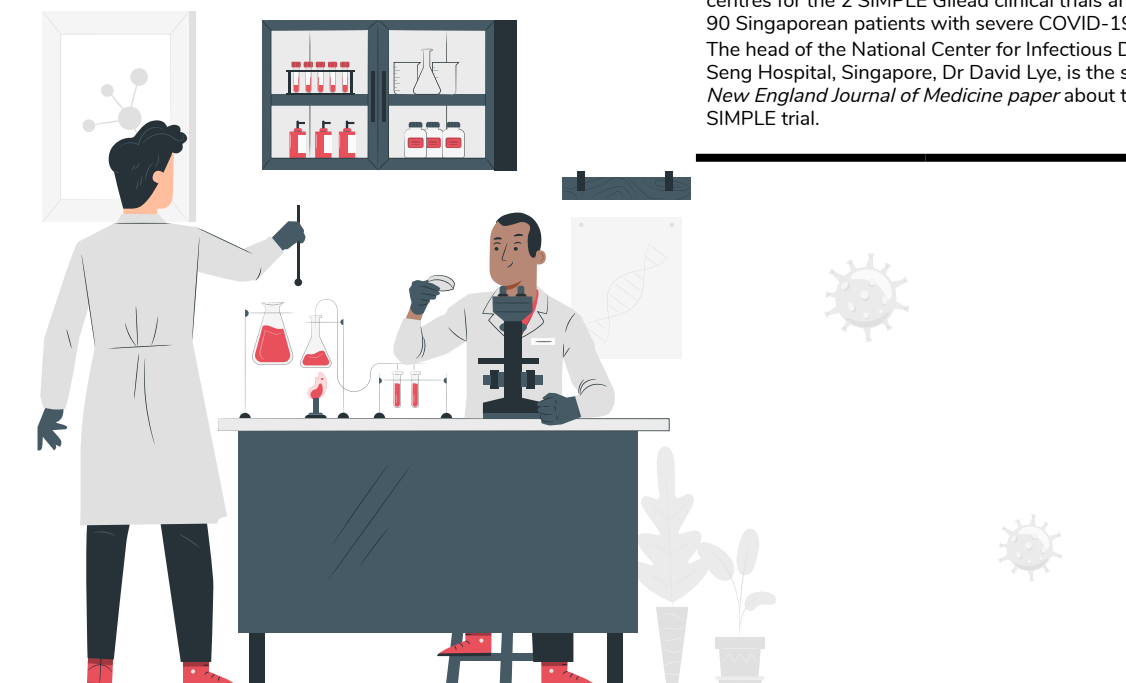
Two clinical trials are ongoing in China, one with mild-to-moderate COVID-19 patients and the other with severe COVID-19 patients. Trials stopped early due to low enrollment. Gilead countered reports of lack of efficacy in one study, saying that results were due to inclusion of severe patients and flawed by small sample size.

On 1 May, remdesivir was approved by FDA for emergency use in patients.

### Singapore's Involvement

Singapore's National Centre for Infectious Disease (NCID) is one of the centres for the 2 SIMPLE Gilead clinical trials and the NIAID trial, with 90 Singaporean patients with severe COVID-19 enrolled.

The head of the National Center for Infectious Diseases at Tan Tock Seng Hospital, Singapore, Dr David Lye, is the second author on the *New England Journal of Medicine* paper about the results of the first SIMPLE trial.



## Antiviral Drug Candidate

**Lopinavir and Ritonavir (Kaletra®)**

(original indication: HIV infection)

## Developed By

Abbvie (U.S.)

## How It Works

Combination of 2 protease inhibitors that block the HIV protease, an enzyme that HIV needs to infect cells. Rationale is that the drug combination could also block the protease of SARS-CoV-2.

## Stage of Development and Early Results

Currently tested in more than 20 trials (according to Clinicaltrials.gov) to treat COVID-19 or to prevent disease in people who have come into close contact with a confirmed case.

Clinical trial in patients with severe COVID-19 at a hospital in Wuhan, China showed no benefit of combination over standard of care.<sup>37</sup>

## Singapore's Involvement

A study led by Prof Dean Ho at NUS, using an AI platform (iIdentif.AI), identified the combination of remdesivir with lopinavir and ritonavir as an optimal therapy, 6.5x more potent than remdesivir alone. Published in a preprint paper (*not peer-reviewed*).<sup>38</sup>

Identif.AI also predicted that lopinavir & ritonavir, as well as hydroxychloroquine & azithromycin would not be effective.

## Antiviral Drug Candidate

**Dexamethasone**

(original indications: allergies, skin conditions, gastrointestinal disorders, rheumatic disorders, endocrine disorders, etc.)

## Developed By

Multiple companies manufacture this generic drug

## How It Works

Dexamethasone is a steroid that reduces inflammation. Goal is to combat lung inflammation in severe COVID-19 disease, to prevent progression to respiratory failure and death.

## Stage of Development and Early Results

The recovery trial of hospitalised COVID-19 patients compared 4,321 patients on standard care vs 2,104 patients on standard care plus dexamethasone. A preprint paper (*not peer-reviewed*) reported that dexamethasone reduced deaths most effectively (by 35%) in the most severe patients, who required mechanical ventilation.<sup>39</sup> It was less effective in less severe patients, who required oxygen support only (reduced deaths by 20%), and not effective in the least severe patients who did not require respiratory support.

## Antiviral Drug Candidate

**Camostat mesylate**

(original indication: chronic pancreatitis)

## Developed By

Ono Pharmaceutical (Japan)

## How It Works

Inhibits the TMPRSS2 protease, which is required for the SARS-CoV-2 virus to infect cells.

## Stage of Development and Early Results

Phase 2a trial of 114 people with early-stage COVID-19 (within 2 days of diagnosis) is ongoing. Efficacy for reducing viral load (number of virus particles), changing COVID-19-positive status, and lessening COVID-19 symptoms will be evaluated in the 2 weeks after starting a 7-day treatment regimen.<sup>40</sup>

## Antiviral Drug Candidate

**Favipiravir (Avigan®)** (original indication: influenza)

## Developed By

Tayoma Chemical, a subsidiary of Fujifilm (Japan)

## How It Works

Inhibits RNA polymerase of virus, thus preventing viral replication

## Stage of Development and Early Results

Interim clinical trial results reported on May 20 did not show efficacy against COVID-19.<sup>41</sup> Stanford Medicine is testing the drug in 120 newly diagnosed COVID-19 outpatients to see if it reduces virus shedding.

## Antiviral Drug Candidate

**Chloroquine and hydroxy-chloroquine**

(original indication: malaria)

## Developed By

Multiple companies manufacture these generic drugs

## How It Works

These drugs block cellular processes and inhibit production of molecules involved in inflammation and other functions.

## Stage of Development and Early Results

Initially promoted by U.S. President Trump, the FDA approved the drugs for emergency use on 28 March (allowing use for certain hospitalised patients outside of clinical trials). Pharmaceutical and generic drug manufacturers donated millions of doses of both drugs to the U.S. government.<sup>42</sup>

However, because of studies reporting a lack of efficacy of the drugs, the FDA withdrew the emergency use authorisation for both drugs on June 15, 2020.<sup>43</sup>

More recently, a study in Michigan, U.S., showed a lower death rate in hospitalised COVID-19 patients treated with hydroxychloroquine or hydroxychloroquine & azithromycin.



## Will be tested in upcoming clinical trials in 2020

### Antibodies

**Antiviral Drug Candidate** **NEW**  
**VIR-7831 and VIR-7832, human monoclonal antibodies targeting ACE2 receptor of SARS-CoV-2**

**Developed By**  
**Vir Biotechnology (U.S.), NIAID (U.S. government), GSK (U.K.), WuXi Biologics (China), and Biogen (U.S.)**

**How It Works**  
 Derived from an antibody (S309) obtained from the blood of a patient who had recovered from SARS. The antibody targets ACE2, the receptor used by the virus to enter cells, and could neutralize SARS-CoV-2 in cell culture.<sup>44</sup>  
 Vir and Biogen will collaborate on the manufacture of both antibodies.

**Stage of Development and Early Results**  
 Aiming to start a Phase 2 trial (without a Phase 1 trial) in summer 2020.<sup>45</sup>

**Antiviral Drug Candidate** **NEW**  
**COVI-SHIELD antibody cocktail**

**Developed By**  
**Sorrento Therapeutics, Mount Sinai Health System, and University of Texas Medical Branch (all U.S.-based)**

**How It Works**  
 Cocktail of 3 antibodies will include Sorrento's star neutralising antibody against SARS-CoV-2, STI-1499, which inhibits the virus from binding to its receptor on cells and was reportedly able to stop 100% of infections by the virus in cells.<sup>46</sup>

**Stage of Development and Early Results**  
 Phase 1 trial is expected to start end July or early August 2020, with a larger trial planned for October 2020.<sup>46</sup>

**Antiviral Drug Candidate** **NEW**  
**AOD01, human monoclonal antibody that neutralises SARS-CoV-2**

**Developed By**  
**DSO National Laboratories, NUS Yong Loo Lin School of Medicine (Singapore)**

**How It Works**  
 One of five human monoclonal antibodies isolated from the blood of patients who recovered from COVID-19, using a high-throughput screening method that the team developed. The ability of the antibodies to block SARS-CoV-2 from infecting cells is the highest reported to date.<sup>47</sup>

**Stage of Development and Early Results**  
 Clinical trials of AOD01 projected to start in the upcoming months.<sup>47</sup>

**Singapore's Involvement**  
 Only COVID-19 therapy to be wholly developed in Singapore.

## SO WHERE DOES THAT LEAVE US?

Despite the extremely rapid pace at which COVID-19 vaccine and drug candidates are being developed, more time is needed to properly test the most promising candidates in clinical trials. At the moment, some of the brightest antiviral stars on the horizon are remdesivir and dexamethasone, which have been around for a while. Although remdesivir is approved for emergency use for COVID-19 by the FDA (meaning it can be used in certain patients in hospitals outside of clinical trials), it would likely take at least several months before it is approved for more widespread use. A COVID-19 vaccine will take longer, partly because almost all of the candidate vaccines are new and have never been used before. Many experts think it will be early- to mid-2021 at the earliest (12 to 18 months after SARS-CoV-2 was first characterised) before a COVID-19 vaccine is available.<sup>48</sup>

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Dr Tam Wai Jia engaging the migrant workers in an interactive health engagement activity to encourage them to be health ambassadors.

# BEFORE SINGAPORE EXITS CIRCUIT BREAKER, LET'S REFLECT ON OUR BIASES AGAINST MIGRANT WORKERS

by Tam Wai Jia

**“It’s okay to break circuit breaker rules, this is a migrant worker problem anyway.”**

I heard this spoken by a passerby one afternoon on my way home, after volunteering as a frontline worker at a migrant dormitory, my N95 mask and goggle marks still etched on my face.

Since then, the segregation between “them” and “us” seems to have grown.

I have been travelling between two worlds — one at work, where I don personal protective equipment and see migrant workers as a doctor, explaining in simple English, sometimes with a translator, what

the quarantine measures mean and what the future holds; the other, where I overhear lift banter of when one might next expect to have bubble tea again.

I rush home to two rambunctious toddlers aged three and one, oblivious of this new world in which we live.

“Mama, when the *cowona*-virus is over, you will take me to sit on the swing,” says my three-year-old emphatically.

That afternoon, I was reminded of the reality that while these two worlds had always existed, one has been largely hidden beneath our harried lives.

As we prepare to exit the circuit breaker, I’ve been wondering about the message that many of us have been hearing: “Be vigilant. Don’t let our efforts go to waste.”

I also wonder if we have made full use of the pause in our lives to reflect on the gravity of the outbreak amidst our migrant worker community, and our part in it.

For if we race towards normalcy in our lives, I fear we might have had wasted the treasured opportunity this circuit breaker had provided for us to engage in self-examination, as individuals, and as a nation.

“You’re a young lady, spending time with migrant workers is not appropriate.”

“Don’t you understand, they’re having it much better here than they ever would have had it otherwise.”

“Why has the migrant worker problem not sorted itself out?”

Of late, these have been some of the chides I have been hearing, as I transitioned from my role as a medical educator to a frontline public health doctor at migrant worker dormitories and community care facilities, curating multilingual health communication resources and conducting health engagement sessions for them.

Such comments, while appearing valid, reflect innate biases and assumptions made towards our migrant brothers.

“Doctor,” one migrant worker told me, “thank you for visiting us. Singapore Government is very good. Doctors here all very good. We will be strong. Thank you for looking after us.”

I held back tears behind my foggy goggles and N95 mask.

As I reflected on a photo of my three-year-old daughter admiring the Singapore skyline just before the circuit breaker started, I mused over the story I would tell her about mama’s country, what made it distinct from papa’s Canada, through the outbreak she had lived through.

I gazed at the spectacular buildings and pondered upon the many lives that had a hand to play in smoothing those cement floors, tiling the offices, sculpturing the trees. I pondered over the trajectory those lives took, to land in ours in such a time as this.

Dr Tam Wai Jia’s 3-year-old daughter admiring the Marina Bay skyline earlier this year.



Dreamily, I watched my three-year-old pointing at the Merlion and wondered about the narrative I would share with her about living through COVID-19 when she was older.

Would I tell her a two-dimensional story of self-righteous meritocracy and dogged success amidst trials; or would I have the chance to tell her a more nuanced but no less glorious narrative of introspective discovery and compassionate inclusivity?

For I have seen how some of our migrant brothers have lived—and those images cannot be erased. Like a movie with special effects gone wrong, they are played over the backdrop of the beautiful Marina Bay skyline and a bleeding sunset in my mind.

Yes, we cannot dismiss the outpouring of love of several groups. Donors and charities have generously stepped up to provide fans, food and masks; churches have adopted dormitories to meet the physical needs of migrant workers and many non-profits and healthcare groups have developed virtual befriending platforms to ease the mental burden of our migrant friends.

Yet, I wonder, if as individuals, we might still be a little too eager with resuming our own lives without sufficiently addressing the burdens carried by our migrant workers, burdens which reflect prejudices our society has built on over the years to keep them “out of sight” and “out of our backyards”.

Don’t get me wrong. I, too, miss my privileges—to take my toddlers to the playground, to take them to the food court to have a (gasp) decadent ice kacang, to take them out on play dates again.

Nonetheless, as we gripe about the challenges of home-based learning and working from home, have we paused to also empathise with our migrant brothers who worry about when they can return to work?

As we complain about not being able to leave home, have we paused to think of our brothers who cannot step out of their rooms, shared with many other men, in living quarters that could use just one more fan?

“Doctor, today was very, very hot in our room,” is something I often hear them say.

I bristle at comments made in jest by some —“the migrant workers should be happy to receive money when they need not work” —reflecting with heart-wrenching oblivion the lack of insight to the challenges of being quarantined away from home, and transferred from one facility to another, without a full grasp of ever-changing rules in a slippery pandemic.

As individuals, let’s examine the thoughts we’ve held against the people who’ve built our nation with us. Let’s volunteer for migrant worker befriending services and prepare our hearts to smile at them instead of shunning them when they resume work.

And as a nation, let’s journey with them. Let us remember that they, too, are an intrinsic part of the fabric of our Singaporean community.

More than a time to deal with the virus, perhaps it is also a time to deal with our hearts.

Let’s not waste this great opportunity to rewrite the Singapore narrative with genuine contrition, deep compassion and great love.

#### ABOUT THE AUTHOR

**Tam Wai Jia** is a medical doctor with a background in public and global health. A Lee Kuan Yew Scholarship holder, she is the founder of Kitesong Global, an international non-profit that empowers underserved communities.

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# PATHOGEN CENTRAL

Have you ever wondered where viruses are studied? What goes into studying virus samples? Who are the people who support the day-to-day research operations? The answers lie inside the largest research-focused biocontainment facility in Singapore, currently housed on campus at Yong Loo Lin School of Medicine, and known as the Biosafety Level-3 Core Facility.





Opened in November 2014, the NUS Medicine Biosafety Level-3 (BSL-3) core facility is currently the largest research-focused biocontainment facility in Singapore that is properly equipped to handle work involving indigenous or exotic biological agents. At a time when COVID-19 is causing health, economic and social devastation around the world, the race to find a globally-viable vaccine has been running at full speed in the BSL-3 Core Facility at NUS Medicine.

## BEHIND THE BSL-3 LABORATORY DOORS

A BSL-3 core facility is designed and certified to work on indigenous or exotic infectious agents, which can potentially develop into lethal diseases through inhalation. This includes viruses such as the West Nile virus, the causative agent of tuberculosis (*Mycobacterium tuberculosis*), and SARS-CoV-2. Experimental practices such as virus isolation and characterisation of viral agents recovered in cultures of specimens can only be handled in a specialised level three facility, where trained expertise is available.

The NUS Medicine facility has a suite of specialised equipment needed for diagnosis, in vivo and in vitro research on Risk Group 3 pathogens. Typically, biological labs are ranked from one to four, with one being lowest biosafety lab level and four being a highly specialised research laboratory that deals with deadly infectious agents such as Ebola.

Gazetted as Protected Place under the Infrastructure Protection Act and to achieve the highest biosafety and biocontainment, the entire infrastructure of the core facility, down to its Heating, Ventilation and Air Conditioning (HVAC) systems, have been specially designed to ensure no airborne particles can exit the enclosed space.

It takes competent and experienced, specially-trained personnel to run such a lab. They consist of the Operation Team, Research Team and Science Service Support Team, under the leadership of the BSL-3 Core Facility Director. From running engineering and lab operations to assisting in COVID-19 work alongside clinicians, and managing scientific programmes according to biorisk policies and guidelines, it takes tremendous work as well as the efforts of many to run a safe and efficient biosafety lab. These consistent efforts earned the NUS Medicine BSL-3 facility a reputation for managing a very comprehensive biorisk management programme.

## KEY WORK IN INFECTIOUS DISEASES

As NUS Medicine is a founding institutional member of the National University Health System (NUHS), an academic health system, researchers at laboratory are able to tap on the wealth of resources at the National University Hospital (NUH) to fuel COVID-19 research.

Disease surveillance is a key agenda of this core facility. The success of a national outbreak response depends on a well-managed surveillance programme for accurate and rapid diagnoses and outbreak responses, which in turn, could bring about a significant decrease in intensity and duration of disease outbreaks. In this regard, the NUS Medicine BSL-3 facility supports the National Public Health Laboratories in disease surveillance and plays an important role in combating endemic diseases including COVID-19, outbreak situations, and national emergencies of many highly infectious and zoonotic diseases of public health importance. Besides, the laboratory simultaneously conducts research on potential treatments, therapies and vaccines.

The world will continue to see outbreaks and threats of new pandemics beyond COVID-19, amplified by globalisation, urbanisation and increased farming activity. As an international trade and commerce centre, Singapore is particularly susceptible infectious diseases, evident with outbreaks of Zika, H1N1 influenza, that have appeared after the Severe Acute Respiratory Syndrome (SARS) outbreak in 2003.

Since infectious diseases remain a major burden for mortality and morbidity in Singapore, cutting-edge facilities like the NUS Medicine BSL-3 core facility are needed to improve surveillance and research technologies and capabilities, in anticipation of other novel infectious diseases.



## How are scientists protected from viruses in the BSL-3 lab?

-  All personnel entering the BSL-3 facility are highly trained
-  They wear dedicated, special Personal BSL-3 Protective Equipment (PPE)
-  This includes breathing through a Powered Air-Purifying Respirator (PAPR)
-  No personal belongings are allowed
-  Scientists observe appropriate safety equipment and practices
-  Labs are designed with negative pressure rooms, with clean air moving into the space in higher supply than the exhaust air leaving the facility
-  Air flows only in one direction
-  Exhaust air is High Efficiency Particulate Air (HEPA) filtered to remove tiny, airborne particles as part of contamination control

# The ENABL Collaboration **PARTNERING WITH PHARMA TO DETECT AND STOP MAJOR CAUSE OF LIVER CANCER**

by Dr Khor Ing Wei  
Dean's Office



From left: Prof Ng Huck Hui (Co-Principal Investigator of this research programme and Assistant Chief Executive of A\*STAR's Biomedical Research Council), Prof Patrick Tan (Executive Director of GIS), Dr Karin Conde-Knape (Corporate Vice President at Novo Nordisk), Dr Ivan Formentini (Vice President at Novo Nordisk), and Assoc Prof Dan Yock Young (Co-Principal Investigator of this research and Head of the Department of Medicine at NUS Medicine). Photo taken at the EMULSION-Novo Nordisk Asian Biomarker Laboratory (ENABL). Copyright: A\*STAR's Genome Institute of Singapore

**N**on alcoholic fatty liver disease (NAFLD), the presence of fat in the liver that is unrelated to excessive alcohol consumption, is the most common chronic liver disease, affecting 30% to 40% of adults in the U.S.<sup>1</sup> The prevalence of NAFLD is even higher in parts of Southeast Asia, reaching 40% in Singapore and Malaysia and over 50% in Indonesia.<sup>2</sup>

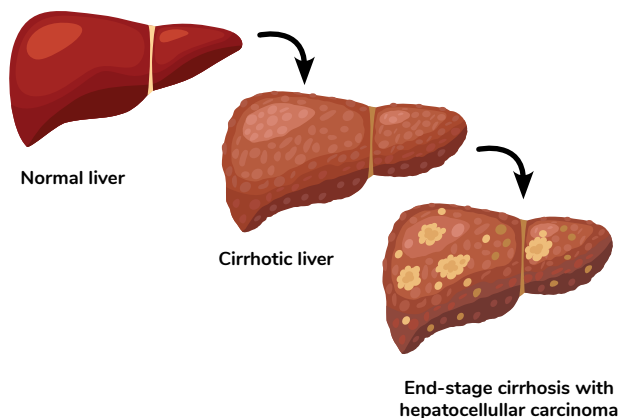
Although NAFLD is relatively benign in most cases, 20% of NAFLD patients have a more serious condition called nonalcoholic steatohepatitis (NASH), in which fat in the liver is associated with inflammation and liver damage.<sup>3</sup> NASH can progress to cirrhosis (scarring in the liver) and liver cancer, at which point few treatment options besides liver transplantation exist. Both NAFLD and NASH are growing in prevalence, and NASH is now the third most common cause of liver cancer and the second most common indication for a liver transplant in the U.S.<sup>4</sup>

NAFLD is strongly associated with metabolic syndrome, with each condition being the cause and the consequence of the other.<sup>5</sup> The majority of NAFLD patients (80%) are overweight or obese, and 44% have type 2 diabetes.<sup>6</sup> Asian NAFLD patients tend to be leaner and younger than Western patients.<sup>7</sup> A study of 1061 NAFLD patients, published in abstract form, found that those with “lean NAFLD” had a lower survival than those with non-lean NAFLD, with lower insulin resistance and fibrosis but more liver inflammation in the lean subjects.<sup>8</sup> These findings suggest that different mechanisms underlie NAFLD in Asians vs Westerners.

To learn more about how NAFLD develops in Asian patients, NUS Yong Loo Lin School of Medicine (NUS Medicine) and the Genome Institute of Singapore at the Agency for Science, Technology and Research (A\*STAR) formed a strategic partnership, ENABL (EMULSION-Novo Nordisk Asian NAFLD Biomarker Laboratory), with Novo Nordisk, a Danish pharmaceutical company that develops medications for diabetes, obesity and NASH.

This partnership is an important development for the Ensemble of Multi-disciplinary Systems and Integrated Omics for NAFLD (EMULSION), a national effort to establish a world-class fatty liver program that is funded by A\*STAR’s Industry Alignment Fund – Prepositioning Program. EMULSION is co-led by the NUS and GIS.

ENABL aims to find new solutions to help diagnose, assess prognosis and treat NAFLD. The first clue that someone may have NAFLD is usually elevated levels of alanine transaminase in the blood, in the absence of other causes such as excessive alcohol use or viral infection. After that, liver biopsy and examination of the extracted tissue sample under the microscope is the “gold standard” used to establish the diagnosis. However, because liver biopsy is invasive and painful, it is not feasible for screening large populations of people. This is one of the reasons why many cases of NAFLD and NASH go undiagnosed.<sup>9</sup>



Although some studies have used ultrasound, blood tests or imaging with MRI or CT, these methods are not as sensitive as biopsy for diagnosing NASH. Development of more sensitive, non-invasive methods to diagnose NAFLD and NASH, such as tests based on biomarkers, will facilitate screening in a broader population. However, such tests require good biochemical markers for NAFLD, which are sorely lacking. The ENABL collaboration aims to address this urgent need by combining the strengths of the various partners. This would help more people with NAFLD, especially those in earlier stages of the disease, to obtain a diagnosis and start interventions to prevent their conditions from progressing to more severe stages, which are associated with much higher morbidity and mortality.

**By defining the optimal thresholds for non-invasive blood or imaging tests, we would be able to make a diagnosis of those who are at highest risk [of NAFLD],” said Professor Dan Yock Young, Head of the Department of Medicine at NUS Medicine and one of the principal investigators of the joint programme.**

“This strategic partnership with Novo Nordisk will enable EMULSION to look into biomarkers that are applicable across different populations,” added Professor Ng Huck Hui, Senior Group Leader GIS and Co-lead Investigator for the EMULSION programme. “This will enable rapid adoption of any diagnostic kits developed for these markers.”

Modifying existing non-invasive tests for NAFLD is another approach that the team of researchers will explore.

“By defining the optimal thresholds for non-invasive blood or imaging tests, we would be able to make a diagnosis of those who are at highest risk [of NAFLD],” said Professor Dan Yock Young, Head of the Department of Medicine at NUS Medicine and one of the principal investigators of the joint programme.

Similar to all metabolic diseases, the main interventions used to prevent or slow down NAFLD are diet and lifestyle changes. Although these preventive measures can be very effective, many people find it difficult to maintain these for a lifetime. This leads to another aim of the academic-industry partnership.

“We hope to be able to develop more specific, targeted and efficacious treatment strategies to add to the universal general recommendations of dietary and lifestyle management,” explained Prof Dan.

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# WHAT DO DIABETES AND ALCOHOL METABOLISM HAVE IN COMMON?

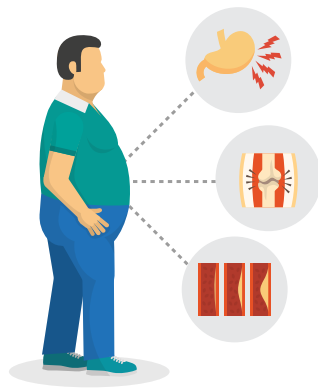
New study discovers links between diabetes and genes involved in alcohol metabolism and belly fat, among others.





by Dr Khor Ing Wei  
Dean's Office

In the largest non-European diabetes genetics study to date that involved 433,540 East Asian individuals from China, Hong Kong, Japan, the Philippines, Singapore, South Korea, Taiwan and USA, an international team of 113 investigators co-led by 5 senior authors<sup>1</sup>, including Dr Xueling Sim from NUS Saw Swee Hock School of Public Health (NUS SSHSPH) and Dr Karen Mohlke from University of North Carolina, identified 61 new genetic variants associated with Type 2 diabetes (T2D).



Findings include discovery of variants near genes involved in skeletal muscle, pancreatic functions, and alcohol metabolism (e.g. *GDAP1*, *PTF1A*, *SIX3*, *ALDH2*), as well as in genes linked to higher levels of fat around the belly in East Asian individuals, e.g. *NID2*. These genes had not been linked with T2D before and may help explain why East Asian individuals get T2D even though they are not obese according to their body mass

index (BMI) measurements. The study was published online in the prestigious scientific journal, *Nature*, on 6 May 2020.

“While a recent study of 900,000 European individuals discovered many new genetic variants linked to T2D2, we were still able to make novel findings as we were studying such a large number of East Asian individuals, where these variants are more common. The identified variants are relatively rare in Europeans and thus missed in the European studies,” said Dr Sim. She added, “We learnt over the years that European and East Asian individuals share many T2D genetic variants, but studying East Asian individuals in such an unprecedented collaborative scale allows us to expand the number of genetic variants associated with diabetes. This can help us understand population differences in the development of T2D.”

The researchers made another striking observation: genetic variants can act through multiple close-by genes in different tissues to influence T2D development. For example, one gene may influence the production of insulin in the pancreas, while another gene close by could affect the use of insulin in the muscle.

...genetic variants can act through multiple close-by genes in different tissues to influence T2D development. For example, one gene may influence the production of insulin in the pancreas, while another gene close by could affect the use of insulin in the muscle.

“These results help further our understanding of the genetic basis for T2D across populations and provide new targets for T2D drug discovery,” said Dr Karen Mohlke of the University of North Carolina, one of the co-senior authors.

“Genetic variants are present in all our genomes, some of which predispose individuals to disease like T2D. Due to differences in the population history, some variants are more common in one population than another. This study emphasises the importance of including large numbers of individuals from different parts of the world in these studies, so that we can better understand the cause of diseases. Singapore, with its multi-ethnic populations from different parts of the world, is an ideal environment for studying this,” said Professor Tai E Shyong, Professor, Department of Medicine, NUS Yong Loo Lin School of Medicine and Professor at NUS SSHSPH, who is also Senior Consultant from the Division of Endocrinology at the National University Hospital and a co-author of the *Nature* article.

These findings serve as a valuable public resource for precision medicine efforts in diabetes. The next steps are to identify which genes are altered by the genetic variants and to determine which of these genes may be targets for new diabetes drugs and treatments.

The large-scale study brought together 23 cohort studies from the Asian Genetic Epidemiology Network (AGEN), a consortium with over 10 years of collaborative history. It includes local cohort studies such as the Singapore Population Health Studies (SPHS), the Singapore Chinese Health Studies (SCHS) from NUS SSHSPH, and the Singapore Epidemiology of Eye Diseases (SEED) studies from the Singapore Eye Research Institute (SERI).

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Assoc Prof Shirley Ooi speaking during the NUHS Residency Graduation ceremony in 2016

# KEEPER OF THE FLAME

A familiar face in the NUHS Residency programme since 2009, *Associate Professor Shirley Ooi* handed the reins to her successor at the start of July 2020. She tells why helming the NUHS Residency programme for more than a decade has been a deeply satisfying and meaningful chapter in her professional career.

**1**036 residents, 32 residency specialist streams, 11 years. The numbers tell the story of how the NUHS nurtures and develops its corps of residents and prepares them for the rigours and challenges of medical practice. For Associate Professor Shirley Ooi, the erstwhile Designated Institutional Official (DIO) of the NUHS Residency training programme, it is also the tale of her personal journey in stewarding the programme from its inception, culminating in her receiving the 2020 Accreditation Council for Graduate Medical Education—International (ACGME-I) Physician Leader award and to her handing over the reins to her Emergency Medicine colleague and successor, Assoc Prof Malcolm Mahadevan on 1 July 2020.

As the DIO, NUHS Residency, Assoc Prof Ooi serves as keeper of the flame, responsible for driving the training and development of junior doctors so that they become competent doctors and specialists who bear the NUHS hallmark of excellence in medical practice and service.

The NUHS Residency training programme was recognised by the ACGME-I in 2009, branching out from its parent organisation, the ACGME. For a residency programme to be ACGME-I-accredited means that the residents are taught based on a model that emphasises on professionalism, selfless responsibility and patient-centeredness that goes beyond book knowledge.

The DIO works in collaboration with a Graduate Medical Education Committee to oversee all Joint Committee on Specialist Training and ACGME-I-accredited residency training programmes in NUHS. On a daily basis, the DIO bears the hefty responsibility of handling all the administration systems, processes, programme directors and residents that counts towards establishing a good residency training programme.

## MANY HATS

Assoc Prof Ooi holds the distinction of being the longest serving DIO among Singapore's three healthcare clusters, having been there right at the start of the ACGME programme in 2009. For the first 8 months, her new tenure as DIO coincided with her day job as Head of the NUH Emergency Medicine Department and her position as Chair of the Specialist Training Committee (STC) of Emergency Medicine at the national level. Yet, the mother of three not only remain unfazed by these responsibilities, but juggled them deftly and with relish. Looking back, she remains grateful for teachable moments like this, which have translated into numerous valuable learning opportunities that have helped shaped lifelong core values she holds dearly.

"The DIO job has its fair share of challenges," said Assoc Prof Ooi. These range from dealing with multiple stakeholders who hold differing views and negotiating policies to better apply them to the local context. Caring for her flock of programme residents and trainee doctors takes additional effort, especially when they have concerns and issues that required her input and intervention. To top it off, the DIO must always keep abreast of constant changes in the educational and residency landscape to ensure that the programmes remain relevant. It also takes some degree of moral courage to tackle difficult issues in a fair and objective manner.

"To put it simply, the DIO is like an octopus with many tentacles that have to work simultaneously and in coordination to survive!" Assoc Prof Ooi said.

Along with the challenges come the delights. They include working with and getting to know colleagues across the medical disciplines, moulding and mentoring a generation of doctors, forming lasting bonds of friendship. These, as well as the scope, scale and intensity of the DIO role, proved to be so absorbing that the 11 years she held the appointment seemed to go by in a flash.

The broad disciplines offered by the NUHS residency programme, its strong teaching culture and a reputation for clinical excellence today—these came about over the years of effort put in by the dedicated and enthusiastic team of programme directors and faculty staff that she assembled and led when the ACGME programme began. It was a very busy and hectic time, Assoc Prof Ooi recalled. "When I look back, I can only say it is by the grace of God that I managed to succeed!"

## STRONG BONDS

She is gratified that her efforts at building up a cohesive and like-minded team that set out to fulfil a vision of transforming graduate medical education at the NUHS has paid off.

"The bond between me and the pioneer batch of Programme Directors is particularly strong as we faced unprecedented challenges of getting all our programmes accredited by ACGME-I within a very short timeline."

Besides attracting the best and most promising residents, the NUHS Residency training programme seeks to provide opportunities to acquire additional skills through the distinction tracks in medical education, quality and innovation and research which runs in parallel with the core residency programme. Residents can even train and cultivate leadership skills through an in-house Residency Leadership Development Programme.

As part of the residency programme, Assoc Prof Ooi and then-NUH CEO Joe Sim as well as then-CMB Professor Aymeric Lim wanted to ground the young doctors in the NUHS values of teamwork, respect, integrity, compassion and patient-centredness. They packed the residents off for bootcamp—3 days and 2 nights at the Outward Bound Singapore (OBS) on Pulau Ubin. There, the trainees soaked up an intensive orientation programme that was designed to develop teamwork, mutual interdependency and resilience in the face of mental and physical challenges.

Leaders lead through modelling exemplary behaviour, and Assoc Prof Ooi decided that she would not shy away from the course. That decision led to her attending 19 consecutive runs at the OBS. It paid off, as through the numerous opportunities for interaction with the residents, she got to know many of them.

"I am far from being sporty. I can't even swim, but I mustered enough courage to kayak 18-km each time with the residents. I have been advised by my orthopaedic surgeon not to do it because of back problems but thankfully with regular gym sessions, my back can still take the exertion."



Assoc Prof Shirley Ooi and her residents on a 3 days and 2 nights orientation programme at the Outward Bound Singapore (OBS) on Pulau Ubin.



Assoc Prof Shirley Ooi (second from left) and her residents bonding over a kayaking session at OBS.

Spending time together with the residents away from the clinical setting also gave her many occasions to hear from the residents on how the NUHS residency programme could be improved. This translated to better supervision and more effective management of the entire NUHS residency programme.

“Knowing the residents well beyond just Emergency Medicine residents meant that I have a mental database to call upon when I saw an opportunity for them to contribute beyond their programme level. It also enabled me to get ground feedback easily since they would have known me already at a personal level and I could just call them up to talk to them.”

In the early days, she got to know every single one of the residents in the initial batches. It became increasingly hard to do so as their numbers grew.

But while she's doffed her DIO hat, her educator's cap sits firmly in place. In her new role as Associate Dean at the National University Hospital (NUH), Assoc Prof Ooi will be involved in undergraduate medical education, something she has long experience in, having taught healthcare professionals ranging from medical students, PGY1s (House officers), medical officers, residents, senior residents and nurses. It is a role she is looking forward to and which looks just as likely to lead to future generations of well-trained, confident and compassionate NUS Medicine graduates.

# LEVELLING UP!

## Enhancing Teaching with Gamification and Technology

by Associate Professor Alfred Kow

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Senior Consultant, Division of Hepatobiliary & Pancreatic Surgery, Department of Surgery, University Surgical Cluster, National University Hospital

Senior Consultant, Liver Transplant Programme,  
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Senior Consultant, Division of Surgical Oncology,  
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Associate Consultant, Division of Hepatobiliary & Pancreatic Surgery, Department of Surgery,  
University Surgical Cluster, National University Hospital

The learning habits of our students change from time to time, and as generations evolve, so must teaching and learning methods. Immediate access to the internet, the widespread ownership of smartphones, electronic and mobile devices, all lead to students growing up as tech-savvy digital natives. Importantly, these factors have changed the way they search for and retain information in their learning. In addition, the continuous influx of knowledge and boom of discoveries in medical fields, particularly where technology plays a large role, is challenging the relevance of traditional ways of teaching and learning which are rapidly becoming outdated. However, developments in virtual and mixed reality, gamification tools, simulation tools and other tech can now be used to fill the gaps in current training methods in medical education, opening up endless possibilities for teaching and learning.

While the fundamentals of medical education should and must still be between the students and real patients, other innovative and interactive learning encounters can enhance the learning experience. As such, NUS Medicine aims to be the leader in developing innovative models of teaching and learning in this respect. Many of these technologies leverage on the daily learning habits of the students, by prompting and tracking learning, facilitating recall and training of knowledge and skills. Importantly, the tools complete the triangle of teaching, learning and assessment.

Through this learning tool, learners are exposed to diverse clinical scenarios involving patients of various demographic profiles which require their decision-making on the ordering of investigations and management procedures.





**Figure 1.**  
Case scenario of a straightforward community-acquired pneumonia



**Figure 2.**  
The cartoon scene of HEALING as the background of the game



**Figure 3.**  
The cost of treatment (or investigation) demonstrated on the screen after the player made the selection



**Figure 4.**  
The final bill of the patient showing player's invoice and the "correct" invoice, including all the costs of investigations and treatment as well as the methods of payment

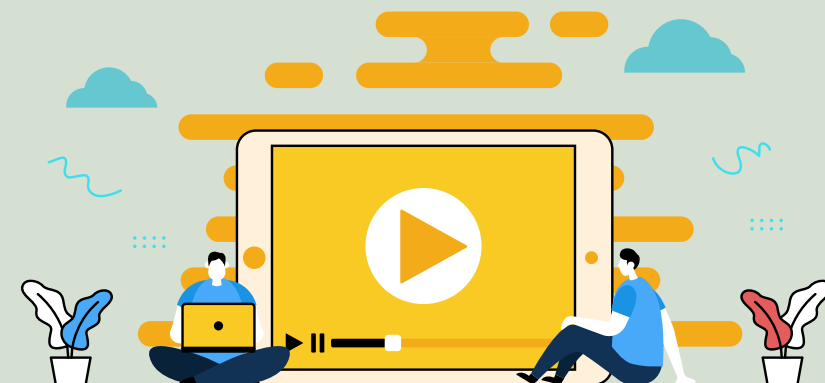
## UNDERSTANDING HEALTH ECONOMIC ASPECTS WITH HEALING

A recent innovation the School created is HEALING, or Health Economics Awareness Learning, a technology-enhanced simulation game that educates medical students on the importance of healthcare economics. The main pedagogy in this game utilises information and knowledge in healthcare spending, including cost of investigations and treatments as well as methods of financing hospital bills, to train players on what constitutes optimal cost-efficient clinical care to patients.

Through this learning tool, learners are exposed to diverse clinical scenarios involving patients of various demographic profiles which require their decision-making on the ordering of investigations and management procedures. At the end of the game, learners obtain feedback on the cost and the appropriateness of treatment they have administered compared to the necessary, cost-effective treatment. Through this experience, learners are made aware of the financial impact of their decisions, while gaining knowledge about the different categories of charges and subsidies, which are useful in guiding their behaviours and decisions in future practice.

Since the emphasis of this game is not on clinical decision making, scenarios are categorised into straightforward and complex ones. For example, a case of simple community-acquired pneumonia with straightforward investigations and treatment options, illustrates the cheapest and most straightforward cost of treatment. On the other end of the spectrum is a scenario of an elderly patient with multiple comorbidities and complicated pneumonia, requiring prolonged treatment and multiple investigations, and who as a result faces elevated costs. More importantly, the game also teaches students the various payment options in Singapore, to illustrate cost differences from one scheme to another. We hope to strengthen our students' knowledge in this area and build a healthy habit of choosing wisely when they enter into clinical practice in the future.

HEALING is easily accessible for use on iPads and is available on the App Store. As the app facilitates synchronous learning, students are able to access it to learn anytime and anywhere. With HEALING incorporated into the Healthcare Economic Series in the School's core curriculum, it will supplement students' learning from actual interactions with patients and learning encounters surrounding this topic.





# INTRODUCING THE VIP: AN AI RESPONSE TO CLINICAL TEACHING IN THE TIME OF COVID-19

by **Juanita Kong**

Research Assistant, Department of Pharmacology

Dr **Judy Sng**

Senior Lecturer, Department of Pharmacology

Face-to-face classes cancelled, and lessons moved online? Can't practise your skills? Not allowed into clinics? Fret not, Virtual Integrated Patient (VIP) is a virtual hospital aimed at allowing medical students and practitioners to hone their skills further.

The screenshot displays the Virtual Integrated Patient (VIP) interface. The top section features a chat window where a doctor asks "how are you?" and the patient responds "I'm coughing and feel a bit breathless." The doctor then asks "Do you have fever?" and the patient replies "this time, I don't have any fever." The doctor asks "tell me about your cough" and the patient says "it's a dry cough." The interface includes a "Random Patient Generator" and a "Medical Record" section with tabs for Patient History, Physical Examination, Lab Examination, Diagnosis, and Treatment. A table of laboratory test results is shown, including WBC, Neutrophil, Lymphocyte, Monocyte, Eosinophil, Basophil, and Neutrophil percentage. The interface also includes a 3D anatomical model of a human body with a BMI of 23.4, weight of 70kgs, and height of 1.73m. The interface is designed to be easy to navigate and provide realistic case information.

Test	Result	Unit	Ref Ranges
Haematology			
Full blood count			
WBC	11.07	$\times 10^9/\mu\text{L}$	(4.0 - 10.0)
Differential Count			
Neutrophil%	6.68	$\times 10^9/\mu\text{L}$	(2.0-7.6)
Lymphocyte%	1.48	$\times 10^9/\mu\text{L}$	(1.0-3.0)
Monocyte%	0.64	$\times 10^9/\mu\text{L}$	(0.2-0.8)
Eosinophil%	2.00	$\times 10^9/\mu\text{L}$	(0.0-0.4)
Basophil%	0.07	$\times 10^9/\mu\text{L}$	(0.0-0.1)
Neutrophil	76.16	%	(40.0-75.0)

The picture above shows the interface of the VIP.

**From left, first panel:** Every patient in this database is unique and the VIP can randomly generate patients for the user (Random Patient Generator). The interface is designed like a chat room where doctor and patient can hold a realistic conversation about the symptoms felt and recommended course of treatment.

**Second and third panels (bottom):** This portal is multidimensional, where users can perform physical examinations and run realistic lab investigations for their virtual patients, to gather more evidence, should the history-taking component be insufficient. Case information provided is realistic and based on results that occur in real life.

Like how pilots train flying aircrafts on flight simulators before taking to the skies, the Virtual Integrated Patient (VIP) seeks to complement medical education by providing medical students with a safe space to practise their clinical skills anywhere and anytime. This allows them to gain confidence before stepping into an actual clinical environment.

Equipped with a random patient generator, students are exposed to different clinical cases. They are tasked to identify symptoms based on asking the virtual patient questions that would lead them to make an appropriate diagnosis. One remarkable feature of the VIP programme is its conversational technology. A chatroom with a virtual patient is set up, where learners can converse with him or her like how a consultation session with a doctor would be like on a messaging app. This includes patients detailing how they are feeling and why they have come for a consult. Information collected from the conversations between the patient and the doctor are compiled into datasets subsequently to enable a smoother AI-learning experience.

The VIP was recently piloted with Phase II (Year 2) medical students as part of the “Communication with Patients” module. A survey was conducted among these students after using the learning portal, to further understand what they liked about it and how it can be improved to better serve their learning needs. The first batch of students who trialed this website welcomed it as this allowed them to accumulate additional practice in patient diagnosis, in addition to the Standardised Patients (SPs) that they were clerking weekly. Our students find this helpful as an additional learning resource that they can leverage on the go and at any time when they are busy. The launch of this VIP programme also coincided with the transition to online classes due to the COVID-19 pandemic, so that learning was not disrupted and students could still continue to hone their clinical skills despite moving to home-based learning.

Besides bettering their clinical acumen and jogging their memory on what they have learnt during their curriculum time, students also gave feedback that these simulations help them improve their ability to assess a patient from symptom to diagnosis, which is the reality of what students encounter when they go to clinics to meet their real patients. A key objective of VIP is its focus on the process taken to get to the end point, rather than the diagnosis itself.

One remarkable feature of the VIP programme is its conversational technology. A chatroom with a virtual patient is set up, where learners can converse with her or him like how a consultation session with a doctor would be like on a messaging app.

With the COVID-19 circuit breaker in place, we have also provided Phase IV (Year 4) students with hands-on experience to develop the VIP platform with us under their elective module “Inspiring Health for All” under the topic of Education Innovation. Over 12 weeks, the students developed their symptom of choice and took it through the development of history-taking conversations with their virtual patient, the physical exam and investigations to perform on their virtual patient and the appropriate provisional and differential diagnoses at the end of the process. The platform was shortlisted as one of the two top Education Innovation projects and selected for a webinar presentation in the Pathway-Based Elective Programme Grand Finale to faculty members and their fellow students.

The Phase IV students felt positively about the experience, such as their work in the development of a couple of diagnoses. Overall, they believe

in the value of the VIP as a learning platform for themselves and students in the medical school.

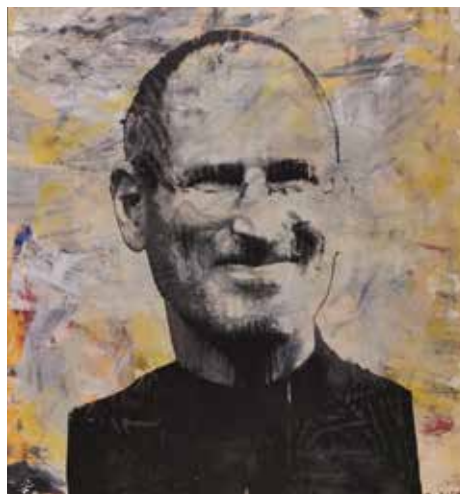
The uptake for the VIP platform has been largely enthusiastic. This diversity of different clinical cases gives rise to more active discussions among the tutorial or student groups, allowing the students to share their experiences of different patient types with their peers, discuss the process of arriving at a diagnosis and learn new or different ways of approaching a case. Indeed, this VIP portal has been flexible and beneficial for the education of students from different years, which will be impactful when introduced into the medical community.

The VIP was initially funded by the MOE Tertiary Research Funding 2018-2020 and is currently supported by the Yong Loo Lin School of Medicine under the Innovation Project. It was shortlisted under the Graduate Research Innovation Project (GRIP) and hot-housed for venture creation, but the team decided to further develop the platform for our students before moving it out to be used commercially.



The VIP team (from left): Research Assistant Lee Yueh Jia, Research Programmer Pabba Anubharath, Principal Investigators Professor Edmund Lee and Dr Judy Sng, Research Assistant Juanita Kong, GRIP PI Dr Viveka Kalidasan and her husband





Paintings by artist Raouf Rifai

# ART FOR CHILDREN WITH CANCER

by Ng Hwee Koon  
Senior Assistant Director, NUS Medicine  
International Council, Dean's Office

The NUS Medicine International Council (NIC) of the Dean's Office of NUS Medicine, is launching an "Art for Kids with Cancer Charity Donation Drive" to raise funds for paediatric oncology research and education at the School. The fundraising campaign highlights NUS Medicine's commitment to innovation in education and research, this time expressed through art.

Cancer is one of the top causes of death for children around the world. There is urgent need to improve the cure rates of children with cancer in Asia and the NUS Yong Loo Lin School of Medicine (NUS Medicine) is well positioned to help.

You may recall the days—some 25 years ago—when almost every Singapore family with a child with cancer would leave for either Australia, the United States or the United Kingdom—if their family can afford it. Since then, our healthcare has improved tremendously because of investments in clinical training and research. Now, most Singaporean children with cancers are successfully treated in Singapore with about 8 in 10 cured.

In a recent case, Oscar Saxey-Lee—a 6-year-old British boy came to Singapore to seek help from NUS Medicine's Professor Dario Campana and Associate Professor Allen Yeoh, whose ground-breaking work made a profound difference for Oscar who had exhausted all treatment options in UK. After six cancer-free months, he returned home in June 2020.

Yes, it is remarkable how we have turned the situation around, making a difference not just for Singaporeans but for children in other parts of the world. But the situation in most parts of Asia remains dire. Fifty percent of the world's burden of childhood cancer reside in Asia. Of those, only 20% are cured.

The NUS Medicine International Council (NIC) of the Dean's Office of NUS Medicine, is launching an "Art for Kids with Cancer Charity Donation Drive" to raise funds for paediatric oncology research and education at the School. The fundraising campaign highlights NUS Medicine's commitment to innovation in education and research, this time expressed through art.

A series of portraits by renowned artist Raouf Rifai, who has depicted transformational innovators of the world on canvas, will be exhibited for silent auction at a suitable time to be announced. Rifai's paintings in this "Disruptors" collection pay homage to leading, innovative icons such as Steve Jobs, Bill Gates, Elon Musk, Jack Ma, Jeff Bezos, Mark Zuckerberg, Pony Ma, Sergei Brin and Yayoi Kusama.

Meanwhile, our initial round of fundraising soft-launched during the COVID-19 pandemic in April raised close to \$350,000 in two months, almost halfway to our goal of \$750,000. We would like to acknowledge all our kind supporters including Mr Ng Yu Zhi, Founder and Managing Director of Envy Capital, as well as our contributors from 21 various countries.

You can also do your part to help. Participate now in this "Art for Kids with Cancer" initiative at the NIC website at [nic.nus.edu.sg](http://nic.nus.edu.sg).



# THE DUTY TO INFORM AND THE DOCTOR'S DILEMMA

by Professor Kumaralingam Amirthalingam  
Faculty of Law and Centre for Biomedical Ethics,  
Yong Loo Lin School of Medicine

While the Chief Justice in Hii Chii Kok emphatically stressed the importance of striking a balance between autonomy and beneficence, doctors in clinical practice remain fearful, wondering what risks will be deemed material and how far they can go to persuade a patient to accept beneficial treatment without violating patient autonomy.

Doctors provide patients with information and advice in order to provide the best care for the patient (the principle of beneficence) and to enable the patient to make an informed decision (the principle of autonomy)<sup>1</sup>. These two objectives should exist in harmony but more often than not, they end up at odds with each other. When things go wrong, doctors face complaints or lawsuits. It is then up to the courts to decide which information should have been provided or withheld. Should the information be based on what the doctor believes is material to the patient's health; what the patient believes is material to the patient's interests; or what the court determines on hindsight is material to the patient's autonomy? This decision involves a complex balancing of professional, ethical and legal considerations. In an ideal world where the doctor-patient relationship is based on trust and mutual respect, these considerations should converge and result in the right decision.

However, the real world is far from ideal. A series of recent decisions on the scope of the duty to inform has left doctors bewildered because what the law apparently requires does not seem to align with the medical understanding of professional and ethical obligations. Reflecting on the polarized

world we live in, patient autonomy and medical beneficence are set against each other instead of reinforcing each other. This has a corrosive effect on the doctor-patient relationship as well as on the morale of doctors. Importantly for clinical practice, doctors are unsure what information they should disclose and what advice they can give to guide patients without infringing patient autonomy and falling foul of the law. This article argues that much of the current concerns stem from a misunderstanding of what the law is. In doing so, the article aims to explain the law, to clarify some misconceptions and to point to a recent English legal decision that should provide some reassurance for doctors.

The starting point is the seminal decision of *Bolam v Friern Hospital Management Committee*<sup>2</sup> in which it was held that a doctor may not be found liable if his or her practice is accepted as proper by a respected body of medical opinion, even if there is another group of medical experts who disapprove of the practice. In short, the standard of care is determined by peer practice. Applied sensibly, this provides a pragmatic and fair approach to medical judgments pertaining to diagnosis, treatment and care where professional differences legitimately exist. However, the application of *Bolam* to the doctor's duty to inform was problematic as it resulted in doctors controlling information that was essential to enable patients to make informed decisions. *Bolam* had the effect of undermining patient autonomy, and not surprisingly, it has been rejected across the major common law jurisdictions. Singapore and the United Kingdom are latecomers to this trend. The law governing the duty to inform, set out in the United





Kingdom Supreme Court in *Montgomery v Lanarkshire Health Board*<sup>3</sup> (“*Montgomery*”), was adopted by the Singapore Court of Appeal in *Hii Chii Kok v Ooi Peng Jin London Lucien*<sup>4</sup> (“*Hii Chii Kok*”).

Under the *Montgomery/Hii Chii Kok* test, a doctor is under a duty to inform a patient of material risks. A risk is material if a reasonable patient would attach significance to it or if the doctor knows or ought reasonably to know that the patient would attach significance to it. Some doctors have misunderstood the second part of the test to mean that the doctor must disclose any information that the patient desires. Not so. If the doctor has no reason to know that the patient would attach significance to a particular risk, there is no negligence. A controversial decision of the Singapore Medical Council (SMC) Disciplinary Tribunal, wrongly finding a doctor guilty of professional misconduct for failing to inform his patient of a trivial risk sent the medical profession into a panic. The received message: Inform or be damned. The fact that the High Court reversed the decision and acquitted the doctor has been ignored<sup>5</sup>.

There is a gulf between doctors and lawyers/ethicists on the meaning of patient autonomy and its place in the doctor-patient relationship. For lawyers and ethicists, autonomy is first amongst equals; for doctors, beneficence is their beacon. Autonomy is a complex concept with ethical, philosophical, legal, social and political layers. These complexities cannot be explored in this forum, but suffice to say that much of the tension between autonomy and beneficence is due to a narrow, liberal conception of autonomy born out of civil rights that does not fit comfortably in the medical context<sup>6</sup>. While the Chief Justice in *Hii Chii Kok* emphatically stressed the importance of striking a balance between autonomy and beneficence, doctors in clinical practice remain fearful, wondering what risks will be deemed material and how far they can go to persuade a patient to accept beneficial treatment without violating patient autonomy.

A recent English legal decision provides some helpful guidance. The plaintiff in *Pepper v Royal Free London NHS*

*Foundation Trust*<sup>7</sup> (“*Pepper*”), who was 56 years old at the time of the incident, underwent a pancreaticoduodenectomy [Whipple surgery] at the hands of the defendant surgeon. The plaintiff had presented at the emergency department with abdominal pain. A series of tests including repeated computed tomography, magnetic resonance imaging and endoscopic ultrasound were carried out. The tests were inconclusive, suggesting possible malignancy or an inflammatory lesion. The plaintiff consented to investigative surgery and Whipple surgery if there was evidence of malignancy. An intraoperative biopsy was negative for a tumour but the defendant, feeling that the pancreas was hard, made a clinical judgment to proceed with the Whipple surgery. The histopathology results post-surgery showed no malignancy; the plaintiff had acute pancreatitis and cholecystitis. She brought an action in negligence, alleging that she had undergone unnecessary surgery that had resulted in adverse consequences.

The key issues were whether the defendant surgeon had been negligent in advising the patient to undergo surgery and whether she had given her consent. The judge began his judgment with this salutary reminder of the doctor’s role in the doctor-patient relationship:

... a doctor’s role is to ensure that patient understands the serious consequences of her condition, her treatment options and the risks of undergoing or not undergoing such treatment and that it is a patient’s right to make an informed decision as to whether to undergo the treatment which is offered to her. I bear in mind the inequality in the position of doctor and patient, given that the former will be highly experienced and the latter may well have little or imperfect knowledge and that it may not be easy for a patient to question a doctor about what he proposes.<sup>8</sup>

On the first issue of negligent advice to have the surgery, the judge noted that the defendant had been quite forceful in warning the plaintiff about the risk of the cancer becoming inoperable if quick action were not taken. Nonetheless, the judge held

that the defendant was not negligent in using “stark language” to impress upon the patient the gravity of the situation. Indeed, the judge went on to say that the doctor may well be negligent in failing to be forceful in cases where the patient does not “fully appreciate the gravity of her situation.”<sup>9</sup> On the facts, it was found that the defendant had carefully drawn the line between his duty to give appropriate information as a professional and the plaintiff’s right to make an informed decision. There had been no undue influence.

On the second issue of consent, the patient alleged that she had given consent to the surgery only if the biopsy was reported as positive. The defendant argued that the plaintiff had given consent to the surgery even if the biopsy were negative if the defendant nonetheless formed a professional opinion based on his assessment of the pancreas that it could be malignant. The judge accepted this argument and went on to determine whether the defendant had been negligent in assessing the pancreas to be malignant when in fact it was not. Here, the judge weighed the evidence of the experts and found that as there were experts who would have made the same assessment, the defendant could not be found negligent on the *Bolam/Bolitho* test.

*Pepper* is a significant decision that should reassure doctors that they can and should act in the best interests of their patients while providing them with the necessary information and guidance, and that they can do this without the fear of being held liable. Indeed, a close reading of *Hii Chii Kok* and *Lim Lian Arn* would provide similar reassurance. The law on the duty to inform set out in *Montgomery* and *Hii Chii Kok* strikes a balance between beneficence and autonomy. Unfortunately, it has occasionally been misunderstood or misapplied, leading to a trust deficit. Doctors understand that trust is central to the doctor-patient relationship—perhaps some of that trust should also be placed in the law.

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'WHAT IS INCONVENIENT FOR YOU IS LIFE-SAVING FOR ME':

# HOW HEALTH INEQUITIES ARE PLAYING OUT DURING THE COVID-19 PANDEMIC

by Dr Vicki Xafis

Senior Research Fellow, Centre for Biomedical Ethics



The COVID-19 pandemic has had a significant impact globally. Most affected, however, are those individuals and groups routinely disadvantaged by the social injustice created by the misdistribution of power, money, and resources. Simple measures that prevent the spread of COVID-19, such as frequent hand washing and social distancing, are unavailable to millions of people in the wealthiest of nations and in the poorest of nations. Disadvantaged groups are impacted more directly and in disproportionately higher numbers due to existing poor health, and the disruption of services central to securing an income and an education will have lasting consequences for their futures. The unintended effect of exclusionary government policies is that privileged citizens and healthcare systems are also at greater risk.

This paper explores ways in which certain groups who already experience disadvantage are being affected by COVID-19 through a brief examination of some of the social determinants of health that impact health outcomes in both affluent and poorer nations. The areas considered in this paper include income and wealth, employment and access to health services, housing, food environment, education, and safety. Examples are given to highlight the way health inequities play out for different groups but it should be remembered throughout that one form of disadvantage often leads to being impacted by other forms. For example, inability to access education will most often impact on health, and life more broadly, in numerous direct and indirect ways at various stages of a person's life.

## DEEP INSIGHT AND A NEW OPPORTUNITY

This pandemic has already brought about a new awareness. For example, it is only now that low paid workers have finally been recognised for the vital contributions they make to keeping cities and countries functional. People we have previously walked past as if they were invisible have suddenly come into sharp focus; the supermarket worker stacking the shelves has become our hero because he not only replenishes stocks but, in doing so, also unwittingly provides psychological relief; the homeless person lying in the entrance of a building has suddenly become the subject of our concern...or of our fear; the factory worker who works tirelessly to make the mask which may save our life is another such hero.

The COVID-19 pandemic has demonstrated, in profound ways, that all sectors of society and all members of society are interlinked and interdependent. The risks disadvantaged members of societies are exposed to have impacted the whole of society with devastating consequences on mortality and on healthcare systems which, in many parts of the world, have struggled to cope with the rapid rates of infection. Despite the global turmoil COVID-19 has created, governments around the world are now presented with an opportunity to correct the health inequity course we have been on for decades.

Had governments of wealthy nations invested with commitment in programmes and policies that aim to reduce health inequity, thousands of lives may have been spared and billions of dollars may have been saved.

In the months ahead, governments will need to reflect on what has become the greatest challenge of our lifetime. Had governments of wealthy nations invested with commitment in programmes and policies aimed at reducing health inequity, thousands of lives may have been spared and billions of dollars may have been saved. The reduction of health inequities is an ethical imperative but is also prudent from an economic sense, as it ultimately leads to greater productivity, less strain on healthcare systems, and fewer welfare programmes.

It will never be possible to fully eradicate health inequity. However, the multidisciplinary approach that needs to be taken from the start of a child's life has been articulated multiple times for multiple groups by world renowned experts and focuses on 'early child development; education and skills development; employment and working conditions; minimum income for healthy living; sustainable communities; and a social-determinants approach to prevention.' (Marmot 2011). Closing the health inequity gap will entail many years of dedicated efforts but governments around the world now have a rare opportunity to achieve this.

Finally, it has emerged that the character traits of our leaders have played a decisive role in responding to this pandemic. Likewise, during the recovery efforts, leaders around the world will either guide us prudently through this lengthy phase or contribute to widening the health inequity gaps locally and worldwide.

# FROM CLASSROOM TO FRONTLINE

The disruptions caused by COVID-19 have been widespread. Graduates from the Yong Loo Lin School of Medicine Class of 2020 were deployed earlier than expected to work in hospitals islandwide to meet the nation's call for healthcare professionals, and most faced a heavy workload from the get-go. Hear from some of our newest alumni as they share their thoughts on graduating early and answering the call to serve during a pandemic.



## Joshua Chia

SGH Internal Medicine

Initially, most of us were understandably disappointed when our grad trips were cancelled, but it has been an honour to be able to contribute to society in such a time of need. Adjusting to life as a doctor is never easy. The pandemic makes doctoring a little more challenging, but I have been privileged to work with great seniors who are always looking out for us and lending a helping hand to help us cope.

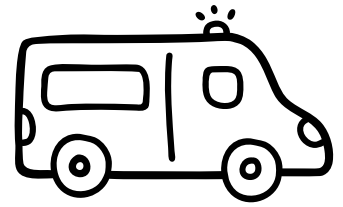
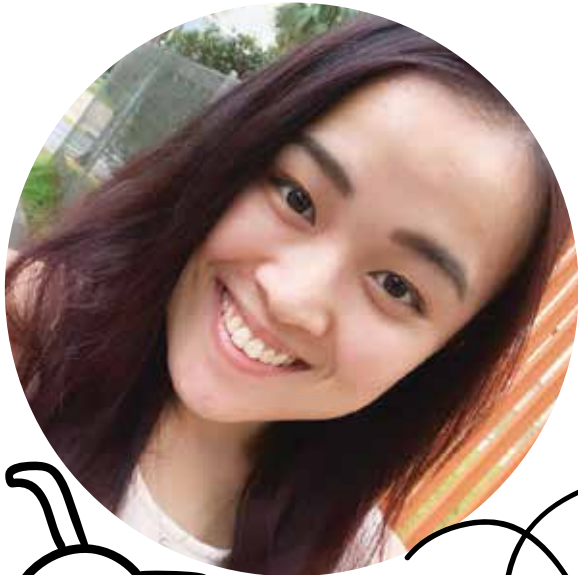
## Sarah Tham

SGH Internal Medicine

While there are many new protocols in place, the hospitals have made a lot more effort to integrate us this year. Unlike our seniors, we had a one week orientation and one more week of overlap with the senior house officers (HO), as well as "tag on" calls when we would be attached to a senior HO. Our seniors also conducted Zoom lessons to teach us the ropes. I am reminded that every day is an opportunity for us to offer love where there is none, comfort where there is despair, and hope where there is uncertainty.







## Amanda Chia

SGH Obstetrics and Gynaecology

I was nervous at first, but also, the seriousness of the situation sank in and seeing so many of my seniors giving so much of themselves made me want to do the same too. I think the difference is that our department's manpower is halved and all of us have to step up to cover multiple stations. The learning curve is really very steep. However, no matter how long the night might seem, the sun will rise tomorrow!

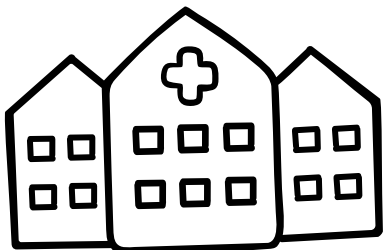


## Thaddeus Cheong

KKH Paediatrics

I think we were all surprised when we were told that we would be starting work earlier than usual and nervous about starting work in such uncertain conditions. There was a lot of self-doubt about whether we would be up to the task but what struck me most has been the dedication and encouragement of our seniors and colleagues. The nurturing and resilient attitude they modelled for us is something I hope to one day carry as well. So as we continue in our first steps of this journey, we owe a huge thank you to all who have guided us along!

Dr Thaddeus Cheong (far right)  
with his colleagues





# FIRST SAF FEMALE MEDICAL OFFICER TO DON KHAKI BERET

Story by Koh Eng Beng  
Photos by Chua Soon Lye & Courtesy of Cpt (Dr) Ng





“  
Coming in, as a young 24-year-old girl, I felt that I need to go through some kind of common experience with them so that I can connect with them at a different level.

— CPT (Dr) Ng on why she chose to go through the gruelling GCC

**TOP**  
Better known as the ADF, the Army Deployment Force is an all-Regular combat unit that conducts niche operations in counter-terrorism, overseas peace support, and more.

## Tough as nails: Captain (Dr) Ng Chen Hui volunteered for the gruelling Guards Conversion Course to win the respect of her boys in the Army Deployment Force (ADF).

After completing her medical studies at the National University of Singapore, Captain (CPT) (Dr) Ng Chen Hui returned to the Singapore Armed Forces (SAF) last year to resume her career as a medical officer. The 25-year-old was a recipient of the SAF Medicine Scholarship.

Her first tour of duty? Battalion medical officer of the ADF.

Under her command is a team of about 10 combat medics. Most of them are highly experienced Guardsmen—elite infantry soldiers who specialise in heliborne operations.

Two weeks into her job, CPT (Dr) Ng requested to undergo the Guards Conversion Course (GCC). This is not a requirement for an ADF battalion medical officer.

### PULLING HER OWN WEIGHT

The 1.56m-tall doctor was the only female trainee during the five-week long GCC, and went through the same gruelling training as the men. This included heli-rappelling, a 1km coastal swim and the painful 10km combat march.

“It was very, very tough. We were already hunched over with our load which weighed over 30kg. The terrain was up and down; the ground was rocky. On top of that, we had to meet a passing timing so at times we had to run.”

Whether during basic military training or officer cadet training, CPT (Dr) Ng never expected to be treated differently from the men.

She was quick to play down her achievement of being the first female medical officer in the SAF to complete the GCC, noting that other women before her had done it as well.



“  
I pulled my own weight, and the guys respected me for that. During a section firefight, we would take turns to carry the signal set. I also carried the Matador (an anti-tank weapon that weighs almost 9kg) and did the firefight together (with the guys).

— CPT (Dr) Ng on keeping up with the guys during training

**LEFT**  
A proud CPT (Dr) Ng with her hard-earned khaki beret at the Guards Conversion Course graduation parade last year.

“

I train my BCS boys personally. I take it as my responsibility because their proficiency will affect casualties that we would face in real operations... It's very important for the ADF because we are an operational unit...training for the real thing.”

— CPT (Dr) Ng on working with her team of ADF medics



GCC trainees rappelling down from a helicopter.



CPT (Dr) Ng (left) working with Staff Sergeant Muhammad Amir Bin Amat to treat a simulated casualty inside a BCS.

## A POSITIVE SPIRIT

Throughout the interview, she would repeatedly say that training was *siong* (Hokkien for tough) but fun.

Looking back at the Battle Inoculation course, the toughest part of her BMT, she laughed as she recalled: “It was raining very badly; it was like I was crawling in *teh peng* (Hokkien for milk tea)! It's just disgusting! Very sad because I was just so wet and tired!”

She also likened the 1km coastal swim during the GCC to a fun swim in the ocean, noting that it was a smooth start when swimming with the tide.

“But on the way back, you can get stuck at a certain point. It was so painful; the swim was endless,” she reminisced. “Towards the end, we just all held on to each other and swam together (to reach the shore).”

And while some guys like to get their training over and done with, she prefers to enjoy the moment—especially during activities that involve high elements like heli-rappelling.

“It's a whole new world up there because the helicopter blades are spinning just directly above your head; the wind is very, very strong,” she elaborated.

“A lot of the guys, because they are very young—all 18 or 19 years old—speed down 'cos they think it's a race. But I took my time 'cos I wanted to enjoy the scenery!”



## DOCTOR, COMMANDER & TRAINER

Day to day, CPT (Dr) Ng takes care of the health of the ADF troops, attending to their medical needs.

During missions, she will be out with the troops in their area of operations, providing medical cover from a field hospital known as the Battalion Casualty Station (BCS).

She takes her job very seriously as the ADF is a high-readiness unit.

As a commander, she is responsible for the well-being of her “boys”, many of whom are older than her and have children. She makes it a point to hear their concerns, noting that “sometimes all they need is a listening ear”.

“This is really a privilege of command—nowhere else would you have this chance to take charge of someone else’s life. So I am thankful for this opportunity.”



CPT (Dr) Ng (far left) with her team of ADF medics.



GCC trainees undergoing the combat march with full combat load weighing more than 30kg.

“

Physical fitness can always be trained. For those who want to sign on, you just need to be clear about what your goal is. Are you here to serve? If you are, then a lot of these concerns are secondary. You must have faith in yourself and believe that you can do it.

— CPT (Dr) Ng’s message to ladies thinking of joining the SAF



As part of the GCC, the 1km coastal swim builds trainees’ confidence in operating in open waters.

## HER FITNESS USED TO BE JUST AVERAGE

For the record, she wasn’t so fit when she enlisted in 2013. Her timing for the 2.4km run was over 16 minutes.

Today, her total score for the Individual Physical Proficiency Test is 98 out of 100 points!

She can complete the 2.4km run in 10:20 min, and do 60 push-ups in one minute. Her only weakness is sit-ups – she can only manage the “low 50s”.

Her message for women who are on the fence about joining the military?

**Inspiring Health For All**



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Yong Loo Lin  
School of Medicine