Rapporteur's Report: ASHM Inaugural COVID-19 Conference Day 2021

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Preamble

The ASHM Inaugural COVID-19 Conference Day 2021 'Devils in the Details – Making sense of COVID-19' was a one-day conference, bringing together an array of experts from the disciplines of basic science, clinical care, epidemiology, and social science.

The conference featured thematic sessions from a range of speakers presenting new and unpublished science, with an emphasis on interdisciplinary collaboration and open access to information.

The conference was open to health professionals, non-specialists and the general public on a complimentary basis, in the spirit of the partnership approach adopted by Australia's response to the HIV pandemic. The day was an opportunity for the sector and the public to come together to learn about the science of COVID-19 and to strengthen collaboration between research groups nationally and internationally.

Plenary

Chair: Sharon Lewin, Peter Doherty Institute for Infection and Immunity

Professor Sharon Lewin opened the conference with the refection that "any good science is open to dialogue, debate and interaction".

She recognised that many HIV researchers are leading the coronavirus response and that many the communities vulnerable to HIV are also vulnerable to COVID-19.

As a conference day that has been designed to be open to the public, it was expected that people from all different backgrounds could be joining as well as the possibility of hundreds of delegates continuing on from the Australasian Joint HIV & Sexual Health Conference 2021 which had just finished earlier in the week.

Plenary Lecture: Challenges of designing a COVID-19 vaccine

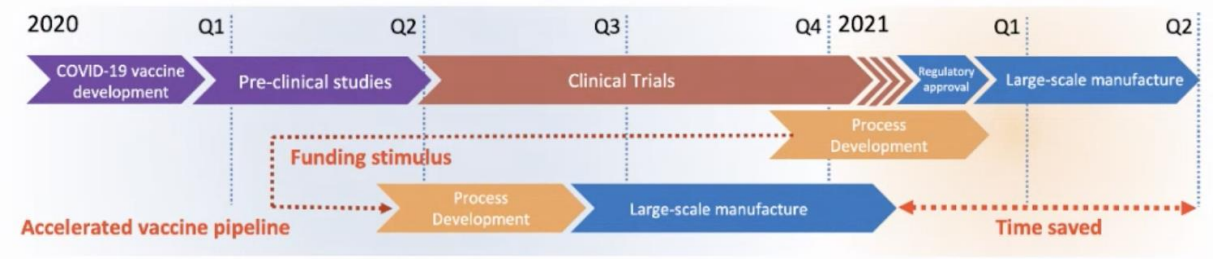
Speaker: Professor Paul Young, The University of Queensland

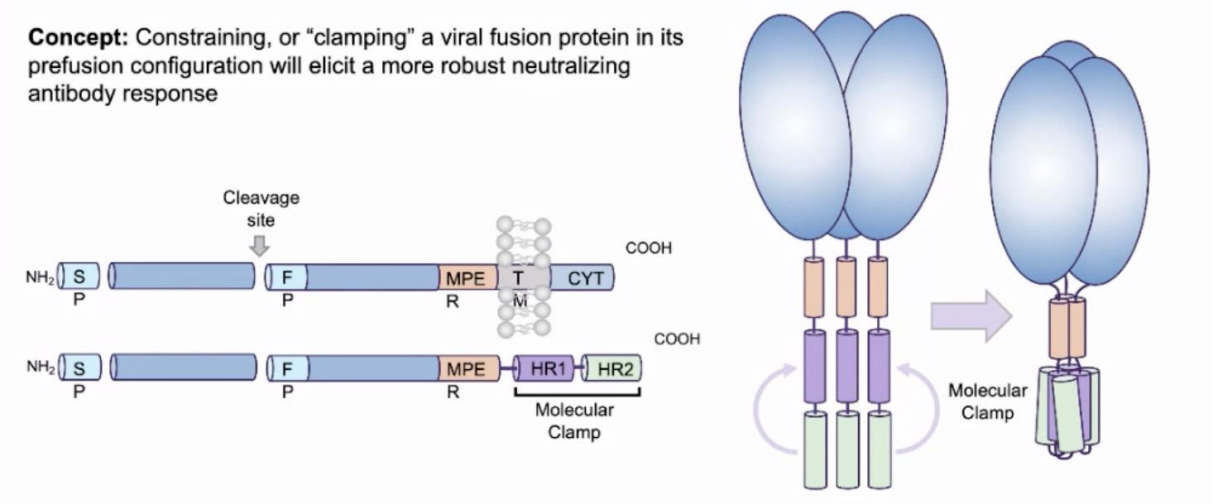
Researchers at the University of Queensland (UQ) led by Professor Paul Young developed an MF59-adjuvanted subunit vaccine for COVID-19 based on recombinant SARS-CoV-2 spike glycoprotein stabilised in a pre-fusion conformation by a novel molecular clamp.

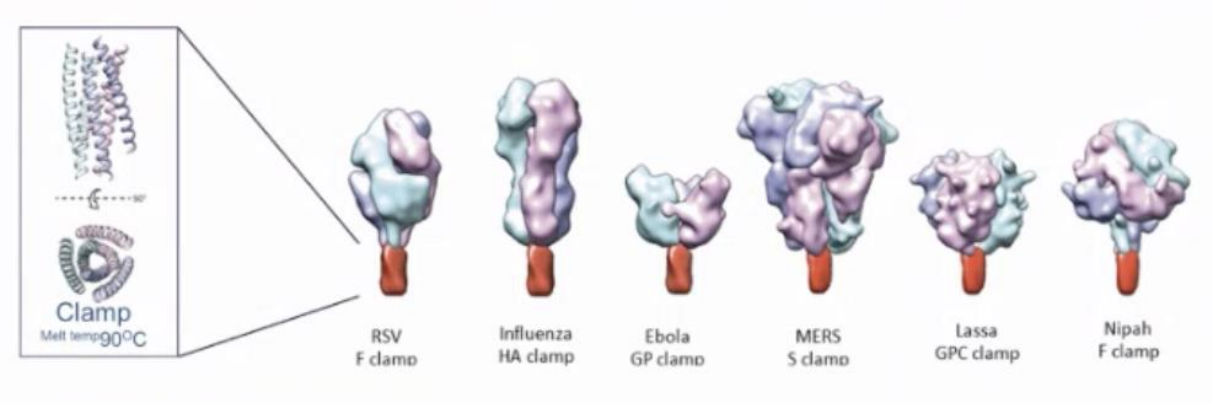
The UQ vaccine development entailed an innovative rapid response strategy with concurrent human trials alongside process development and large-scale manufacturing to produce the vaccine at speed. By the time of clinical trials, approximately 10 million doses had been manufactured.

The first iteration of the COVID-19 clamp induced high levels of COVID-19 antibodies, would predict 90% efficacy and showed good thermal stability, demonstrating its clear utility in low-income countries where refrigeration might be an issue. Further, it was

clear that the molecular clamp platform technology could be applied to a number of viruses, including regular flu variants and HTLV-1.







The decision to not proceed with the UQ COVID-19 vaccine was due, in part, to concerns about HIV diagnostic interference caused by the use of the six-helix bundle of HIV-1 glycoprotein 41 in the vaccine (red component in the figure below). The vaccine caused cross-reactivity in some but not all HIV testing assays. However, the main concern particularly from the Federal government was the likelihood of vaccine hesitancy due to HIV stigma.

The UQ researchers are currently working on a re-engineered 'Clamp 2.0' which has the potential to be in the next generation of COVID-19 vaccines.

The story of the UQ vaccine, as told by Professor Young, is a testament to the power of partnerships that underpin bio-medical research in Australia. Professor Young emphasised the importance of public-private partnerships in the development process and the need for investment in the biomedical sector.

"It was really a rollercoaster to move at the speed we needed to... the level of collaboration in Australia is just extraordinary."

– Professor Paul Young

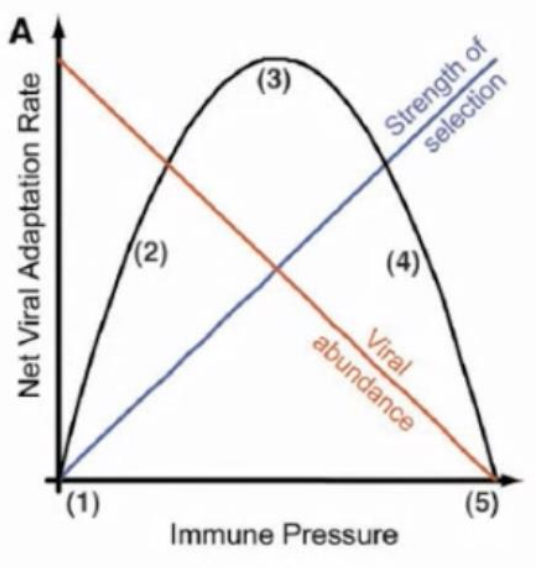
Plenary Summary:

1. The story of the UQ vaccine development is testament to the power of partnerships and the need for Australia to invest in the biomedical sector.
2. UQ innovation of concurrent human trials alongside process development and large-scale manufacturing to save time and produce a vaccine more quickly.
3. UQ COVID-19 clamp vaccine showed good thermal stability with clear utility in low-income countries where refrigeration might be an issue. Molecular clamp platform technology broadly applicable to a number of viruses, including regular flu variants and HTLV-1.
4. Decision to not proceed with UQ COVID-19 vaccine due to concerns about HIV diagnostic interference and anticipated vaccine hesitancy due to HIV stigma.

Session 1: New Basic Science on SARS-CoV-2 Origins, Variants, and Immune Responses

Chairs: Professor Heidi Drummer, Burnet Institute & Dr Wei Zhao, Peter Doherty Institute
Speakers: Professor Edward Holmes, University of Sydney; Professor Jennifer Juno, University of Melbourne & Associate Professor Stuart Turville, Kirby Institute

Professor Holmes opened the session with an analysis of the origins of COVID-19. The virus has previously been linked to horseshoe bats but from the intermediary host remains unclear. Both pangolins and racoon dogs, as well as many other species can carry similar viruses.



Holmes explained that there is no evidence that the virus was manufactured in a laboratory, noting that the virus has a suboptimal furin cleavage site which "not even the worst PhD student would insert".

He argued that the emergence of COVID-19 was strongly linked to the way that humans engage with wildlife and warned that it would not be the last virus to emerge unless practices change, including the way that wet markets are designed and monitored.

"We will have COVID-19 with us forever… we will have good years and bad years."
– Professor Edward Holmes

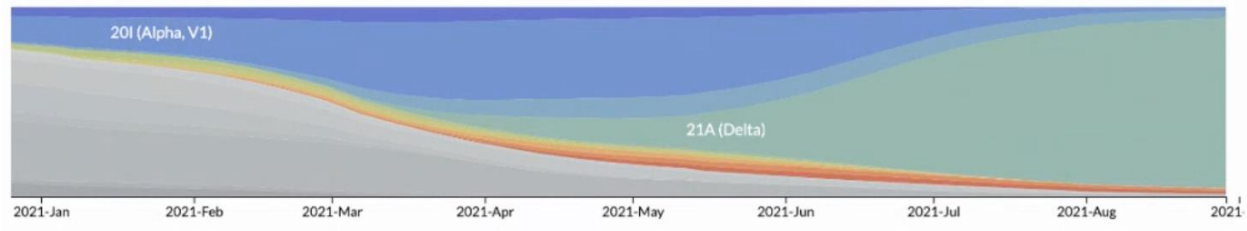
The Professor closed with the prediction that the capacity of the SARS-CoV-2 virus for immune escape will be strongest in the immediate future but will decrease over time. He predicted that going forward we will have "good years and bad years" with COVID-19 but overall, the disease will get milder. In the Q&A, he discussed the moral imperative to provide vaccine coverage globally, as well as the critical need to ensure good data sharing between countries.

Professor Jennifer Juno's research focused on CD4+ T Cells and their capacity to help B cell antibody responses. Juno explained that infection provided stronger immunity than vaccination, while a combination of the two provided an extremely robust neutralising antibody response.

However, her research suggests that antibodies wane over time regardless of how immunity was acquired, whether through infection or vaccination, so booster shots will likely be needed to maintain neutralising antibody titres.

Later in Q&A, Professor Juno indicated that boosters especially for immunocompromised individuals, and mixed-dose schedules would be beneficial. Juno also proposed that vaccination might help against long COVID, though further research is required to confirm this.

Associate Professor Stuart Turville clarified that Delta has displaced Alpha, Beta, Gamma and Lambda due to its fitness gain and its capacity to efficiently infect cells. What makes Delta particularly dangerous is its speed to achieving peak viral loads and its infectiousness.



New developments in variants of concern (VOC) and variants of interest (VOI) include changes in RBD, N-Terminal deletions and shuffling in the furin cleavage site, especially P681 H/R, which is present in what Turville dubbed the "big hitter" variants such as delta.

Nevertheless, Professor Turville drew attention to the fact that viruses have a "limited backpack of tools" and that it is "easy for a virus to break". For these reasons he

reminded attendees to be wary of what he termed "scariants" (i.e., new variants) that have not yet earned their Greek letter.

> *"What really vexes me is that large parts of the world have no vaccinations. Booster shots are good but* not *if they're at the expense of other countries… we're not going to move on until the whole world is vaccinated."*
>
> – Professor Edward Holmes

Session 1 Summary:

1. COVID-19 does not necessarily originate from bats (possibly pangolins or racoon dogs) or from Yunan province in China. There's no evidence of COVID-19 study or manufacture at Wuhan laboratories and evidence against the idea it was human-made, such as a sub-optimal furin cleavage site.
2. Research suggests that antibodies wane over time regardless of how immunity was acquired, whether through infection or vaccination. Booster shots very likely in the future to maintain neutralizing antibody titres and mixed-dose schedules may be beneficial.
3. Developments in variants of concern and interest include changes in RBD, N-Terminal Deletions and shuffling in the furin cleavage site especially P681 H/R, which is present in the COVID "big hitter" variants. Delta is especially concerning due to its fitness gain and its capacity to evade an immune response.
4. Data sharing remains critical, as does the need to change practices of human-animal interaction (i.e., live animal markets) and ensure global vaccination coverage.

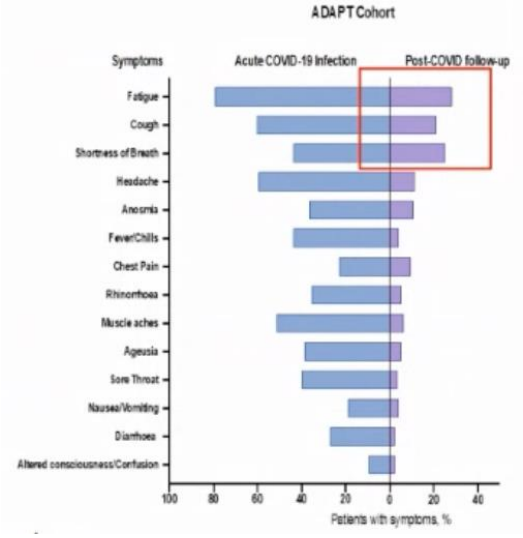
Session 2: Clinical sequelae following SARS-CoV-2 infection and emerging treatments for SARS-CoV-2 infection

Chairs: Adeeba Kamarulzaman, University of Malaysia & James McMahon, Alfred Hospital, Monash University
Speakers: Associate Professor Edwina Wright, Alfred Health and Monash University; Mirabai Nicholson-McKellar; Professor Gail Matthews, The Kirby Institute; Professor Ole Schmeltz Søgarrd, Aarhus University, Denmark & Professor Steve Webb, Monash University

This session opened with a Q&A presentation between Professor Edwina Wright and long-COVID survivor Mirabai Nicholson-McKellar. Nicholson-McKellar outlined the physical experiences of her symptoms such as headaches, fatigue and shortness of breath, describing how she is barely able to function 18 months on.

Nicholson-McKellar spoke at length about feeling misunderstood by the healthcare system and her sense of isolation from friends and co-workers, who know very little about long COVID. Conversely, she emphasised the importance of social media, COVID-19 support groups, who were the first groups to describe long COVID and the informal peer support these provided.

"No-one knows if I'll recover and that's very challenging... It's been critical for my wellbeing to have people who intimately know what I'm going through."
– Mirabai Nicholson-McKellar



Professor Gail Matthews presented sobering news on how little is known about the cause, duration, and prevalence of Post Acute Sequelae of SARS-CoV-2 (PASC), also known as long COVID. Symptoms include fatigue, chest pain, headaches, fogginess, poor concentration, and issues with smell, among dozens of others.

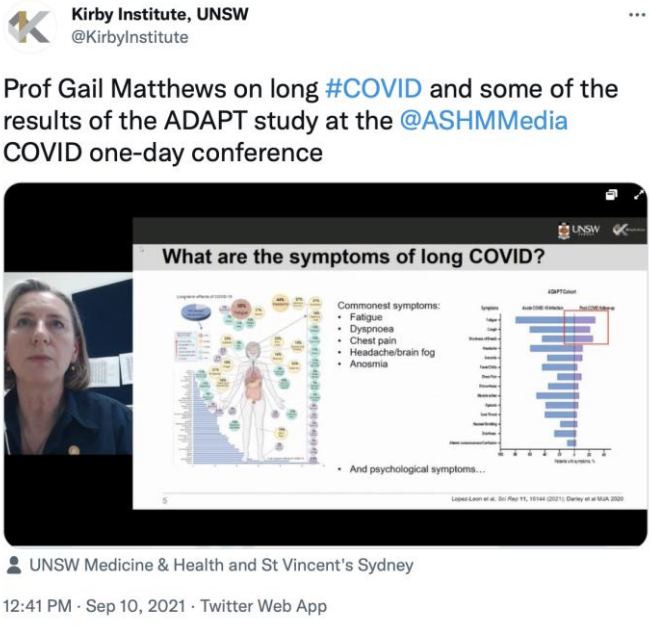
It is likely that long COVID represents several separate syndromes, but the cause(s) remain unknown. Evidence to date suggests that long COVID may last up to 8 months after acute infection but in some cases may last longer, and that women and people with pre-existing disease are at particular risk.

Professor Matthews emphasised the need for multidisciplinary care in the absence of available therapeutics and warned that even a conservative prevalence of 10% of COVID-19 cases developing long COVID would potentially represent tens of millions of cases. In the Q & A it was emphasised that we do not yet currently know whether initially receiving treatment for COVID reduces the risk of long COVID.

Professor Ole Schmeltz Søgaard presented the findings of a double-blind, randomised controlled trial into the effectiveness of camostat mesylate, a trans-membrane protease serine 2 (TMPRSS2) inhibitor, in patients hospitalised with COVID-19.

At the cellular level, TMPRSS2 cleaves the spike protein of human coronaviruses thereby facilitating cell entry and infection. As a protease inhibitor, camostat mesylate had the potential to block this process.

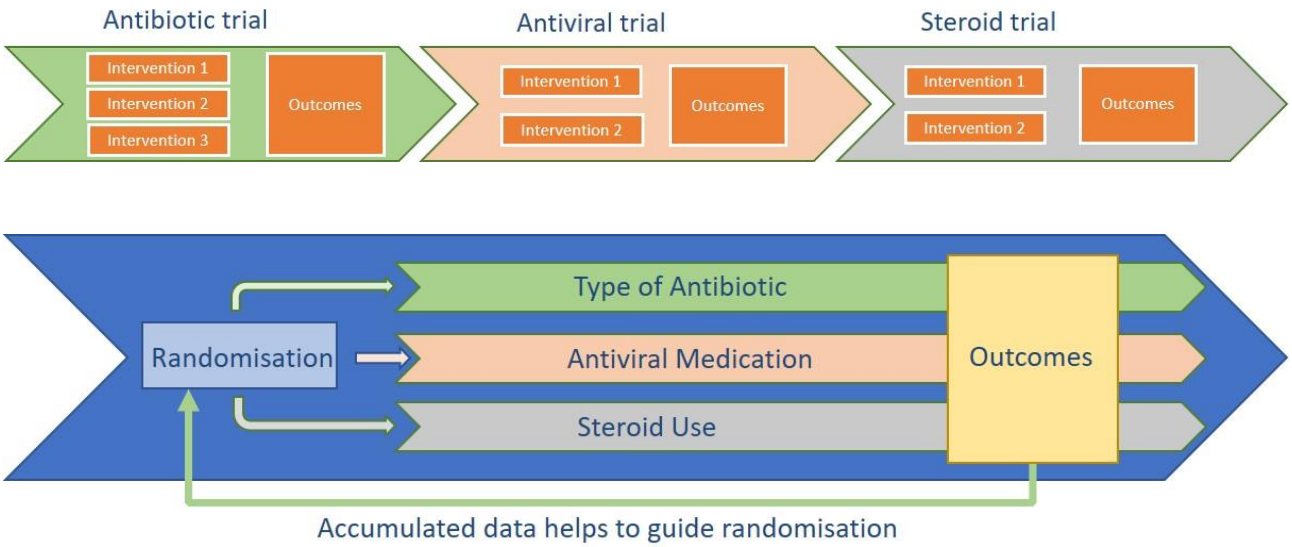
Though it has previously been shown to be an antiviral agent against SARS-CoV-2 in vitro and against SARS-CoV-1 in mice, the study found camostat mesylate to have no significant effect on COVID-19 viral load or mortality.

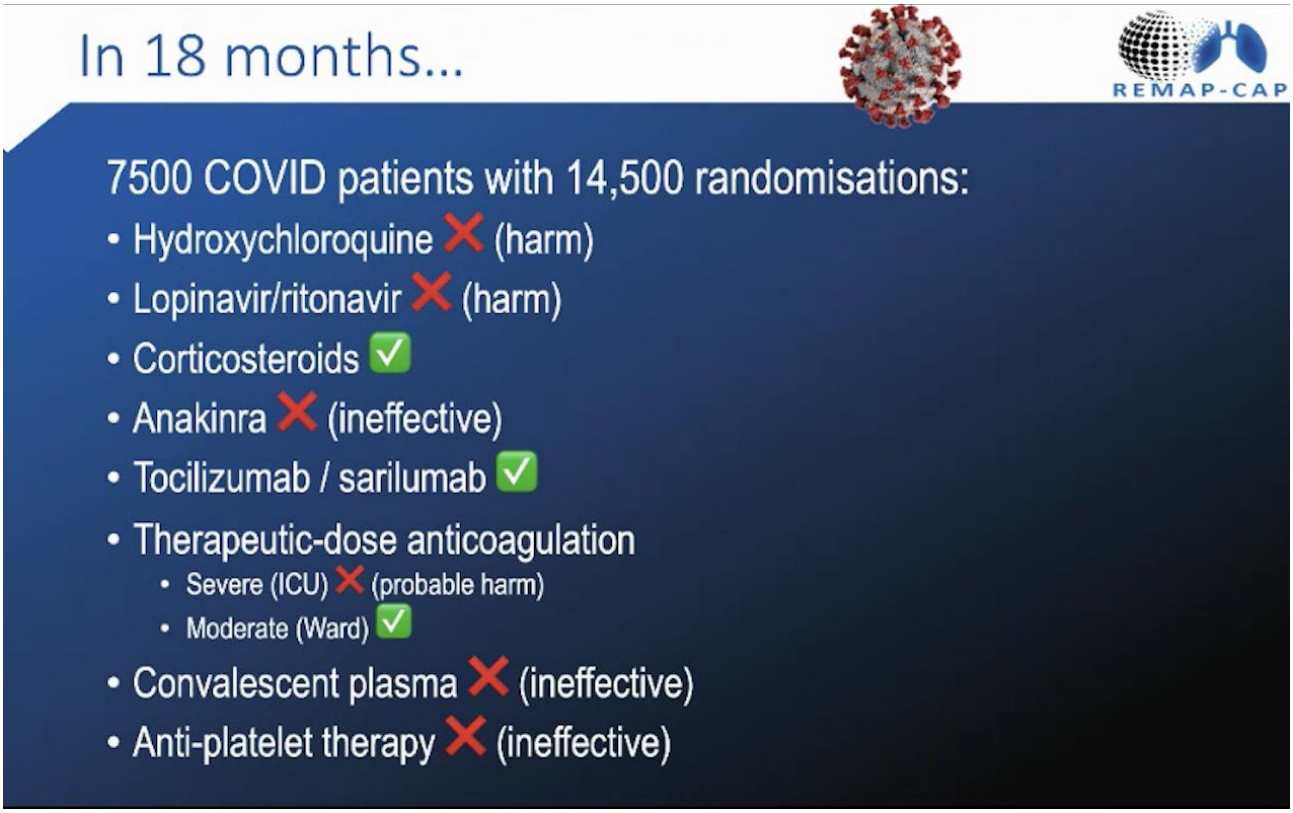


"The cost of long COVID is going to be enormous."
– Professor Steve Webb

Professor Steve Webb introduced REMAP-CAP, a randomised and adaptive clinical trial currently investigating clinical treatment options for COVID-19. Instead of the sequential testing of a traditional trial, the program tests several interventions simultaneously.

REMAP CAP's trials enrolled approximately 7,500 COVID-19 patients who underwent 15,000 randomisations. The REMAP-CAP study has provided a number of key findings that have influenced clinical practice in Australia and internationally in the management of people with COVID-19 illness. Their studies found that tocilizumab and sarilumab are effective treatments and supported the very important findings from the UK RECOVERY study that corticosteroids are effective treatment for COVID-19. REMAP-CAP has demonstrated that therapeutic dose anticoagulation showed some promise in moderate ward cases, but not in severe ICU cases where it was potentially harmful. The study has also reported that hydroxychloroquine and lopinavir/ritonavir are harmful, while anakinra, convalescent plasma and anti-platelet therapy are ineffective treatments.





Session 2 Summary:

1. Post acute sequelae of SARS-CoV-2 (PASC) or 'long Covid' includes dozens of symptoms and is likely several separate syndromes. However, the cause(s) remain unknown. Evidence to date suggests that PASC may last up to 8 months after acute infection and that women and people with severe disease are at greater risk.
2. Survivors of long COVID require greater care, including multidisciplinary care and peer support. Conservative estimates of prevalence suggest that long covid cases might eventually number in the millions, and experts suggest that the costs of the syndrome(s) will be high.
3. Camostat mesylate found to have no significant effect on COVID-19 viral load or mortality.
4. REMAP CAP's adaptive platform trials with 7,500 patients suggest that corticosteroids, tocilizumab and sarilumab were effective treatments. Therapeutic dose anticoagulation showed some promise in moderate ward cases, but not in severe ICU cases.

Session 3: Epidemiological tools required for heavy lifting during the COVID-19 pandemic: Nowcasting, mandatory masking wearing and prioritisation of Indigenous leadership

Chairs: Associate Professor Margie Danchin, Murdoch Children's Research Institute & Scientia Professor John Kaldor, Kirby Institute
Speakers: Professor James Ward, Poche Centre for Indigenous Health, University of Queensland; Assistant Professor Kathy Leung, University of Hong Kong & Dr Nick Scott, Burnet Institute

Professor James Ward opened this session with an analysis of Indigenous engagement during the COVIDF-19 pandemic in Australia. Aboriginal communities called for biosecurity measures such as border closures very early in the COVID-19 pandemic to protect vulnerable communities and especially Elders.

Ward suggested that the long lockdown that Victorians experienced in 2020 encouraged vaccine uptake in the state as compared to the other jurisdictions, where Aboriginal vaccination rates are 50% lower than those of the general population. He briefly discussed the hesitancy caused by, among other factors, miscommunication, and distrust in the health system.

> *"[First Nation peoples] will be left vulnerable if we open up at 70% population vaccination. At the heart of all this is inequity, our healthcare systems are not optimal."*
> – Professor James Ward

Professor Ward emphasised issues around access to healthcare, education and housing and emphasised the need for an equity lens across the whole pandemic response. He concluded by saying Aboriginal communities will be left vulnerable if Australia 'opens up 'when 70% of the overall population is vaccinated and that Australia needs a national campaign for indigenous people, especially those under 20 years of age.

Assistant Professor Kathy Leung presented on pandemic nowcasting, reporting on modelling conducted in Honk Kong. Leung's research utilised data from the Octopus smart card, which is used in Hong Kong for transport, entertainment, shopping, and dining. The use of the data on transport use from the smart card was the best indicator

to track COVID-19 transmissibility in near to real-time and to generate short term forecasts.

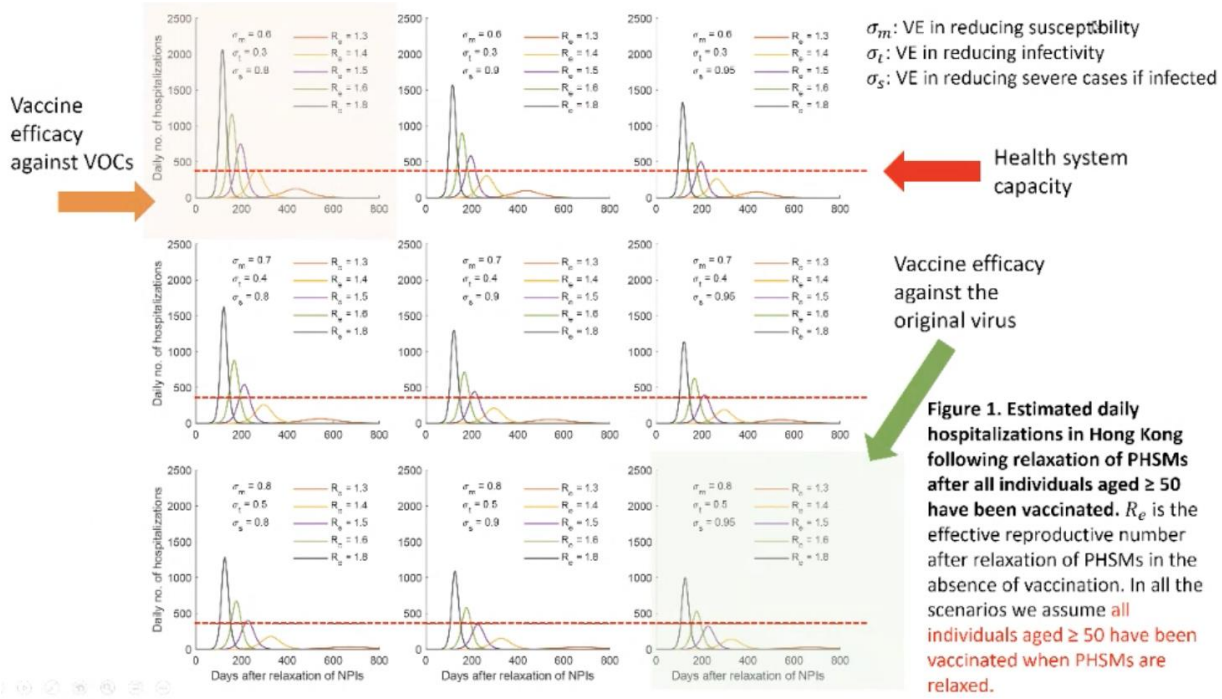


Figure 1. Estimated daily hospitalizations in Hong Kong following relaxation of PHSMs after all individuals aged ≥ 50 have been vaccinated. R_e is the effective reproductive number after relaxation of PHSMs in the absence of vaccination. In all the scenarios we assume all individuals aged ≥ 50 have been vaccinated when PHSMs are relaxed.

What this investigation yielded was a model, which could predict the point at which the health system capacity would be overloaded if public health social measures were simultaneously relaxed.

Professor Leung's models suggests that public health measures can be gradually relaxed with decent vaccine coverage (~70-80%) but not completely and not all at once. The Professor also suggested that rapid testing might be a valuable avenue to explore in the future.

Dr Nick Scott reported the findings of a study into the effects of the mandatory mask policy in Melbourne during the second COVID wave in 2020. The efficacy of masks was demonstrable in a controlled setting, but this project investigated their use and efficacy in a real-world setting.

The study examined journalistic photography taken in Melbourne from before and after the mask mandate to measure uptake in addition to self-report data. This showed that the mandatory mask police substantially increased mask use and was associated with a significant decline in epidemic growth rate.

"Mandatory mask mandates slow the spread of the virus. This is a fact proven without a doubt."
– Dr Nick Scott

Dr Scott concluded that this represents strong evidence that the mandatory mask policy was strongly associated with reducing COVID-19 cases in a community setting. He suggested that facemasks should be considered elsewhere and at other times to reduce community transmission, potentially even after Australia reaches 70-80% vaccine coverage.

Session 3 Summary:

1. An equity lens is required for the whole pandemic response, especially around issues such as access to healthcare, education, and housing. As it stands Aboriginal communities stand to remain highly vulnerable to COVID-19 if Australia opens up at the proposed 70-80% overall population vaccination rate.
2. The modelling from Hong Kong suggests that public health measures can be gradually relaxed with decent vaccine uptake but not completely and not all at once. Rapid testing might be a beneficial avenue to explore.
3. There is strong evidence that the mandatory mask policy was strongly associated with reducing COVID-19 cases in a community setting. Face masks should be considered elsewhere and at other times, including potentially after Australia reaches 70-80% vaccine coverage.

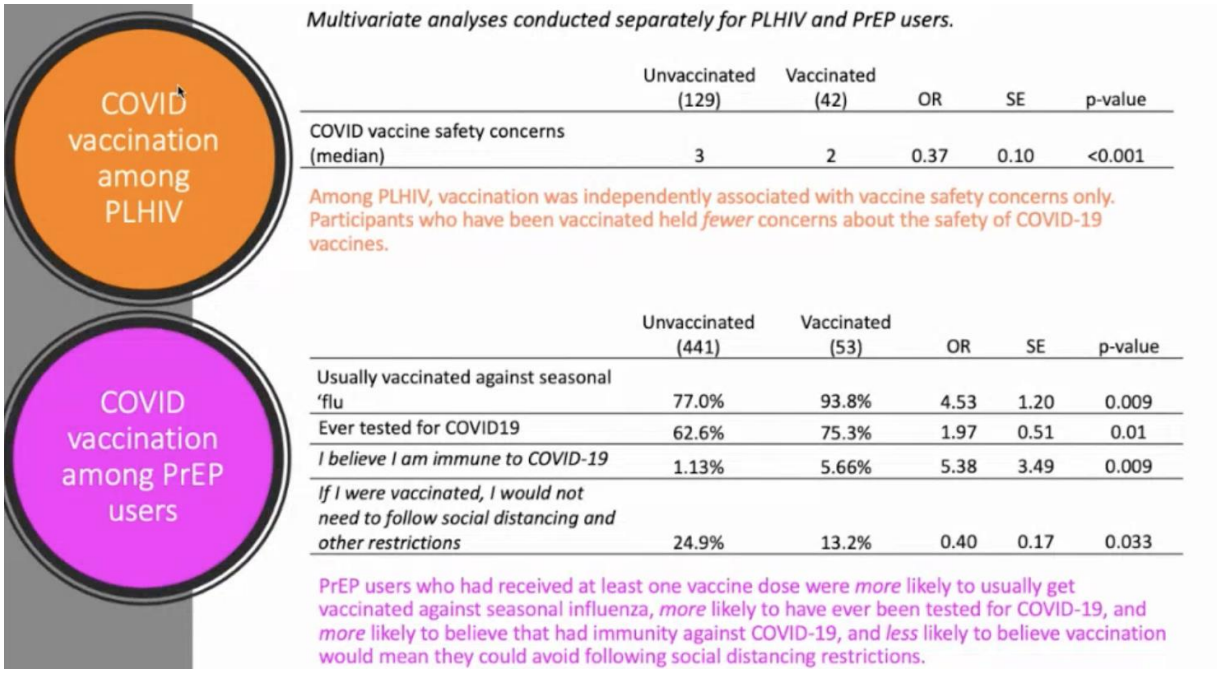
Session 4: An examination of the Social Aspects of Masks, Mathematical Models and Vaccine acceptability in PLWHIV and PrEP Users

Chairs: Dr Kiran Pienaar, Deakin University & Dr Bridget Haire, Kirby Institute
Speakers: Dr Dean Murphy, Alfred Hospital; Professor Deborah Lupton, UNSW & Dr Kari Lancaster, UNSW

> *"There was very little advocacy for mask wearing early on... but behaviours changed rapidly [after the introduction of mandatory mask policies]."*
> – Professor Deborah Lupton

Dr Dean Murphy presented the findings of an Australia-wide study into COVID-19 vaccine acceptability in people living with HIV (PLHIV) as compared to pre-exposure prophylaxis (PrEP) users, the VAX-PLORE study. Murphy and his co-authors hypothesised that PLHIV would be more likely to accept a COVID vaccine.

The study showed that PLHIV were significantly less likely to trust the health system and the government to manage the pandemic. Contrary to the hypothesis, PrEP users are more likely than PLHIV to be vaccinated against COVID-19 for a variety of attitudinal and social reasons.



	Unvaccinated (129)	Vaccinated (42)	OR	SE	p-value
COVID vaccine safety concerns (median)	3	2	0.37	0.10	<0.001

	Unvaccinated (441)	Vaccinated (53)	OR	SE	p-value
Usually vaccinated against seasonal 'flu	77.0%	93.8%	4.53	1.20	0.009
Ever tested for COVID19	62.6%	75.3%	1.97	0.51	0.01
I believe I am immune to COVID-19	1.13%	5.66%	5.38	3.49	0.009
If I were vaccinated, I would not need to follow social distancing and other restrictions	24.9%	13.2%	0.40	0.17	0.033

PLHIV tended to have greater safety concerns with regarding to a COVID-19 vaccine, though both groups remained very likely to be vaccinated, with 81% PLHIV reporting that they were likely or very likely to get the COVID-19 vaccine, versus 90% of PrEP users. In the Q&A, Dr Murphy discussed the "biomedical enthusiasm" of PrEP users compared to the greater distrust of PLHIV.

Professor Deborah Lupton, introduced longitudinal research concerning the rapidly developing mask use behaviours in Australia. According to the ABS Household Impacts of COVID-19 Survey, only 15% of Australians were wearing facemasks regularly, but this grew to a high of 64% by February 2021.

Mask use has varied across domestic jurisdictions and has been highest in Victoria due to the state's mandatory mask policy. Mask use in Victoria has remained above 90% since September 2020. As of June 2021, nearly half of all Australians report wearing masks.

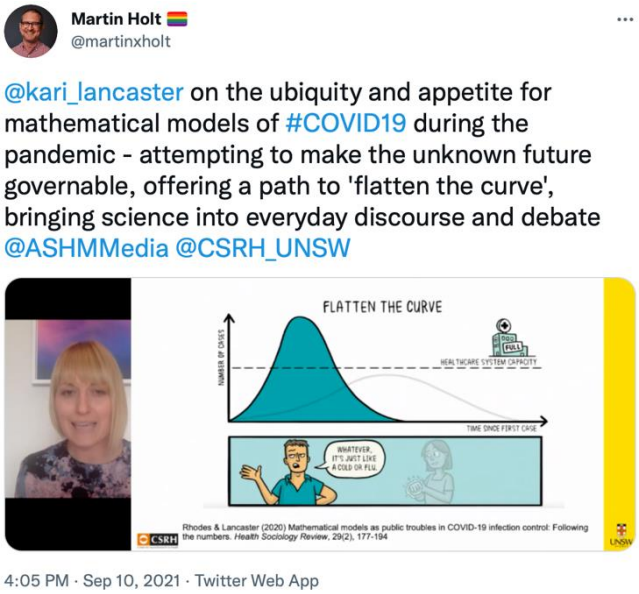
Professor Lupton's research provided historical context and situated mask use in a complex schema that encompasses a variety of social, cultural, political, and economic factors, as well as individual, medical and data practices.

"Epidemiological projections are no longer limited to the scientific community but embroiled in the everyday… models are nothing without their social and political relations."

– Dr Kari Lancaster

Finally, Dr Kari Lancaster summarised her research into mathematical modelling and public understanding. In her presentation, she proposed that scientific models are not mere theories but lived projections that are actualised in the social sphere which help people grapple with anxieties of the unknown.

Dr Lancaster discussed the way that models detach from scientific discourses to exist as their own objects in the public sphere, becoming embroiled in social and political



relations. After COVID-19, epidemic projects are no longer limited to a select group of experts but have become entangled in the everyday.

In the Q&A, Dr Lancaster considered how this process reveals the operation of the "evidence-based policy paradigm" where evidence is often conflictual and deeply political. She additionally stressed the importance of non-expert and community knowledge, such as the lived experiences of PLHIV.

Session 4 Summary:

1. PrEP users are more likely than PLHIV to be vaccinated against COVID-19 for a variety of attitudinal and social reasons, though PLHIV are still very likely to be vaccinated.
2. COVID prevention, especially masks, extend across a variety of social, cultural, political, and economic factors, as well as individual, medical and data practices. Further, mask behaviours have changed rapidly since the start of the pandemic.
3. Scientific models are not mere theories but lived projections which are actualised in the social sphere which help people grapple with anxieties of the unknown.

Conference Wrap Up

Chair: Associate Professor Edwina Wright, Alfred Health and Monash University

To close the conference, co-convenor Associate Professor Edwina Wright reflected on six themes that she felt had emerged during the conference: the power of partnerships (including the importance of data sharing), issues relating to equity and resilience, the complexity of human behaviour, hope and the unknown.

Professor Wright closed with some brief comments about the challenge posed by long Covid and concerns about new and emerging variants. The Professor challenged attendees to "keep talking to each other" and insisted that

communication and data sharing will be key to helping control the COVID-19 pandemic.