NSW Health

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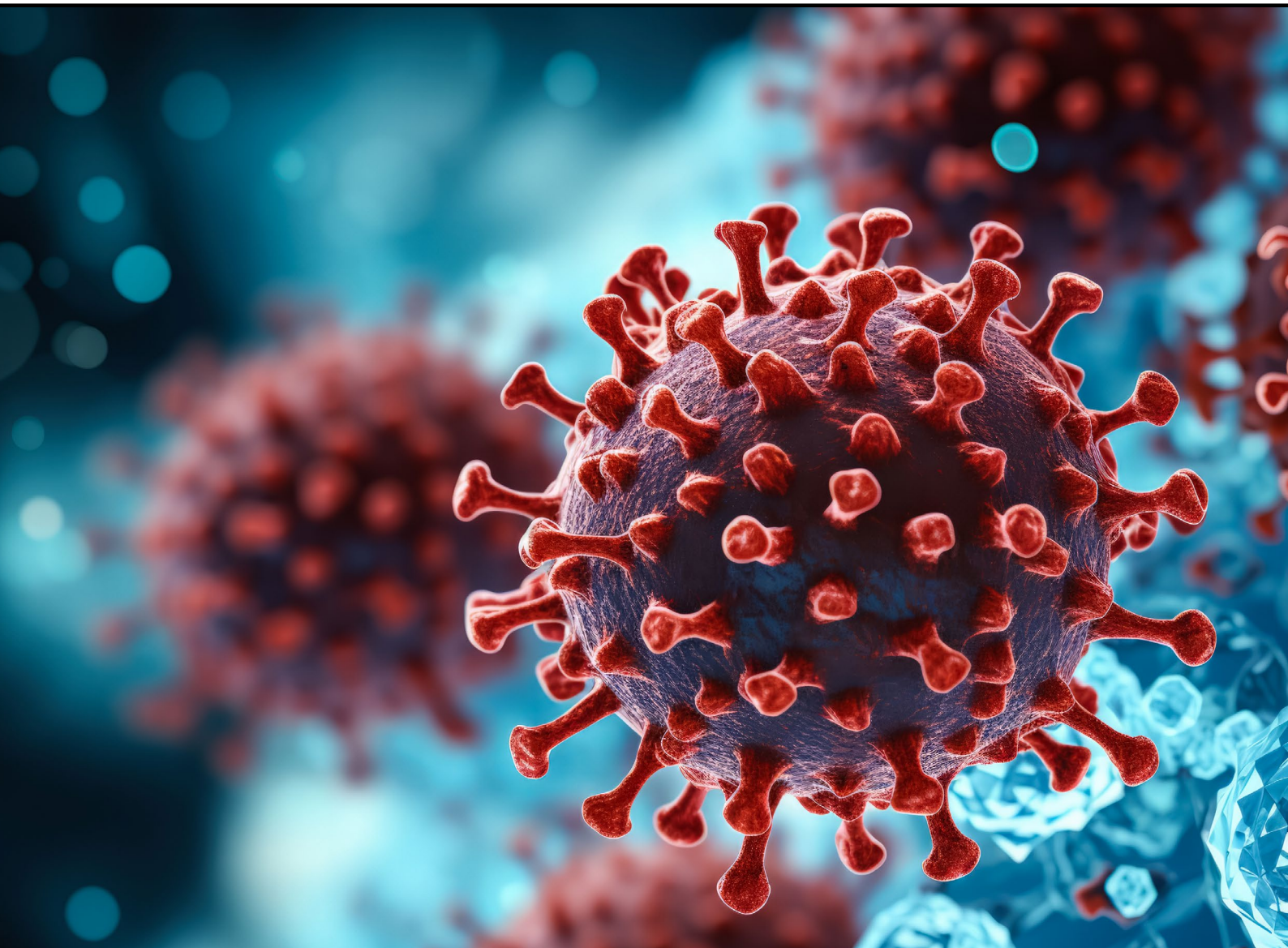
COVID-19 Research Program

Outcomes Report



NSW Ministry of Health
1 Reserve Road
ST LEONARDS NSW 2065
Tel. (02) 9391 9774
Fax. (02) 9391 9101
TTY. (02) 9391 9900
www.health.nsw.gov.au
Email: moh-ohmr@health.nsw.gov.au

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The NSW Ministry for Health acknowledges the traditional custodians of the lands across NSW. We acknowledge that we live and work on Aboriginal lands. We pay our respects to Elders past and present and to all Aboriginal people.

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Principal authors:
Centre for Epidemiology and Evidence
Office of Health and Medical Research

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Contents

Glossary

ACCHO	Aboriginal Community Controlled Health Organisation
ACCHS	Aboriginal Community Controlled Health Service
ASCOT	Australasian COVID-19 Trial
ATAGI	Australian Technical Advisory Group on Immunisation
eICU	Electronic Intensive Care Unit
ELISA	Enzyme Linked Immunosorbent Assay
EOI	Expression of Interest
HREC	Human Research Ethics Committees
ICPMR	Institute of Clinical Pathology and Medical Research
ICU	Intensive Care Unit
LGA	Local Government Area
MDF	Medical Devices Fund
MRFF	Medical Research Future Fund
NACCHO	National Aboriginal Community Controlled Health Organisation
NCIRS	National Centre for Immunisation Research and Surveillance
NSW RPRN	NSW RNA Production and Research Network
OHMR	Office for Health and Medical Research
PIMS-TS	Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2
PRSP	Prevention Research Support Program
REMAP-CAP	Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia
RNA	Ribonucleic acid
SARS-CoV-2	The virus that causes COVID-19
SSAs	Site Specific Assessments
TRGS	Translational Research Grants Scheme
UNSW	University of New South Wales
VIIM	The Vaccine, Infection and Immunology Collaborative Research Group
VRGS	Virtual Rural Generalist Service
WGS	Whole Genome Sequencing

Executive Summary

Between April 2020 to June 2023, the NSW Government invested almost $30 million for research and infrastructure through the COVID-19 Research Program ('the Program'). The Program was established to fund research in priority areas that could directly contribute knowledge to minimise the health and social impacts of the COVID-19 pandemic in NSW.

Four cross-cutting themes were identified that highlight the key strengths of the Program:

1. **Capitalising on existing research infrastructure**: NSW had significant research infrastructure and expertise in place before the pandemic began, supported by historic funding from the NSW Government
2. **Collaboration between researchers and decision makers**: Clinicians, managers, researchers and government worked effectively together to provide robust evidence to decision makers, to help reduce the impact of the pandemic and improve outcomes
3. **Enabling new partnerships through targeted and leveraged funding**: The pandemic resulted in rapid escalation of targeted research and proliferation of multidisciplinary teams working on projects from basic science to translation into practice. Many of those research partnerships have continued, funded by many different state and national grant bodies
4. **Facilitating future preparedness**: NSW continues to prepare for future pandemics by investing in cutting edge research facilities. Networks of NSW researchers are well established, as well as relationships across Australia and internationally. NSW is better prepared than ever to respond rapidly and effectively to health emergencies.

Together, these themes demonstrate how previous strategic investment into health and medical research infrastructure, coupled with the permissive and innovative partnerships developed during the pandemic, supported better health outcomes, and reduced social and economic impacts of the response to COVID-19. The impact of the Program was enhanced by improved processes to identify and distribute research funding, and the introduction of strategies that enabled rapid translation to occur. Improved diagnostic techniques help improve case identification and access to treatment, and rapid modelling approaches helped explore scenarios that could improve pandemic outcomes. Collectively, these themes place NSW in a strong position to respond effectively to future health emergencies, including pandemics.

Other branches and organisations within NSW Health implemented initiatives that complemented the work of the Program, particularly around the flow of information between researchers and policy makers. In early 2020, the Agency for Clinical Innovation created the Critical Intelligence Unit which brought together clinical, analytic, research, organisational and policy experts to provide timely and considered advice to decision makers (CIU 2022). The Unit played a complementary role to frontline pandemic response teams, providing real-time, synthesised advice and options to be considered by system leaders. It also maintained communities of practice that facilitated engagement between the research sector and policy teams.

Work is underway to ensure these improvements are embedded as business-as-usual practices, to further strengthen the response to future large-scale emergencies, and to support and develop the NSW research ecosystem.

Using this report

This is the final Outcomes Report for the COVID-19 Research Program. It builds on the impacts detailed in the earlier *Interim Report* (Centre for Epidemiology and Evidence, 2021), which reviewed early outcomes of the Program to 31 January 2021 (approximately nine months after Program initiation). This Outcomes Report provides an update on progress to July 2023 and documents the outcomes and outputs of the Program. Due to how rapidly research was translated in the early days of the pandemic, the Interim Report should be read in conjunction with this final report to ensure full understanding of the overall impact of the Program.

The Outcomes Report includes information on the new workstream dedicated to providing Vaccine Research Support. This was funded after the Interim Report was produced and includes the establishment of two collaborative initiatives aimed at:

1. developing the mRNA production industry in NSW; and
2. research into the clinical and immunological responses to COVID-19 vaccines.

In addition, this report features four *Case Studies* selected from across the Program. These illustrate the breadth and depth of outcomes and impacts achieved and provide key insights into the benefits for NSW from health, social and economic perspectives. They also demonstrate how the outputs from these strategically funded research projects were used to inform the COVID-19 response across the health system.

Introduction

The COVID-19 Research Program ('the Program') was established to contribute to minimising the health, social and economic impacts of the COVID-19 pandemic in NSW. In total the NSW Government invested almost $30 million into research to support the NSW COVID-19 response and recovery. Investment in some aspects of the Program was supplemented by other existing and newly established funding sources. The Program consisted of several interconnected workstreams across key themes.

The **Research Funding Scheme** financed research projects in priority areas to directly support the NSW Health COVID-19 response and recovery. Two separate workstreams were developed to facilitate this critical research.

- The **COVID-19 Research Grants** workstream established a pathway to create knowledge and innovation to support the COVID-19 pandemic response through two rounds of competitive funding. Seven studies were funded in round one and ten studies in round two. This workstream was managed by the Office for Health and Medical Research.

  Round one had short application and scientific review timeframes; designed for projects that were ready to start within four weeks of funding, with preliminary data available within six months to support the short-term needs of the pandemic response. Research priorities for round one covered diagnostics research, prevention of infection, treatment, and public and population health.

  Round two provided slightly longer timeframes and included an Expression of Interest (EOI) process to streamline the number of research organisations submitting full applications. This round was designed to support the medium- and long-term needs of the response and recovery. Round two priorities covered identification of effective models of care, mental health impacts of COVID-19, public health messaging, prevention and therapeutics, and diagnostics.
- The **Emergency Response Priority Research** workstream enabled rapid creation of evidence to support urgent operational work for the public health management of the COVID-19 epidemic in NSW. This workstream was managed by the Centre for Epidemiology and Evidence.

  This workstream leveraged existing research infrastructure and partnerships to rapidly generate local evidence to inform policy and practice throughout the COVID-19 pandemic. A key mechanism to achieve this was embedding research personnel in the pandemic response, allowing them to work directly with key policy decision makers and frontline workers within NSW Health, and to use NSW Health datasets to inform the response. The Emergency Response Priority Research workstream consisted of eight funded research projects across a range of priority areas.

The **Vaccine Research Support** program established two networks comprised of leading vaccine, infection and immunology researchers and practitioners in NSW, which aimed to advance vaccine research and production.

- The NSW RNA Production and Research Network (NSW-RPRN) aimed to create an RNA medical research and manufacturing industry, positioning NSW as a hub for the development and production of RNA therapeutics. The network provides high-quality genetic materials for use in pre-clinical studies relating to COVID-19, and consists of three pillars: production, pilot research, and services and support.
- The Vaccine, Infection and Immunology (VIIM) Collaborative Research Group was established to study the clinical and immunological responses to COVID-19 vaccines in NSW recipients.

The **Clinical Trials** workstream aimed to develop infrastructure and build capacity in NSW to conduct adaptive clinical trials for the treatment of COVID-19, while linking NSW researchers to a global network of experts. Several networks and advisory groups were consequently established to provide expert advice.

The **Industry Scheme** workstream was established to:

1. support the life science industry sector to pivot to the production of COVID-19 diagnostics, therapeutics and devices, and
2. assist medical device businesses funded through the Medical Devices Fund (MDF) to remain viable during the pandemic to contribute to a sustained infrastructure and the NSW recovery. This stream also established the OHMR COVID Triage Service, providing an information portal and knowledge brokerage service for industry and researchers.

In addition to the funded workstreams, supplementary components of work were built into the structure and administration of the funding stream to enhance the research ecosystem and infrastructure, in response to COVID-19.

Processes were put in place to expedite statewide administrative processes thereby minimising unnecessary delays in research ethics application approvals and site-specific approvals for COVID-19 related research, as well as monitoring the impact of the pandemic on approval numbers and times for non-COVID-19 related research.

Research translation from the funded research into the COVID-19 pandemic response and recovery was facilitated in various ways. This was done through a combination of synthesising COVID-19 Research Program outputs and targeted dissemination to key decision makers as required, as well as a more direct lines of communication between researchers and key decision makers to expedite the flow of critical, time sensitive information.

A range of external communication channels were also utilised enabling key activities and research outcomes to be shared publicly, including through the NSW Health and Medical Research website and social media accounts, such as the @NSWMedResearch X (Twitter) account.

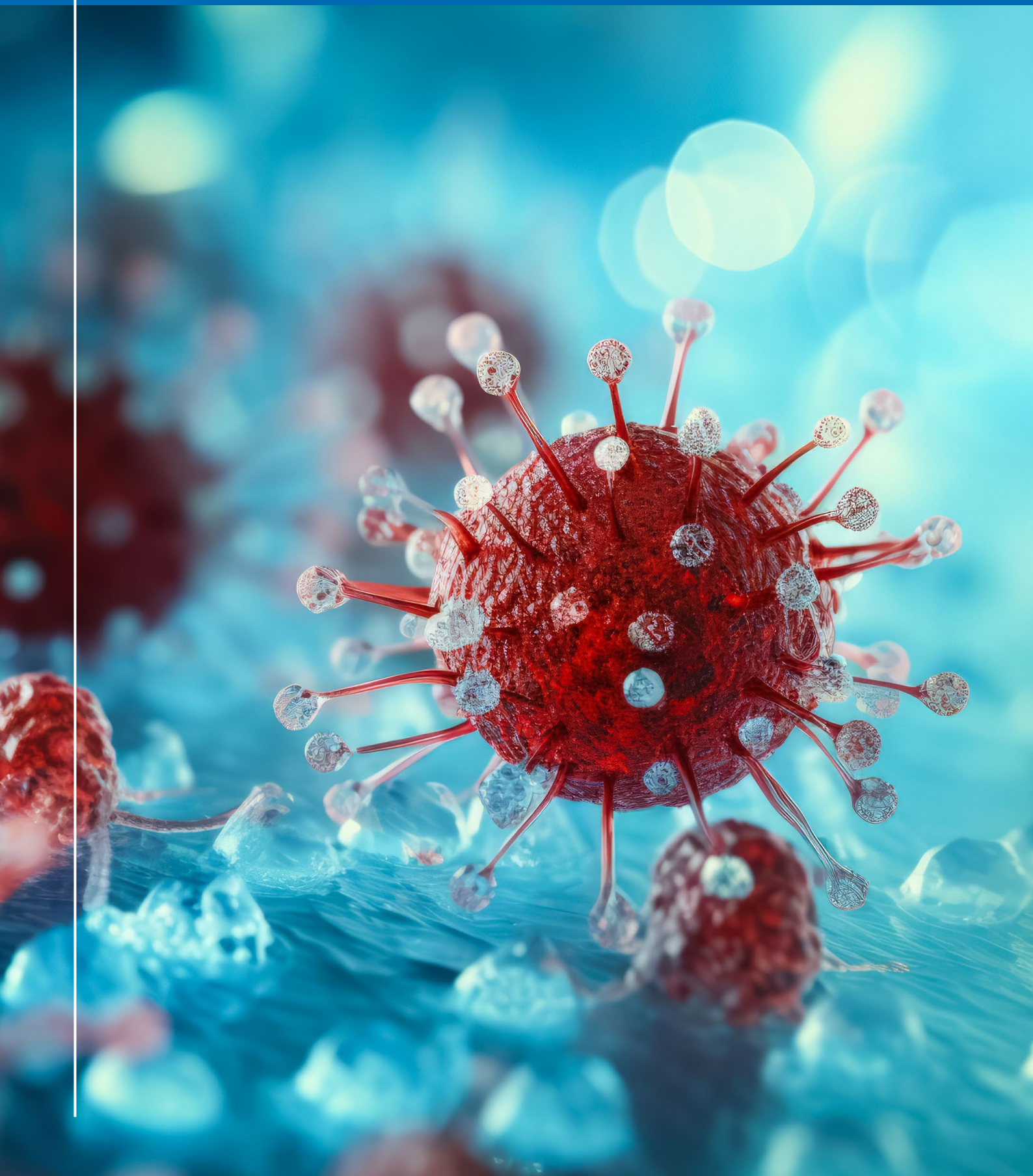
Funding

The following table summarises the funding for the COVID-19 Research Program from April 2020 to June 2023.

WORKSTREAM	FUNDING
COVID-19 Research Grants	**$8,013,987**
▪ Round 1	$3,237,129
▪ Round 2	$4,776,858
Emergency Response Priority Research	**$3,754,199**
Vaccine Research Support	**$9,595,223**
▪ VIIM	$4,696,272
▪ NSW RPRN	$4,898,951
Additional vaccine support activities	**$2,494,141**
▪ Waratah Vaccine Trial Alliance	$498,274
▪ COVID-19 Vaccine Acceleration Program	$1,995,867
Clinical Trials	**$3,096,669**
▪ REMAP-CAP	$1,380,000
▪ ASCOT-ADAPT	$617,232
▪ BEAT-COVID19	$1,099,437
Industry Schemes	**$2,012,381**
▪ Kico Knee Innovations Pty Ltd	$1,000,000
▪ Tetratherix Pty Ltd	$481,381
▪ Perx Health Pty Ltd	$380,000
▪ Beyond700 Pty Ltd	$151,000
Operational expenses*	**$360,796**
Total	**$29,327,396**

*Operational expenditure to support the implementation of the COVID-19 Research Program comprised $196,144 for administration, $36,950 for reviewer payments, $70,000 for communication support, and $57,000 to support the Research Impact Assessment reported in the *NSW Health COVID-19 Research Program Interim Impact Evaluation Report*.

Workstream Updates
Project-level Impacts



COVID-19 Research Grants

This section provides an overview of the final outcomes of the projects that received a competitive COVID-19 Research Grant. These projects focused on priority areas to directly support the NSW Health response to the pandemic. Funding was awarded across two staggered rounds.

For all research topics, NSW Health prioritised projects that could fulfill the following criteria:

1. research using a system-wide approach so that findings could be scaled in NSW;
2. research that had high potential for translation into policy and practice;
3. studies measuring clinically important outcomes;
4. large, multidisciplinary and/or collaborative projects and trials; and
5. research that included consideration of health equity between different population groups.

The projects are grouped according to priority areas of *diagnostics, priority populations, mental health impacts, public health messaging and models of care*.

Completed projects

Of the 17 projects funded under this workstream, 11 were complete at the time of writing, eight of which are detailed below. A further three research projects are featured as in-depth case studies.

DIAGNOSTICS

Improved confirmatory diagnosis of COVID-19 infection using protein mass spectrometry

Professor William Rawlinson, University of Sydney

Confirmatory diagnosis of COVID-19 at the commencement of the pandemic utilising nucleic acid amplification testing (NAAT), frequently continued to return positive results after the typical window of infection when symptoms had cleared. Continued re-testing of these patients placed additional workload on laboratories and reduced testing capacity. This project therefore aimed to create diagnostic efficiencies by developing a new test to detect viral proteins in patient samples, as a promising complementary and confirmatory strategy for diagnosis of COVID-19 infection.

Using high-resolution liquid chromatography-mass spectrometry (LC-MS) on viral culture samples, researchers detected COVID-19 Nucleoprotein (N), Spike (S), ORF9b, ORF8, Membrane (M) and protein 7a. These results were used to develop a high-throughput targeted assay for detecting viral proteins. Peptides from N and ORF9b were found to have the highest sensitivity. Specificity of the assay was maximised during development by searching high resolution data from COVID-19 cultures against sequences of human and bovine proteins, as well as those from other respiratory viruses and selecting peptides that matched only to COVID-19 at high confidence (>99%).

Benefits of this method include improved turnaround times compared to standard workflows. Sample preparation time was successfully reduced from 24 to four hours with an analytical run time of less than 3.5 minutes. Additional benefits include the potential for providing a differential diagnosis in a single test, and development of a template for rapid deployment of new LC-MS assays in the event of a future pandemic.

A template for rapid deployment of new LC-MS assays has been developed for future use and is currently being trialled by a small cohort as part of a Quality Assurance Process exercise. The final method intended for clinical use was developed on a mass spectrometry instrument in use for routine testing at the Prince of Wales Hospital Clinical Chemistry laboratory. This method can be transferred to any clinical lab with a sufficiently sensitive triple quadrupole mass spectrometer and properly equipped liquid chromatography system. Within the NSW Health Pathology network, this includes Royal North Shore Hospital, Royal Prince Alfred Hospital, Liverpool Hospital, and the forensic toxicology laboratories at NSW Forensic Analytical Scientific Services. Additionally, the sample preparation methodology has been simplified to be accessible for staff working at any level within NSW Health Pathology Clinical Chemistry laboratories.

Ultra-sensitive PC2 serology and rapid viral outgrowth assays

A/Professor Fabienne Brilot, Sydney Children's Hospitals Network

Neutralisation antibodies against SARS-CoV-2, which block further re-infection were found to be present at very low levels in some patients, making detection very difficult and time consuming. Further, it was unclear whether infection with COVID-19 variants would impact the detection of antibodies. With the emergence of new variants and COVID-19 vaccination on the horizon, this study aimed to improve COVID-19 antibody and virus diagnostic detection of low levels of COVID-19 antibodies.

The team developed platforms that enabled high content serological testing across thousands of biospecimens and many nation-wide cohorts and characterized global variants to determine their relative risk to the community as soon as they emerged in Australia. Researchers were able to phenotype every *Variant of Concern* and over eight *Variants of Interest* spreading globally in 2021. They compared the immune response between adults and in children and evaluated the relative protection of vaccine and boosters in individuals from the general community. Further, the immune responses of individuals at high risk due to immunosuppression, following haematological cancers or multiple sclerosis, were assessed.

Key findings from this research include:

- first characterisation of Omicron BA.1, 2
- similarity of antibody response in breadth and longevity between COVID-19-naïve children and adults infected by SARS-CoV-2, 5
- greater cross-reactivity, induced by some variants of concern, such as Delta generated a greater response characterised by enhanced immunogenicity
- decrease antibody cross-reactivity to newer variants such as BQ.1.1, BA2.75.2, and XBB1 in vaccinated adults and children.

The research was able to support the response in the following ways:

- informing the Australian Technical Advisory Group on Immunisation (ATAGI) national vaccination guidelines and international vaccination guidelines with respect to Omicron BA.1
- informing clinical guidelines with respect to those at risk of a poor vaccine response (haematological cancers, multiple sclerosis)
- informing CDC therapeutic guidelines.

In addition, the research enabled extensive collaboration to guide efforts with respect to therapeutic use, vaccination, and next generation vaccine strategies.

Novel diagnostics for evaluating duration of immunity after COVID-19 and for Phase I/II vaccine trials

Professor Anthony Cunningham, Westmead Institute for Medical Research

Upon establishing that reinfection with COVID-19 can occur, determining the period of natural immunity in recovering patients and the period of time for which immunisation may remain protective, became urgent questions. Understanding the duration of immunity among population groups such as frontline workers and vulnerable populations, especially the elderly, was a particular priority to inform policy decisions. This study aimed to examine the level and duration of immunity to COVID-19, particularly that mediated by white (T) cells, following infection and after immunisation with new candidate vaccines.

The research team was able to define T-cell peptides using an immunoinformatics analysis pipeline to provide COVID-19 specific tests for CD4 and CD8 T-cell immunity, to all viral strains circulating in Australia and globally. The peptides were found to largely avoid areas of mutation that had arisen in different viral variants, including Delta and Omicron, and so were specific for these strains.

It was found that T cell responses induced by natural COVID-19 infection persisted out to 12 months with only a modest decline, which was relatively unaffected by age. Antibodies declined more markedly in older groups, especially above 70 years, but were persisted to at least 12 months.

Commercial COVID-19 peptide pools have a high degree of cross-reactivity with people not exposed to the virus. In their peptide pool, the team could attribute cross reactivity heavily to a single peptide providing them with tools to test for COVID-19 specific responses in recovered patients (by omitting this peptide) and boosting of pre-existing COVID-19 immunity during vaccination (by including this peptide).

The study found that among patients with chronic lymphatic leukaemia only 40% achieved sera conversion after two doses of COVID-19 vaccine, but greater than 90% were able to sera convert with repeated doses (up to eight). However, T cell immunity was achieved in 80% of vaccine recipients with just two doses.

The technology developed in this project has been utilised by the Vaccine, Infection, and Immunology (VIIM) Collaborative Research Group (also funded under the Program) to further investigate vaccine induce immunity. The findings continue to inform NSW Health about the level and durability of vaccine induced immunity in the face of recurrent waves. The team also contributed to the NSW RNA Bioscience Alliance – a partnership across all NSW universities, supporting the development of a vaccine pipeline initiative in NSW.

PRIORITY POPULATIONS

45 and Up COVID Insights
Dr Martin McNamara, Sax Institute

This study sought to apply an agile methodology to the existing database of participants from the *45 and Up Study* – which has tracked the health of more than a quarter of a million elderly NSW residents for the past 15 years. Conducting short online surveys with sub-cohorts of participants and expediting analysis and reporting timelines, enabled the delivery of insights of clinical and policy relevance in relation to the population effects of COVID-19.

A total of 32,115 participants enrolled in the sub-study, which involved a series of five online surveys that were conducted throughout 2020-2022. Survey themes were selected to obtain information on the pandemic's impact on health, loneliness, lifestyle, physical activity, diet, sleep, alcohol use and access to health services, as well as experiences with telehealth, vaccination and more.

From the five surveys, a variation in impacts on the different population groups and stages of the pandemic were reported. Key findings include:

- Missed healthcare: between Feb-Apr 2021 (survey two), 10% reported missed healthcare in the past month due to the pandemic, increasing to 26% by Sep-Nov 2021 (survey four), and subsequently decreasing to 16% in Mar-Apr 2022 (survey five)
- Quality of life: overall this remained high, with more than 90% reporting good, very good or excellent quality of life across the different surveys
- Mental health: as the pandemic progressed, the proportion of participants reporting worsened mental health because of the pandemic, increased from 29% in Jul-Dec 2020 (survey one) to a high of 46% in Sep-Nov 2021 (survey four), before decreasing slightly to 44% in Mar-Apr 2022 (survey five). Disparities were detected in priority groups such as carers and people living with a disability
- COVID-19 vaccination: in Feb-Apr 2021, 89% intended to get the COVID-19 vaccine with 8% unsure. By the end of 2021, vaccination uptake was high with 92% double vaccinated
- COVID-19 prevention: behaviours such as mask wearing showed increased uptake across the first four surveys before decreasing in Mar-Apr 2022 (survey five).

Examples of how insights from this study were considered in policy and planning include:

- decrease in physical activity during the first stay-at-home period – informing messaging during subsequent periods that people should stay active in safe ways
- missed cancer screening – informing future planning for services
- increase in the prevalence of mental health concerns – informing mental health service planning
- negative impact of the pandemic on people with disabilities – informing work on the National Disability Strategy.

Impact of COVID-19 on Indigenous Australians' preventive health behaviours: A mixed methods study, *Professor Kim Usher, University of New England*

This project investigated barriers and enablers of attendance at preventive health services by Indigenous Australians in NSW, with the aim to increase the health system's understanding of the unique experience of Indigenous Australians to engage in preventive health behaviours due to COVID-19.

The study reported that 1,192,293 Indigenous health assessment services were claimed between July 2017 and June 2022 across Australia, including 26,322 telehealth services, and found a 14% reduction (from 3292 to 2852 per 10,000) in claims between 2019-20 and 2021-22. A significant decline in health assessments was observed in April 2020 coinciding with the initial COVID-19 stay-at-home period. Indigenous health assessment claim numbers were found to be higher for females in all age groups over 14 years compared to males.

Findings from 110 interviews revealed several barriers to seeking preventive health care during the height of the pandemic. Issues raised including the inability to travel due to local public health measures, lack of available services, lack of transport, and fear of going out due to COVID-19. These insights into the preventive health seeking behaviour of Indigenous Australians will inform the development and implementation of specific interventions aimed at increasing engagement with preventive health services.

A rapid qualitative assessment of COVID-19 health needs in an urban Aboriginal community

Associate Professor Joanne Bryant, University of NSW

This study aimed to gain insights into the specific health needs of the Aboriginal community and enable a rapid, effective and community-led response. Utilising qualitative peer-led interviewing methods, this research resulted in insights on COVID-19 related prevention knowledge, control strategies, vaccine acceptability and health service needs in two metropolitan and one regional location. The approach aimed to produce meaningful evidence for Aboriginal communities and to support health promotion messaging tailored to their specific concerns.

The results showed that most participants were cautious about the vaccines but did not have a firm view about whether they would get vaccinated, and only a handful had strong negative views. The main reason for scepticism about vaccines was a sense that the current vaccine products were developed too quickly, which participants believed has compromised their safety. Other specific concerns were that: the vaccine includes a fragment of the virus, that the side effects of vaccines could be just as damaging as COVID-19, and that older people were more vulnerable to developing COVID-19 from vaccines. The main reason participants gave for getting vaccinated was that it would permit them to return to their 'normal' lives. For young people (16-29 years) returning to 'normal life' tended to be about travel and socialising, for participants aged 30-50 years, it was about returning to 'normal' work; and for older participants (50+ years) it was about maintaining longevity and staying healthy.

Findings highlighting the need to generate more discussion within Aboriginal communities about vaccination, were shared with the Aboriginal Health and Medical Research Council (AH&MRC). Consequently, an extensive list of additional questions regarding vaccine acceptability were added to their interview protocol, and the results utilised by the AH&MRC in their 'Yarn Up!' campaign. The research findings also directly informed the health promotion efforts of the national governing body of Aboriginal Community Controlled Health Organisations (NACCHO), the South Western Sydney Local Health District Aboriginal Health team and Tharawal Aboriginal Medical Service, specifically around COVID-19 vaccine uptake.

MENTAL HEALTH IMPACTS

Rapid evaluation of a scalable program for reducing common mental disorders during COVID-19

Scientia Professor Richard Bryant, University of NSW

Modelling in Australia projected a significant increase in common mental disorders (CMDs), including anxiety, depression, and suicidality, in coming years due to COVID-19. This project aimed to address the need to mitigate the anticipated mental health problems arising from the pandemic, by adapting a proven intervention with the potential to be rapidly integrated into mental health systems across metropolitan, regional, and remote locations.

The protocol was a randomised control trial into the effectiveness of Problem Management Plus (PM+) therapy delivered remotely through group sessions and supplemented with homework, for the management of COVID-19 anxiety and stress. PM+ program aimed to reduced CMDs arising from COVID-19 stressors relative to those receiving enhanced usual care. The measured outcome was a total score on the Hospital Anxiety and Depression (HADS) anxiety and depression sub-scale assessed at baseline one week, two months and six months post-treatment. Secondary outcomes included measures of worry, sleep impairment, anhedonia, mood, and COVID-19-related stress.

Relative to the enhanced usual care group, participants receiving the intervention showed statistically significant reduction on both the anxiety and depression scales, with effects maintained at six months post intervention. There were also greater reductions of worry, anhedonia, COVID-19-related fears, and contamination fears.

Findings from this study suggest that utilising videoconferencing to deliver a brief group-based intervention can result in moderate reductions in CMDs arising from the COVID-19 pandemic. While the burden of CMDs did not necessitate a statewide rollout of this program as initially intended, the program does offer a viable and scalable method to address mental health problems in the event of future pandemics.

PUBLIC HEALTH MESSAGING

Designing and testing COVID-19 vaccine public health message

Professor Kristine Macartney, NCIRS and Sydney Children's Hospitals Network

This project aimed to understand factors influencing acceptance of COVID-19 vaccines in key groups in NSW populations and to develop communications guidance and messages to strengthen that acceptance.

To achieve this aim, the project team conducted a range of research activities, including: (i) interviews with priority groups to factors influencing acceptance; (ii) survey and interviews with immunisation providers to assess their COVID-19 vaccination communication needs; (iii) interviews with unvaccinated community members to understand communication preferences; and (iv) online experiments to better understand how key groups respond to messages about COVID-19 vaccines framed in different ways.

The study found that key barriers to COVID-19 vaccine acceptance among priority groups were:

- concerns about COVID-19 vaccine safety, including unknown long term negative effects
- concerns that COVID-19 vaccination could exacerbate pre-existing health conditions
- low perceived personal risk of developing COVID-19.

Key facilitators were:

- trust in vaccine development processes
- confidence in health authorities
- perceived personal benefits, such as travel and life returning to 'normal' perceived community benefits such as reduced spread of infection.

Immunisation providers reported factors that increased the difficulty of communicating with patients about COVID-19 vaccination, including time constraints, keeping up to date with a changing information landscape, and language barriers when communicating with culturally and linguistically diverse patients.

Unvaccinated individuals described their perceived lack of transparency in communications about COVID-19 vaccine safety, and their desire to see balance and opposing views in health authority communications about COVID-19 vaccination.

Evidence from message testing suggested that emphasizing non-health benefits of getting a booster dose, like reducing the chance of public health restrictions returning, may have the most positive impact on people's intention to vaccinate.

Ongoing projects

The Chief Investigators of a further six research studies requested an extension of their timeline and were still underway at the time of writing. This was largely due to recruitment challenges, caused in part by the relatively delayed rise in incidence of COVID-19 in NSW. The updates for these projects are based on the information contained in the most recent progress reports.

DIAGNOSTICS

Development, evaluation and validation of Enzyme Linked Immunosorbent Assay (ELISA) assays for both the diagnosis of COVID-19 and utility in seroprevalence in communities

Dr Linda Hueston, NSW Health Pathology

To enable reliable serological diagnosis of COVID-19, tests must be accurate, sensitive and specific, easily performed in high numbers, and achieve rapid turnaround times. Commercial tests in routine use at the start of the pandemic targeted various parts of the spike protein preventing them from being able to distinguish vaccine from naturally acquired antibodies. This project was funded to support both diagnosis of COVID-19 through the accurate detection of COVID-19 antibodies, and for utility in assessing seroprevalence in communities.

To date three IFA tests and two IgG ELISA tests have been developed. Significantly, the Trimeric spike IgG and Nucleoprotein IgG ELISA assays allowed diagnostic services to distinguish between vaccine induced and naturally acquired antibodies, which assisted with contact tracing and pinpointing the timing of infection. Since the introduction of vaccination and the appearance of multiple variants the antibody response using these five tests has changed. The ancestral strain (Wuhan) produced antibodies to IgG, IgA and IgM in most patients, but different patterns were observed between COVID-19 variants: IgM was rarely produced, and IgA was reduced or often absent. The introduction of Omicron variants saw the IgA antibody appear more frequently. Vaccination also occasionally induced the IgA but not the IgM antibody.

An additional round of antibody class capture assays was developed using enzyme-labelled antigens for Spike 1, Spike 2 and Nucleoprotein antigens – this system reduced testing time and allowed automation. The Spike 1 and Spike 2 IgA and IgM assays were successful and research is continuing to investigate future potential. The Nucleoprotein version was not successful due to very high background readings that could not be removed. Another round of testing is underway to develop antibody class capture for IgA and IgM using monoclonal antibodies as the detectors. This technique has proven to be very sensitive and improved specificity with the use of specific monoclonal antibodies.

The five finalised assays were integrated into routine use, enabling NSW Health to understand how the virus changed over time and the impact of those changes on diagnostic processes. These assays have been used by research groups inside and outside NSW to monitor vaccine efficacy.

PRIORITY POPULATIONS

A place-based pandemic response to the strengths and vulnerabilities of Aboriginal communities in south-eastern NSW, *Professor Kathy Clapham, University of Wollongong*

This study aimed to develop a culturally safe, place-based response to COVID-19 for NSW Aboriginal communities and to safeguard effective service provision by Aboriginal Community Controlled Health Organisations (ACCHOs). With a focus on the immediate and long-term physical, social and emotional impacts of the pandemic, this project sought to shed light on the gap in knowledge of how ACCHOs responded to the complex health and social challenges confronting local Aboriginal communities in the COVID-19 context. The study investigated social and cultural disruption, trauma, health and safety education and services, information, messaging and communications within Aboriginal communities. Informed by its findings, the project developed a collaborative protocol for Aboriginal communities to utilise in response to crises.

Stakeholder engagement comprised of in-depth face-to-face or phone interviews (n=14); focus group participation (n=8); meeting and committee engagement (n=15).

Outcomes from the Pandemic Response Rapid Review highlighted that ACCHOs were:

- consistently taking initiative to lead and drive the community response, enabled by their flexible models of care and service delivery and, recent experience in crisis management gained from responding to the bushfires of summer 2019
- collaborating with government to inform/plan the guidelines and toolkits
- developing targeted health messaging, interpreting standardised public health measures and legislation, and engaged in myth debunking.

ACCHOS also experienced:

- rapid re-orientation of service delivery to deliver COVID-19 safe services
- new services and processes to accommodate e.g. welfare checks, food security, clinics, point of care testing, contact tracing
- rapid response to issues of family violence or notification about poor social and emotional wellbeing
- increased workload.

MENTAL HEALTH IMPACTS

Supporting the mental health of health workers at Aboriginal Community Controlled Health Services in NSW during the COVID-19 pandemic and beyond

Ms Sandra Bailey, Sax Institute

Throughout the pandemic health care workers in Aboriginal Community Controlled Health Services (ACCHSs), who were already working under challenging conditions, were at the forefront of managing COVID-19 and its flow-on effects in their communities. This study aimed to examine the mental health of these staff and how it was impacted by the COVID-19 related service-level changes. Further, the study sought to investigate how best to support the mental health of health care workers throughout the changing conditions.

A total of 222 staff from four ACCHSs participated in four surveys over an 18-month period and 31 staff from five ACCHSs joined yarning circles or participated in individual interviews. Key findings include:

- Despite reports of changes to roles, most staff demonstrated low levels of emotional exhaustion and psychological distress, and reported higher job satisfaction
- Since the start of the pandemic, staff have experienced prolonged levels of stress including concern about virus transmissibility, information and workplace uncertainty, and increased burden of providing healthcare
- Awareness about mental health support was variable, and staff considered support difficult to access, or were concerned about privacy issues.

In addition, the research team implemented a mental health training program – *Accidental Counsellor* – that provided staff with strategies to support colleagues and community members.

A digital solution to address the mental health and financial impacts of the pandemic for children and their parents in the first 2000 days

Dr Valsamma Eapen, South Western Sydney Local Health District

Emerging evidence suggested that children and families from disadvantaged backgrounds were experiencing increased psychosocial and mental health stress due to the pandemic. Culturally and linguistically diverse families and those from regional/rural communities face barriers to service access and can be reluctant to seek out mental health support. With most Child and Family Health Nurse (CFHN) clinics closed to in-person consultation during the pandemic, many children were missing health and developmental checks and identification of psychosocial needs.

The *Watch Me Grow – Electronic (WMG-E)* Platform is a free, online, innovative technology that provides unique opportunities to reach vulnerable families at their homes. This study used the WMG-E Platform to engage parents to identify and address parental mental health, psychosocial wellbeing and child developmental needs, thereby optimising the wellbeing of families. The study focused on families of children aged 0-5 years that were hard-to-reach due to sociocultural or geographic barriers as a direct NSW Health COVID-19 response.

A total of 288 families were recruited into the study and 276 completed the six-month follow-up.

Intervention group families received wrap around health and social care and showed significant improvements in service engagement and health outcomes, including:

- numbers in the no-risk group increased
- numbers in the medium-risk intervention group decreased while the number of control families in the medium-risk group increased.

Preliminary evidence suggests that WMG-E may also:

- normalise and de-stigmatise mental health and psychosocial screening
- increase parental engagement and service use
- result in the early identification and management of child developmental needs, parental mental health, and family psychosocial needs
- bed down a new and innovative solution to the current service delivery gap and create mechanisms that can engage families currently not accessing services
- could be embedded into standard CFHN Service protocols across NSW, with targeted initiatives to address any specific population needs.

The eCliPSE COVID-19 project: an electronic pathway to care for NSW residents to reduce depression, anxiety, and alcohol use problems in the face of COVID-19

Dr Milena Heinsch, University of Newcastle

Depression, anxiety and alcohol and other drug use frequently co-occur and were predicted to increased due to COVID-19. While digital treatments can extend the capacity of health services to address this issue, they have not, historically, been well integrated into service provision models. This study set out to develop and test 'MoRE' (Mood Recovery Program), a new digital treatment aimed at improving symptoms of depression and anxiety in adult populations. The study further sought to accelerate translation at scale by implementing and testing the eCliPSE digital portal for mental health and alcohol and other drug use disorders, by digitally enabling services to increase capacity for care. The eCliPSE project was rolled out to all 15 local health districts across NSW.

Over the past 12 months 4472 people have accessed the eCliPSE portal. This highlights the continuing high need and public interest in evidence-based information and support for substance use problems co-occurring with poor mental health.

The eCliPSE portal provides users with access to nine evidence-informed online programs, including the My Healthy Lifestyles Program (MyHeLP), an evidence-based program that helps users reduce or quit smoking and alcohol use, improve their diet, level of exercise, sleep, and overall mood. MyHeLP has been found to be a safe, feasible and effective intervention to assist people with and without mental ill-health to improve and monitor key risk behaviours for chronic disease. This work includes a manual to guide clinicians in supporting people with mental health and substance use issues through the eCliPSE portal's social networking site, 'Breathing Space'. This networking site can provide peer support for those with mental health concerns.

A larger scale eCliPSE trial commences August 2023. This will see a significant increase in the number of Australians who will be provided with mental health support via the portal. There are seven NSW sites currently undergoing ethics and governance processes to participate in the new trial.

MODELS OF CARE

Evaluation of the Virtual Rural Generalist Service as an effective, "COVID-19 resilient" model of care

Dr Shannon Nott, Western NSW Local Health District
Professor Andrew Wilson, University of Sydney

Rural communities experience poorer health outcomes and struggle to recruit and retain a skilled and specialist medical workforce, increasingly relying on locum contracts to support local needs. The COVID-19 pandemic proved particularly challenging for rural communities due to the unique vulnerabilities experienced by rural populations; workforce shortages, reliance on a fly-in-fly-out workforce, and limited ability to cope with a sudden influx of patients. The Virtual Rural Generalist Service (VRGS) was initiated by Western NSW Local Health District (WNSWLHD) to assist communities without a local General Practitioner Visiting Medical Officer, or where fatigue support was required. VRGS supports acute, non-critical care in hospitals when a doctor is unable to be there in person.

The COVID-19 funding supported WNSWLHD to evaluate the impact of the VRGS on health care and workforce outcomes for rural communities in the context of COVID-19, and in addressing the challenges of the rural and remote health workforce.

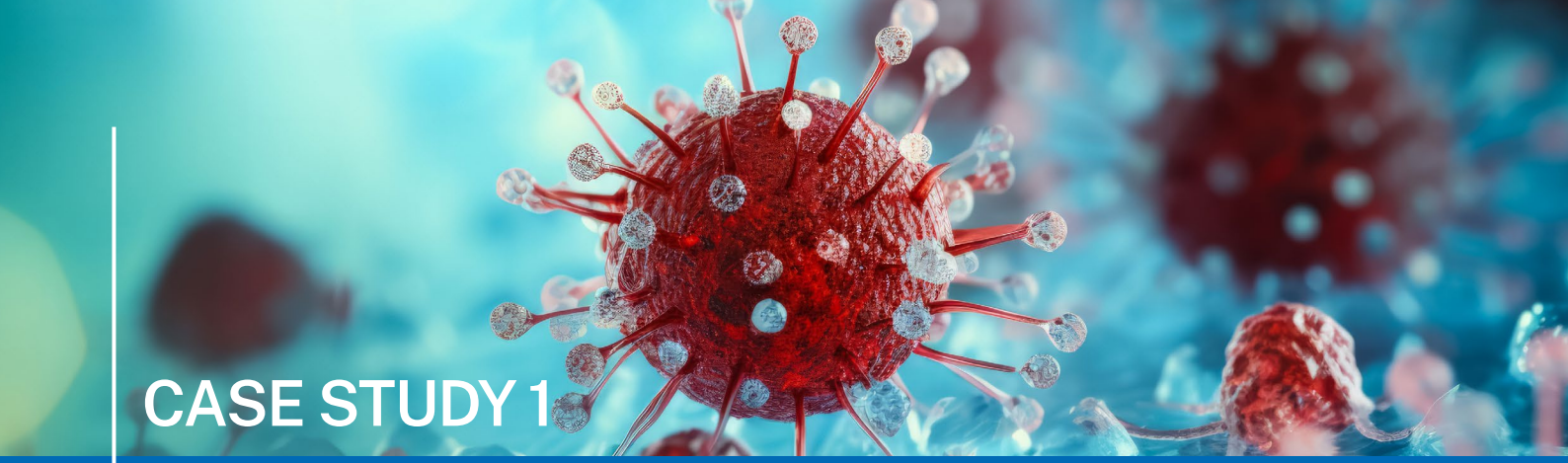
Th evaluation was designed to closely align with key state and local priorities, including the Virtual Care Monitoring and Evaluation Framework and the NSW Health Values Based Healthcare Framework.

Key findings to date include that VRGS:

- delivered care for 34% of 39,701 Emergency Department presentations and 40% of 6328 inpatient admissions between July 2021 and June 2022
- patients, carers, clinicians, and managers are generally positive about the service, and acknowledge the usefulness of the service during the first year of the pandemic
- was a COVID-19 resilient medical model during a period where the existing fly-in-fly-out workforce was unable to travel due to border restrictions in Australia
- the VRGS delivered equivalent patient health outcomes (including mortality rate, emergency department length of stay and unplanned readmissions) to patients who did not access the VRGS
- patients were less likely to be transferred to another hospital
- patients were more likely to have an incomplete Emergency Department attendance, i.e. did not wait for treatment, or left at own risk (i.e., after treatment has commenced, against advice)
- the VRGS model of care demonstrated significant cost reductions when compared to traditional (i.e. non-VRGS) models. The total National Weighted Activity Unit (NWAU) for the VRGS was $2009 per episode compared to $6998 for the non-VRGS group
- Most patients and carers felt that the VRGS provided good quality care and met their needs. They were also positive about the Service being able to provide access to high-quality medical care without leaving their community.

Outcomes of the VRGS address NSW Health's Leading Better Value Care and the quadruple aim, focusing on improving patient experience, improving the health of populations, increasing the effectiveness of healthcare organisations, and ensuring sustainable health care into the future.

In 2022, the Western NSW Local Health District won the NSW Premiers Award in the Excellence in Digital Innovation category for the VRGS service.



CASE STUDY 1

Enhanced Sensitivity of Whole Genome Sequencing

Whole genome sequencing and the COVID-19 pandemic

During the early stages of the COVID-19 pandemic, there was limited understanding of SARS-CoV-2 and its transmission pathways. The pandemic required a response that involved rapid, high-resolution detection to track the spread of COVID-19 in the community and high-risk settings, and with public health follow-up of confirmed cases to identify the source of outbreaks.

Genomic sequencing is recognised as a key diagnostic resource for public health and was already in use in Australia to trace foodborne outbreaks and tuberculosis transmission. Chief Investigator Professor Vitali Sintchenko and the research team were one of the first in NSW to undertake whole genome sequencing (WGS) in the laboratory. Their previous experience in WGS meant the team was able to effectively adapt their work to support the NSW COVID-19 pandemic response, sequencing the genome responsible for the first NSW case of COVID-19 in January 2020.

The research team developed, evaluated and implemented prospective and near real-time public health genomic surveillance, which enabled rapid identification of COVID-19 clusters caused by local transmission or importations into NSW.

The problem: generating genomic sequences for samples with low viral load

A considerable challenge for understanding COVID-19 transmission was generating a full genome sequence from samples with low viral loads, cases with minimal disease, or asymptomatic infections. Generating genome sequences from samples with low viral loads is difficult and consequently, many samples were not sequenced or needed to be re-sequenced. This cost valuable time and resources and delayed the availability of timely information to support decision making.

Outcomes

Enhanced sensitivity of genome sequencing methodologies

The Public Health Pathogen Genomics group, led by Professor Sintchenko, was established as a collaboration between the Centre for Infectious Disease and Microbiology – Public Health, NSW Health Pathology's Institute of Clinical Pathology and Medical Research (ICPMR) and the Sydney Institute for Infectious Diseases of the University of Sydney. Through the NSW Health COVID-19 Research Grant, the team were able to evaluate three novel methodologies to improve the sensitivity of genome sequencing of COVID-19 samples with low viral loads.

In the early phases of the outbreak, it was only possible to generate genomes for 13% of COVID-19 positive cases. The new methodology developed enabled the sequencing of over 40% of COVID-19 samples, significantly reducing the proportion of cases with unconfirmed genomic links. During the pandemic, the Public Health Pathogen Genomics group sequenced over 55,000 genomes, reporting new variants, clusters and transmission links.

Policy and Practice

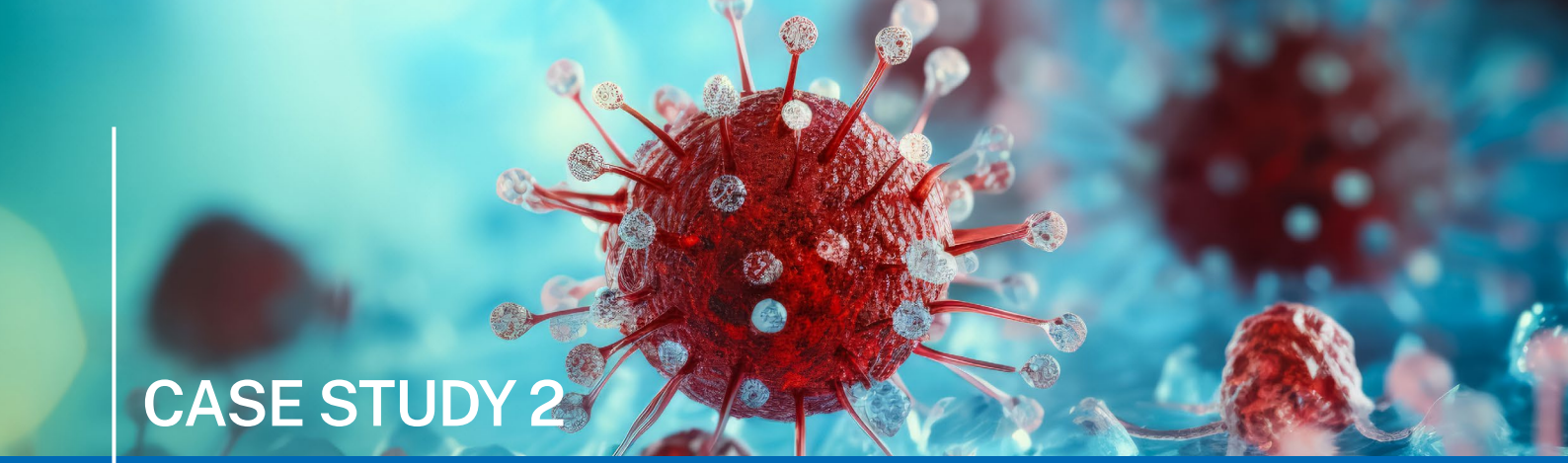
Genomic sequencing has been a pivotal public health tool used to provide insights that enabled an agile whole of system response to pinpoint the source of COVID-19 outbreaks within NSW. The generation of data from WGS provided public health officials with evidence to inform policy and practice decisions and to respond to outbreaks quickly. The evidence generated contributed to identification of COVID-19 transmission pathways, which made it possible to discover cases that were not linked to a known outbreak or cluster, as well as the country the strain was from. This improved understanding of transmission pathways also enabled the NSW public health response to target high risk settings and priority groups and implement strategies to minimise the spread of the COVID-19.

Capacity and capability building

The research contributed to capability building and collaboration between academic and clinical research and the NSW Health system. Professor Vitali Sintchenko and the research team were awarded the NSW Health Secretary's Award – Integrated Value-based Care in 2022 for the project "Unlocking the puzzle of COVID-19 transmission". This award recognises Professor Sintchenko and the research team's pioneering methodology to sequence COVID-19 infections to understand transmission.

Leveraging funding and enabling new partnerships

Prior to the COVID-19 pandemic, Professor Sintchenko through the Centre for Infectious Disease and Microbiology – Public Health and the Public Health Pathogen Genomics research team received research grant funding from NSW Health schemes including the Prevention Research Support Program (PRSP), a competitive scheme investing in research infrastructure for NSW, and the Translational Research Grants Scheme (TRGS). This long-term investment was successfully built upon through the NSW Health COVID-19 Research Program grant, enabling WGS to quickly become an integral resource for the surveillance of COVID-19 cases.



CASE STUDY 2

A 24/7 eICU Model of Care in Regional and Rural NSW ICUs

The problem: Limited intensive care unit capacity and services in regional and rural NSW during a pandemic

During the onset of the COVID-19 pandemic, there was concern regarding the ability of healthcare systems to manage sudden large increases in the number of patients. Of particular concern was the limited capacity of intensive care units (ICUs) and their ability to flex to increase this at short notice. ICUs require specialised medical equipment and highly trained healthcare professionals who can deliver intensive monitoring and treatment to patients facing life-threatening conditions. This issue is greater in regional and rural areas where specialised equipment and staff are more limited. Patients in these areas who require the highest levels of care typically require transfer to more specialised ICUs in Sydney. In case of a sudden surge in COVID-19 cases, regional and rural centres would have to manage critically ill patients themselves, with limited supervision from senior medical professionals trained in intensive care.

Potential solution identified: ICU using virtual care

Virtual care is the use of technology to provide remote healthcare services, such as telehealth and telemedicine. It has been demonstrated to be a solution to some of the challenges of healthcare in rural Australia by offering better access to care, enhancing the efficiency of care delivery, and minimising the need to travel for medical services. This technology provides video advice for clinical staff and supports remote monitoring of symptoms. Virtual care could also enhance the efficiency of care delivery as healthcare professionals can care for more patients over the same period, which is especially critical in regions with limited healthcare resources.

The NSW Virtual Care Strategy seeks to integrate virtual care as a safe, effective and accessible option for healthcare delivery in NSW. However, during the early phase of the pandemic, only descriptive reports of telehealth or virtual care use in ICUs existed, mostly from international jurisdictions.

Chief Investigator Professor Deepak Bhonagiri, an Intensive Care Specialist at Campbelltown and Liverpool Hospitals, has a keen interest in virtual clinical care and remote patient monitoring. The study funded through the COVID-19 Research Program aimed to provide evidence towards the eICU model of care as a safe, effective sustainable model aligned with NSW Health's value-based care.

24/7 eICU Virtual Care Approach

eICU, or electronic Intensive Care Unit, is an innovative model that uses telemedicine to provide continuous monitoring and management of patients, which can lead to better outcomes and reduced mortality rates. To demonstrate the feasibility of this approach, the eICU model of care was set up in three rural ICUs, with a high-level ICU in Sydney providing 24/7 monitoring and support. The eICU operated through an open collaborative model, promoting efficient and effective communication among healthcare providers and ensuring patients receive timely and appropriate care.

Outcomes

Safe, effective, efficient, and acceptable

The eICU model was evaluated against the quadruple aim of value-based healthcare, which includes improving health outcomes, increased effectiveness, and efficiency of healthcare, improving the patient experience of care, and improving the experience of providing care.

The study found that:

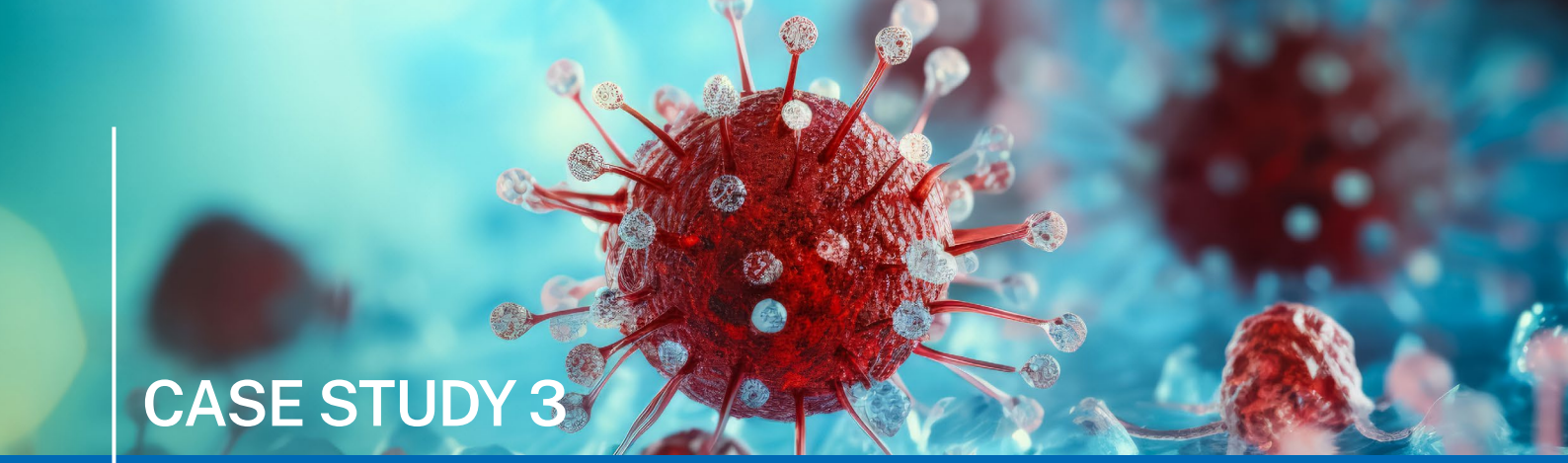
- the model of care was effective in providing the same level of care as other ICUs, as measured against strict standards
- the model of care was associated with a possible reduction in costs, due to a reduction in transfers from rural and regional centres to metropolitan centres
- patients and their families were generally satisfied with the eICU model of care and felt it provided timely and effective care while it reduced the need for transfers to higher levels of care
- clinicians reported positive experiences, finding the model to be effective, efficient, and an opportunity for improved collaboration and communication between healthcare providers. The study also indicated increased access to specialist expertise, and increased confidence in decision-making.

Sustainability

The 24/7 eICU model of care has continued beyond this pilot study. It has been adopted by several other regional ICUs and has shown to be associated with sustained efficiency gains. Five rural and regional centres now have access to higher level ICU clinician expertise, while providing remote monitoring capacity to detect early patient deterioration and provide escalation pathways.

The future for this model of care

This model of care provides potential for care closer to home, improving the patient and carer experience while reducing the need for complex transfers to metropolitan centres. The model has been shown to have the ability to be quickly scaled up and implemented, making it a flexible solution to support the healthcare system during times of crisis. It also has the potential to be extended to rural or regional close observation units with General Practice medical staff.



CASE STUDY 3

A Therapeutic Cell Bank of Virus-Specific Immune Cells Targeting COVID-19

The problem: immunocompromised patients are at risk of severe COVID-19 outcomes and are resistant to existing treatments.

Immunocompromised individuals, such as those with rare disorders and those undergoing cancer treatment, are at a heightened risk for severe outcomes if infected with COVID-19 and have trouble recovering from the virus. They can remain infectious for prolonged periods, which can compromise their ability to receive treatment for their underlying disease, increase the cost of managing their underlying disease, and increase the risk to the community. Despite the development of vaccines, pharmacological treatments and improved clinical management, risks remain for these vulnerable patients. Other novel treatments are required.

Recognition and investment in teams that could help the response

The Westmead Institute for Medical Research is home to groups of clinicians and researchers, among them, Associate Professor Emily Blyth and her team, who focus on improving the safety and effectiveness of patients undergoing blood stem cell transplants. The Institute has over twenty years of experience in T-cell therapy and have made meaningful progress in conducting clinical trials of cell therapies manufactured at the Westmead facility.

The team at Westmead Institute holds intellectual property registered worldwide, serving as a testament to their collaborative research and development efforts. They have worked on several viral and fungal organisms that are problematic in patients with poor immune function, including influenza, which highlights the possible applications of this therapy for infections such as COVID-19.

When the pandemic began, the researchers at Westmead Institute recognised the vulnerability of immunocompromised patients to COVID-19. In response, the research group sought funding through the NSW Health COVID-19 Research Program to explore a new therapeutic for immunocompromised patients.

What is T-cell therapy?

T-cell therapy is a type of treatment where special immune cells that have been taken from donors are given to patients to help their immune system fight disease. It has shown promise in the treatment of viral infections and cancer in patients with a compromised immune system. Unlike antibody therapy, it can target more regions of the virus, making it less susceptible to viral mutations. Moreover, T-cell therapy offers an alternative treatment to existing and other therapeutics currently in development. The potential of T-cell therapy to address this critical need is significant and highlights the importance of continued research in this area. Currently there no commercially available off-the-shelf T-cell therapies in Australia.

Outcomes:

Rapid development of the first COVID-19 T-cell bank for NSW

Despite the development of COVID-19 vaccines and drugs during the pandemic, many people remained vulnerable to adverse outcomes due to limited immunity, reduced responsiveness to vaccines, and an evolving virus rendering existing therapies less effective. The team at the Institute was able to use and adapt existing techniques to rapidly produce a bank of T-cells from donors early in the pandemic that were available when the delta wave of COVID-19 hit Sydney. This T-cell bank is currently accessible to patients under the special access scheme for compassionate use.

Collaboration

This research supported a formal collaboration with Australian Red Cross Lifeblood. Lifeblood is a vital Australian organisation responsible for blood donations and transfusions, providing essential support to the country's healthcare system. It has an active research program led by Professor David Irving, with a strong interest in medical research. This project received an enthusiastic response from the community, resulting in enthusiastic donor participation from people interested in contributing to research. This collaboration has also helped several other projects that are recruiting donors through Lifeblood.

Basic research knowledge

The work done at Westmead Institute for Medical Research in developing T-cell therapy for COVID-19 has contributed to basic scientific knowledge in several ways. Firstly, the research team investigated the characteristics of the immune response to COVID-19, specifically the breadth and specificity of T-cells post-recovery from infection. This has provided valuable insights into the immune response to the virus. Additionally, the research findings have been presented internationally, providing opportunities for other researchers to learn about and build on this work. Together, this work is contributing to the knowledge and innovation of T-cell therapy for COVID-19 and to the field of immunotherapy in general.

Increased capability and knowledge

This work has increased in the knowledge and technology capability in New South Wales. Training and support provided to scientists and clinicians has increased their expertise in this field, providing a valuable resource for the development of cellular therapies. This has resulted in improved processes and speed in developing T-cell therapies, increasing ability to manage other infectious diseases and conditions in the future.

Increased support and leveraging

This project has increased recognition of cellular therapy that is being conducted on Westmead Campus. In addition, the work has helped add momentum to other projects at Westmead including an application to the Therapeutic Goods Administration (TGA) for another project and collaborations with industry partners which are being explored to accelerate the translation of this research into clinical practice.

Patient Story

The team at Westmead Institute have successfully used this therapy to treat a patient who became severely immunocompromised after receiving a stem cell transplant in 2022. Three months later, the patient contracted COVID-19 and was unable to clear the virus for several months, despite being fully vaccinated and having used all registered treatments. The infection compromised the treatment of the patient's underlying disease as it was difficult to attend appointments while potentially infectious to others. After consideration by a multi-disciplinary team, the patient was given this novel treatment through the TGA's special access scheme for compassionate use. After a single dose, the patient was able to clear the COVID-19 infection within two weeks. There was no toxicity or adverse outcomes from the treatment. This case demonstrates the potential of T-cell therapy to provide a treatment option for vulnerable patients.

Future: T-cell therapy trial

The team aims to treat more patients and develop a therapeutic product. To this end, a trial has been designed to evaluate the safety and therapeutic effect of T-cells in treating COVID-19 and hopefully this will facilitate the use of this therapy for more patients in need.

Emergency Response Priority Research

The Emergency Response Priority Research workstream was established to enable the rapid creation of evidence to support operational work for the public health management of COVID-19. In total, 12 projects received targeted funding under this workstream. Several mechanisms were employed to accelerate the implementation and translation of these projects including:

- embedding researchers within NSW Health, which facilitated access to routinely collected data
- adding a COVID-19 component to existing research projects
- using existing research partnerships to rapidly conduct pilot studies directly commissioning urgent projects with researchers with relevant expertise and track records.

COVID-19 NSW outcomes study

Scientia Professor John Kaldor and A/Professor Bette Liu, University of NSW

This research comprised three studies into COVID-19 outcomes among NSW residents. The research questions and methods were developed collaboratively between senior NSW Health epidemiologists and the research team. Analyses were conducted using data from the NSW Notifiable Conditions Information Management System (NCIMS), linked to routinely collected hospitalisation data and death registry records in NSW.

Study one: hospitalisation rates resulting from COVID-19 infections in NSW.

This analysis investigated all confirmed COVID-19 cases diagnosed between 1 January to 31 May 2020. This showed that one in eight people with COVID-19 were hospitalised, one in 25 people were admitted to intensive care and one in 70 people required ventilation. The median time in intensive care was six days and the median time in hospital was nine days (including those who stayed in ICU for part of that stay). The study reinforced that COVID-19 is a serious illness, particularly among the elderly, and highlighted the potential impact that COVID-19 could have on health services.

Study two: high-risk groups for developing severe COVID-19.

This analysis used data from all COVID-19 cases diagnosed between 1 January to 31 October 2020. The study found that the risk of severe COVID-19 increases with age, that a single comorbidity increased the risk of severe COVID-19 two-fold, and that three or more comorbidities resulted in a five-fold higher risk of severe COVID-19.

Study three: systematic estimation of recovery time.

This study focused on COVID-19 cases diagnosed in NSW between 1 January and 31 May 2020. Overall, 94% of people were followed up by telephone interviews each week until resolution of symptoms. Hospitalisation and death data were linked to all these cases to determine recovery from COVID-19 symptoms. Analyses showed that 89% reported full resolution of symptoms, 8% had not fully recovered at the time of the last phone contact and almost 2% had died. Younger age groups were more likely to recover, men were faster to recover than women, and those with pre-existing medical conditions took longer to recover.

Findings from the research were regularly reported to the Public Health Response Branch. Outcomes were also shared with relevant bodies to calibrate forecasting and scenario models of ward and ICU occupancy. The findings informed the development of targeted prevention strategies. Notably this project was selected by the NSW Office of the Chief Scientist for the 2021 NSW Research Impact Showcase.

NSW Health COVID-19 schools transmission investigation project

Professor Kristine Macartney, National Centre for Immunisation Research and Surveillance

This project aimed to survey, evaluate and document the transmission of COVID-19 in educational settings in NSW. This collaboration between the National Centre for Immunisation Research and Surveillance, the NSW Ministry of Health, and the NSW Department of Education resulted in findings that crucially informed policy on school closures in the State and provided a comprehensive understanding of the sources and risks of COVID-19 transmission in these settings.

The Interim Report reported extensively on the findings from the first COVID-19 wave in 2020. These data were used to inform decisions on the return to face-to-face learning in schools following the first wave.

Subsequent monitoring in 2021 demonstrated that most primary cases of COVID-19 occurred in unvaccinated individuals. Among the vaccinated primary cases, secondary COVID-19 infection rates were lower than in the unvaccinated cases. This highlighted the role of vaccination in preventing infection and reducing transmissions.

Results of the study also found that transmission was higher among staff working in educational settings than among students, leading to the prioritisation of teacher vaccination in areas of high community transmission of the virus. This resulted in high uptake of vaccination among teachers, which likely contributed to the decreased rate of primary cases among staff members by late 2021

Findings also suggested that school-based exposures (in comparison with other social activities) were less likely to affect general community COVID-19 transmission rates. Coupled with the emerging evidence that the negative impacts experienced by children and the community from school closures outweighed the impact of COVID-19 infection in schools, the decision to reopen schools for face-to-face learning was made. The findings informed decisions around the introduction of specific precautions including the use of rapid antigen testing to identify infections early, and expanding vaccination recommendations.

Wastewater-based epidemiology for COVID-19

Dr Kaye Power, Sydney Water

The NSW Sewage Surveillance Program was designed to test untreated sewage for fragments of COVID-19 at sewage treatment plants across NSW. Since the virus can be shed and detected in faeces and when washed off hands and bodies, testing sewage helped track infections in the community and provided early warning signs of increases in infection.

The Surveillance Program was developed following a validation pilot study funded through the Emergency Response Priority Research workstream. Sydney Water collected 100 samples from seven wastewater treatment plants servicing six catchment areas in greater metropolitan Sydney over a 14-week period. Analysis was undertaken to verify the sensitivity and specificity of the method, supporting the subsequent use of these methods for monitoring. Results from these tests was used to support NSW Health's response to COVID-19. Public health alerts were routinely issued in relation to detection of COVID-19 in sewage, leading to efficient localised pandemic response measures that minimized the risk of major outbreaks.

The high-specificity of the waste-water surveillance method helped justify prompt public health actions, such as issuing public health alerts to maintain high community testing rates and communications targeting vulnerable subpopulations in the catchment (e.g. residential aged-care facilities or culturally diverse communities). This method also helped to reduce rates of undetected community transmission.

As COVID-19 prevalence increased, the focus of the program shifted from early warning to monitoring of trends to supplement information gathered through Polymerase Chain Reaction (PCR) and Rapid Antigen Testing. The program now samples four sites in Greater Sydney and Newcastle on a weekly basis, publishing results in the weekly NSW Respiratory Surveillance Report. The technical knowledge developed through this study has been shared and cited around the world, demonstrating its contribution to both NSW and international COVID-19 responses.

Vaccine effectiveness

Professor Kristine Macartney, National Centre for Immunisation Research and Surveillance

In parallel to the rollout of the NSW vaccination program, assessment of vaccine effectiveness was undertaken. This enabled clinical and policy decisions to be informed by timely data on vaccine effectiveness across emerging variants. It also supported public health messaging to maintain community confidence in the vaccination program.

Using linked, routinely collected COVID-19 surveillance data, assessment of vaccine effectiveness was conducted against the Delta and Omicron strains. Results showed that receipt of a third COVID-19 vaccine dose in adults aged 40 years and over significantly reduced hospitalisations and deaths from the SARS-CoV-2 Omicron variant, in a population comprised mostly of individuals who had not yet experienced a SARS-CoV-2 infection.

This study generated the first estimates of vaccine effectiveness in Australia, using data from the NSW population. The findings informed decisions around the need for and timing of the booster vaccination schedule at a State and Commonwealth level, were used by ATAGI and other peak bodies, and reinforced the importance of maintaining other public health measures. This work highlights the value of a routinely updated linked data resource to enable timely, ongoing vaccine program evaluations as population immunity and COVID-19 epidemiology changes.

Monitoring and investigating the safety and effectiveness of the COVID-19 vaccination program

Professor Kristine Macartney, National Centre for Immunisation Research and Surveillance

The NSW Immunisation Specialist Service (NSWISS), through a dedicated clinical team of vaccine experts, aimed to strengthen existing vaccine safety surveillance systems to rapidly detect, investigate, assess, report and respond to serious adverse events following immunisation (AEFIs) before and during COVID-19 vaccine introduction. This included vaccine experts at NSWISS providing an on call clinical service to answer questions from healthcare workers delivering the vaccination clinics. This support to the COVID-19 vaccine monitoring and evaluation ensured that adverse events were managed in a comprehensive and timely way, and supported public confidence in the vaccine program.

The clinical team undertook increased vaccine safety surveillance. This occurred through enhanced and timely follow-up of patients with serious-adverse reactions, and close liaison with Public Health Units. There was intense activity (more than 3500 emails and calls to the service in 2021 alone) responding to primary clinicians and vaccine hubs to answer COVID-19 vaccine questions in real time. These measures optimised the vaccination coverage and ensured that any vaccine safety signal was detected and acted upon.

Outputs from the surveillance system:

- ensured that providers were aware of COVID-19 vaccine adverse events
- provided real time advice to clinicians to assist in vaccine delivery
- facilitated the management of AEFIs
- promoted confidence and optimised vaccination coverage.

NSW Covasim analysis

Professor Margaret Hellard, Burnet Institute

In mid-2021, the Burnet Institute was contracted to conduct scenario analysis of the Delta strain outbreak in Sydney using Covasim, an individual-based COVID-19 model. Covasim was able to assess the impact on case and hospitalisation rates, and predict the risk associated with policy interventions such as testing, contract tracing, restrictions, and vaccination. The model could be adjusted to simulate key sub-populations, for example age cohorts and the evolving epidemic dynamics.

The model ran a baseline scenario reproducing the epidemic in Local Government Areas (LGAs) of concern and the rest of greater Sydney between June and July 2021, providing forward projections for 12 weeks, assuming no changes to other public health measures, vaccine rollout or behaviour (e.g. testing and compliance).

Two additional scenarios were then modelled that looked at how the outcomes of interest could be impacted if there was increased vaccination uptake in LGAs of concern, with or without additional public health measures in other areas.

The model simulated public health measures in several ways including reducing the probability of transmission (e.g. masks, social distancing), reducing specific contact networks (e.g. closing schools), or by reducing the number of contacts in each network (e.g. permitting only authorised work). The impact of these potential measures was then calibrated based on observed transmission dynamics of the initial outbreak during which they were introduced. Simulations were presented to the COVID-19 Modelling Science Table established to integrate data from the modelling approaches used in NSW.

Burden of influenza-like illness (ILI) disease in adults ≥65 years in aged care facilities

Professor Robert Booy, University of Sydney and Dr Shopna Bag, Western Sydney LHD

Since the risk of serious illness from COVID-19 increases with age, it was important to gain insights into the effect of COVID-19 in aged care settings. This study set out to estimate incidence, hospitalisation and death rates of viral respiratory infection outbreaks in aged care facilities. Throughout the duration of the study, nurses conducted routine and enhanced testing of residents of age care facilities across Western Sydney. Monthly reporting of influenza activity and data for COVID-19 were provided to the NSW Public Health Response Branch. The study was completed by mid-October 2020 with no COVID-19 outbreaks in aged care facilities in the study area so the serological aspects of the study could not be conducted.

This study published findings that demonstrated how the use of enhanced respiratory surveillance and on-site testing was reliable and practical for early notification of influenza, as well as the identification of other important viral respiratory pathogens. This timely identification of influenza outbreaks facilitated earlier intervention with antiviral treatment and prophylaxis, with a subsequent reduction in hospitalisations and deaths. This enhanced surveillance also shed light on the burden of disease due to non-notifiable viral respiratory pathogens in residential aged care facilities. Enhanced surveillance in these settings was demonstrated to have value for routine management of respiratory outbreaks in the future by reducing outbreak severity and strengthening facility preparedness.

Surveillance of paediatric COVID-19, Kawasaki disease and PIMS-TS via PAEDS

Dr Philip Britton, Sydney Children's Hospital Network

This study aimed to monitor COVID-19, Kawasaki disease, and Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS) in paediatric patients during the pandemic. Data were collected at various paediatric care sites. Case count reports were provided to the NSW Public Health Response Branch and Health Protection NSW on a fortnightly basis. This provided valuable information for policy making and vaccine recommendations in NSW and supported informed action at the national level.

Serosurveillance for COVID-19 infection

Professor Kristine Macartney and Scientia Professor John Kaldor, National Centre for Immunisation Research and Surveillance

This study aimed to measure the seroprevalence of SARS-CoV-2 antibodies to track the spread of infection by age group, gender, geography, and time. It was developed in response to the need to obtain an accurate estimate of how many people had been infected during the first epidemic wave in Sydney (March – April 2020). The study utilised de-identified blood samples collected during routine healthcare interactions unrelated to COVID-19 from three populations: outpatients undergoing blood collection for routine diagnostic pathology, blood donors, and pregnant women undergoing antenatal screening.

SARS-CoV-2 serosurveys became a key component of the Australian National Disease Surveillance Plan for COVID-19 and are listed as a precedent condition necessary to inform public health measures in the Australia's Pandemic Health Intelligence Plan.

The results of the data collected from the sample provided strong evidence that there were relatively few cases of undetected transmission during the first COVID-19 wave. The team then scaled these results to provide an estimate for the whole population of Sydney, calculating that around 7450 people had been infected in the city during the first epidemic wave. This evidence contributed to demonstrating the success of the rapid implementation of measures to reduce the spread of COVID-19 in NSW.

The study provided valuable evidence about the effectiveness of measures in the case of further outbreaks of COVID-19 and other respiratory diseases. The results demonstrate that control measures involving social distancing and good hand hygiene can be effective in reducing transmission and infection rates, allowing time for vaccine development and longer-term sustainable solutions.

Paediatric serosurveys from children in NSW contributed to the national data. The result showed the prevalence of SARS-CoV-2 antibodies in children and adolescents at the beginning of 2021 to be very low, similar to the findings of Australian serosurveys that predominantly sampled adults. This was useful in informing vaccine recommendations.

Retrospective infected health care worker study

Dr Louise Causer, University of NSW

This study aimed to monitor and respond to the risk and transmission of COVID-19 in health care workers in NSW. The study reviewed all reported cases in the NSW Health Notifiable Conditions Information Management System (NCIMS) to identify confirmed COVID-19 infections in HCWs.

An Expert Panel, chaired by the Chief Executive of the Clinical Excellence Commission, and consisting of subject-matter experts in infectious diseases, infection control, public health, epidemiology, laboratory medicine, and quality and safety systems was established to examine these cases and develop the response. The Expert Panel used these data to inform various aspects of the response to reduce infection risk and transmission to protect HCWs, patients, co-workers, and others in the community.

The study found transmission pathways between HCW colleagues, and identified issues related to common staff spaces and lack of adherence by HCWs to physical distancing. In response, the Panel initiated policy advice about matters such as personal protective equipment and use of shared workspaces such as Emergency Department 'flight decks.' The Panel was also able to identify a need for ongoing training in infection prevention and control measures, including donning and doffing of Personal Protective Equipment (PPE) and the need for appropriately skilled staff to care for patients with suspected or known COVID-19.

The data collected in this study provided valuable support for the targeted development of measures to reduce the risk and transmission of COVID-19 in HCWs in NSW and beyond. The questionnaire and accompanying survey database were shared with the Tasmanian outbreak response team and used in a cohort study as part of the investigation of the response to the health facility outbreak in Tasmania.

The Australian First Few 'X' (FFX) project for COVID-19

Professor Kristine Macartney, National Centre for Immunisation Research and Surveillance

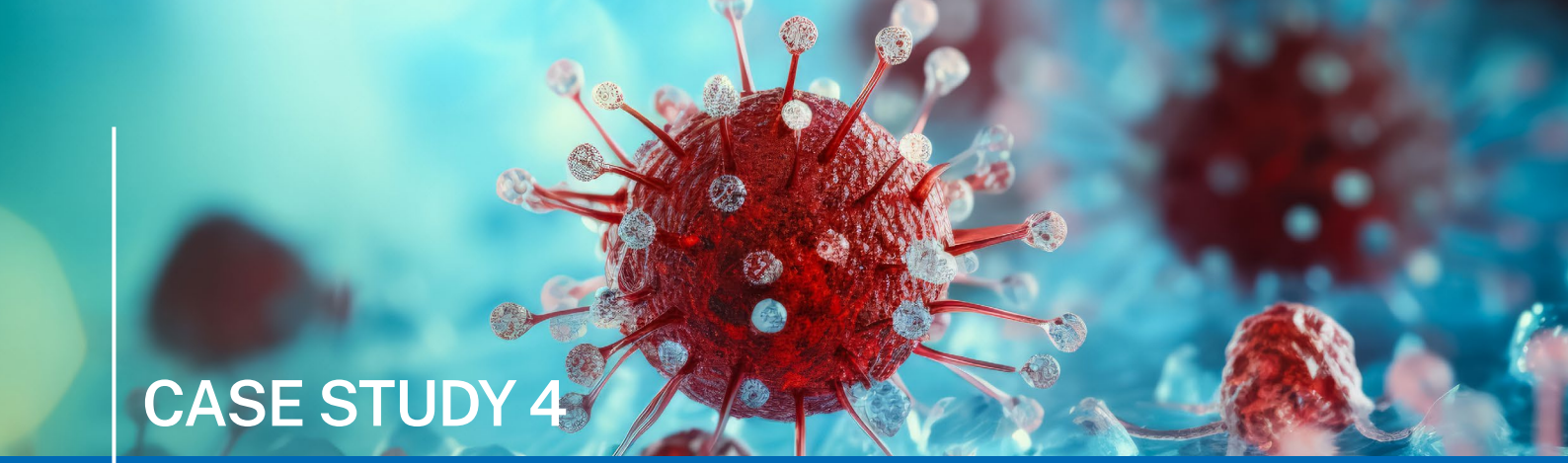
The FFX project was a national, prospective, case-ascertained household transmission study using the collection of enhanced data and specimens from laboratory confirmed cases of COVID-19 and household contacts. The study aimed to provide a response to questions about the transmissibility of COVID-19 within households and support the development of measures to reduce the risk of infection. The study aimed to collect the required epidemiological, clinical, and virological data to help address emerging information needs about the COVID-19 pandemic.

The team recruited households of one or more infected residents and tested non-infected members for COVID-19, retesting on days 7 and 14; and testing those with symptoms again on day 28 after case identification. From early on into the study, the findings helped shape the NSW Health public health response, encouraging the testing of everyone sharing a home with an infected person, regardless of whether COVID-19 symptoms were present. The study was further expanded as part of a national study. Having used the adapted World Health Organisation FFX protocol allowed the results to be shared and compared with similar work internationally.

The national study provided important baseline data characterising the transmission of early SARS-CoV-2 strains from children and adults in Australia, against which properties of future variants of concern can be benchmarked. In addition, valuable lessons were learned to inform future FFX studies in Australia in advance of future outbreaks.

Recognition of the Emergency Response Priority Research Program

NSW Health COVID-19 Emergency Response Priority Research program: a case study of rapid translation of research into health decision making (Campbell 2021) summarised the key findings of the Emergency Response workstream to June 2021. Published in the *Public Health Research and Practice* Journal in November 2021, the paper received a highly commended award in the category "**Best in Practice Paper**" from the *Public Health Research & Practice* Excellence Awards in 2022, acknowledging the contribution to policy and practice from frontline practitioners.



CASE STUDY 4

NSW COVID-19 Modelling and Epidemiological Analysis

The Problem: predicting the effect of control and vaccination measures

The scope and advancement of the Delta strain outbreak in mid-2021 resulted in an urgent need for information to support decisions related to the public health response in NSW. At that time, forecasts of the potential spread of this new strain of COVID-19 in the population were not available. Decision makers were missing critical information they needed to navigate a complex and rapidly evolving situation. Information about the consequences for morbidity and mortality rates, and adjustment of such predictions based on the range of control measures and vaccination efforts being employed across NSW were essential to understanding spread.

NSW-specific scientific modelling and epidemiological analysis

From a public health perspective, statistical modelling enables theoretical examination of the impacts of various combinations of measures and how these may affect outcomes in the short- and long-term. This allows examination of the factors that may affect the future trajectory on an outbreak. A team of researchers from the University of NSW, University of Melbourne and Curtin University was commissioned under the Program to conduct statistical modelling of the Delta outbreak in Sydney. Led by Professor James Wood (UNSW), the team set out to model COVID-19 cases, hospitalisations, ICU admissions and deaths. This information was used to examine the impact of various levels and combinations of public health measures, and to conduct epidemiological analysis of mobility data and other social contact information.

Over the following months, the team updated the baseline model to incorporate the latest data on vaccination, testing, diagnoses and hospitalisations, along with policy changes. Additional funding was provided to Professor Wood's team to examine the impacts of public health measures based on updated epidemiological information and outcomes. Analyses were also undertaken to determine how factors such as socioeconomic status and clustering of low vaccination coverage impacted on epidemic outcomes.

As the pandemic evolved, most public health and social measures were no longer in effect by December 2021. Vaccination rates were high, but the emergence of new COVID-19 variants meant that the focus of modelling changed to understanding the combined effects of vaccination, waning immunity and natural immunity, in the context of these new variants. Further focus areas included modelling the combined impacts of other respiratory viruses during the pandemic. The modelling team also provided independent advice on international trends and the characteristics of emerging variants.

Outcomes

Policy and practice

Statistical modelling directly supported and informed NSW COVID-19 policy and program response efforts. This was accomplished through using COVID-19 case data to model the impact of public health measures and vaccination.

Findings from these projections and scenarios informed government decisions about interventions that could reduce demand on health services. They also informed the implementation of the COVID-19 vaccination program. For example, the UNSW modelling showed the benefits of targeted vaccination at a local government area level during the Delta outbreak of COVID-19 in mid-2021. The spatial concentration of the epidemic indicated that targeted vaccination within the LGAs of concern was likely the most effective additional strategy, and implementation from mid-August led to rapid declines in transmission. This integration of surveillance, short-term projections and scenario analysis using transmission models highlighted the utility of modelling in informing critical public health decisions in real time.

Capability Building

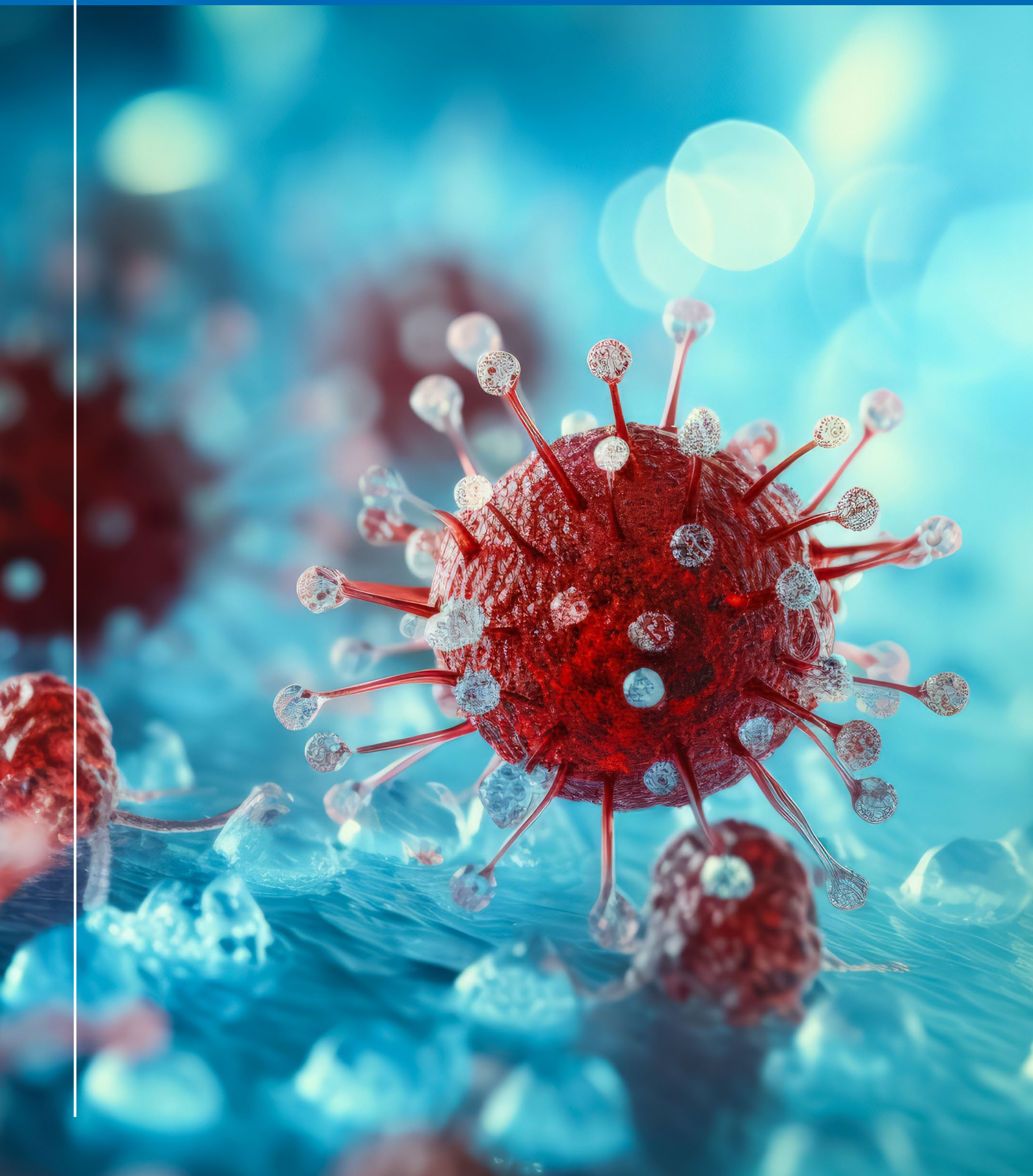
The commissioned statistical modelling by external teams undertaken during the pandemic supplemented internal NSW Health modelling conducted by the System Information and Analytics (SIA) Branch, further enhancing modelling capacity within NSW Health. Enabling researcher access to NSW Health data was critical to facilitating timely and accurate modelling. Having NSW Health teams and researchers collaborate on updating system definitions and generating specific reports to support modelling efforts facilitated efficient incorporation of the latest evidence.

Having expert academic groups involved to provide independent external advice in a challenging environment was particularly valuable as it added another credible voice, independent of government, to provide context and enhance public understanding of the factors influencing public health decision making.

Funding leveraged from this work

Following on from this modelling work, Professor Wood has been awarded an NHMRC Partnership grant in collaboration with NSW Health, Queensland Health and ACT Health. This work aims to further explore approaches to modelling COVID-19, to adapt these to other common respiratory viruses, and to strengthen surveillance systems for respiratory illness.

Vaccine Research Support



Vaccine Research Support

The Vaccine, Infection, and Immunology Collaborative Research Group

In mid-2021, the Vaccine, Infection, and Immunology (VIIM) Collaborative Research Group received approximately $4.7 million to study clinical and immunological responses to COVID-19 vaccines in NSW recipients.

A leading group of NSW experts spearheaded research to inform vaccine policy in the State and beyond. At the time, the population exposure to COVID-19 was still relatively low, allowing NSW to contribute to the global body of knowledge on vaccines and immunity, and to provide timely and robust data to ensure the best outcomes for the people of NSW.

VIIM brings together the leading vaccine, infection and immunology researchers in NSW, incorporating expertise from Western Sydney Local Health District, Sydney Local Health District, Sydney Children's Hospital Network, NSW Health Pathology, the National Centre for Immunisation Research and Surveillance, the University of Sydney's Marie Bashir Institute, the University of NSW, Westmead Institute of Medical Research, the Centenary Institute, and the Kirby Institute, into their research.

With NSW having some of the world's most complete data on virus transmission, scientists can work on answering complex questions about vaccines, across a range of population groups and new variants.

The surveillance and real-world research conducted by the VIIM set out to:

- compare vaccine immunity and natural immunity after COVID-19 to determine how long it lasts, particularly in the elderly
- examine the vaccines' efficacy on variant strains of the virus
- establish an invaluable biobank of specimens which will be crucial to current and future research
- inform vaccine policy that can respond to emerging issues and opportunities
- advise on immunisation schedules, including the potential need for any booster vaccinations for vulnerable groups and the broader community.

The research collaboration has established a prospective cohort of 500 people with live cell binding and neutralisation antibody assays followed up over two years, with a subset of 200 followed with serial cell-mediated immune assays.

Research outputs from VIIM have been provided to the Australian Technical Advisory Group on Immunisation (ATAGI) and accepted for publication in high impact journals. Due to the success and impact of the original funding, in 2022-23, the Office for Health and Medical Research provided an additional $371,000 for VIIM. These new funds will support VIIM to measure antibody and cell-mediated responses to the Moderna bivalent vaccine versus the original vaccine and compare how effective each vaccine is as the fourth booster in protecting against new Omicron variants within the NSW population. This research will add to global efforts in understanding tailored bivalent vaccines.

VIIM investigators were also successful in leveraging further funding from two Medical Research Future Fund (MRFF) grants in 2022, which would not have been possible without the NSW Health investment:

1. COVALIA (COVid vaccine trial for austrALIA): A phase I, double-blind, dose-ranging, randomised, placebo-controlled trial to study the safety and immunogenicity of a DNA-based vaccine against COVID-19 (COVIGEN) in healthy participants aged 18 to 75 years old: $177,780 for VIIM
2. BOOST-IC (Bringing Optimised COVID-19 vaccine Schedules To Immuno-Compromised populations): $204,936 for VIIM.

RNA Production and Research Network

The NSW RNA Production and Research Network (NSW-RPRN) was established in mid-2021 to help scientists translate newly developed RNA therapeutics into advanced pre-clinical studies by enabling access to the required materials, services, and support. The Network has received $4.9 million in funding over three years. It aims to translate newly developed RNA therapeutics from the laboratory to advanced pre-clinical studies. In alignment with a key priority of the NSW Government, the NSW-RPRN also aims to enhance the strength and size of the expert workforce required for advanced biomanufacturing.

The Network consists of major universities and research institutes in NSW and the ACT, including the University of Technology Sydney, Macquarie University, University of Sydney, Australian National University, Children's Medical Research Institute, Kirby Institute, University of New South Wales, Woolcock Institute of Medical Research, Westmead Institute of Medical Research, Children's Cancer Institute, and Royal Prince Alfred Hospital.

The NSW-RPRN consists of three pillars: 1) Production; 2) Pilot Research; and 3) Services and Support.

1. The Production Pillar aims to produce high-quality short RNA, mRNA, and lipid nanoparticles. This is predominantly for pre-clinical evaluation using interlinked pilot production units for mRNA, nucleotide & lipid precursors, synthetic RNAs and lipid nanoparticles, for pre-clinical evaluation.

   This pillar has resulted in the production of high-quality functional mRNA, antiviral siRNA and siRNA-loaded nanoparticles with proven in vitro efficacy, as well as high-quality capping nucleotides (pure raw material for mRNA) and lipids suitable for production of lipid nanoparticles.
2. The Pilot Research Pillar consists of three research projects that enhance existing research excellence within the NSW-RPRN to expedite research towards clinical translation:

   - siRNA loaded lipid nanoparticles to treat SARS-CoV-2
   - mRNA/siRNA nanoparticle delivery systems for the respiratory tract
   - Hybrid mRNA-viral vector delivery to treat genetic disease.

   This pillar has resulted in a high purity antiviral siRNA at > 10 mg scale and the first formulation of m/siRNA loaded nanoparticle. It has also furthered the knowledge available on the value of nanoparticles as carriers for the delivery of siRNAs in the specific therapy of severe respiratory infections like COVID-19, and the potential for nasal dry powders to deliver stable bioactive compounds.
3. The Services and Support Pillar aims to provide scientists with access to a network of world-class service facilities in genomics, proteomics, high-throughput screening, COVID-19 PC3 laboratory and animal testing, and training facilities for both Good Laboratory Practice (GLP) and /GMP manufacturing. Under this pillar, the RPRN has established a Management Board and finalised membership for an External Advisory Board comprised of six institutions as well as an external advisory board comprised of five institutions.

The NSW-RPRN is implementing collaborative projects on RNA-based COVID-19 treatments (antivirals) and RNA lung delivery to treat infections and lung cancer.

In its second year, the NSW-RPRN focused on completing production milestones to facilitate in vitro and in vivo pre-clinical studies. It is expected that these milestones, along with milestones related to analytical services and collaboration across the broader network, will rapidly escalate given that production facilities are now close to fully operational.

In 2022, the NSW Government announced $119 million in funding for a 10-year RNA Research and Development program. The well-established NSW-RPRN will allow the Network to take a leading role in the implementation of this 10-year program.

RPRN investigators were also successful in leveraging further funding from a MRFF COVID-19 grant in 2022, which would not have been possible without the NSW Health investment: *Development of antiviral RNA therapeutics targeting SARS-CoV-2 infection*, to the value of $998,339.

The Inaugural NSW RNA Production and Research Network Annual Symposium was held in March 2023. This symposium brought together RPRN investigators with other key researchers and industry representatives across the sector to increase knowledge-sharing and build collaborations, driving local development and production of innovative RNA-based vaccines and therapeutics.

Additional vaccine support activities

NSW Health undertook two additional programs aimed at supporting vaccine generation and implementation across the State.

The Vaccine Acceleration Program

In April 2023, NSW Health initiated the Vaccine Acceleration Program (VAP) to support NSW-based COVID-19 vaccine research groups who were ready to conduct late-stage preclinical or early phase clinical studies. The VAP aims to rapidly accelerate the development and commercialisation of a next generation COVID-19 vaccine.

The VAP invited applications for a merit-based, competitive process. Applications were assessed by an expert review panel according to published selection criteria. Selection was based on the quality and experience of the research team, the significance and feasibility of the proposed research, and the impact of the project on vaccine production.

Two projects were awarded funding:

- *Nasal delivered COVID vaccine to block transmission of SARS-CoV-2* by the Centenary Institute ($995,867)
- *Development of a 'Universal' mRNA COVID-19 Vaccine resistant to variants* by the Garvan Institute of Medical Research ($1,000,000).

At the time of this report, these projects are in the establishment phase. As yet, there are no significant outcomes to report.

Waratah Vaccine Trial Alliance

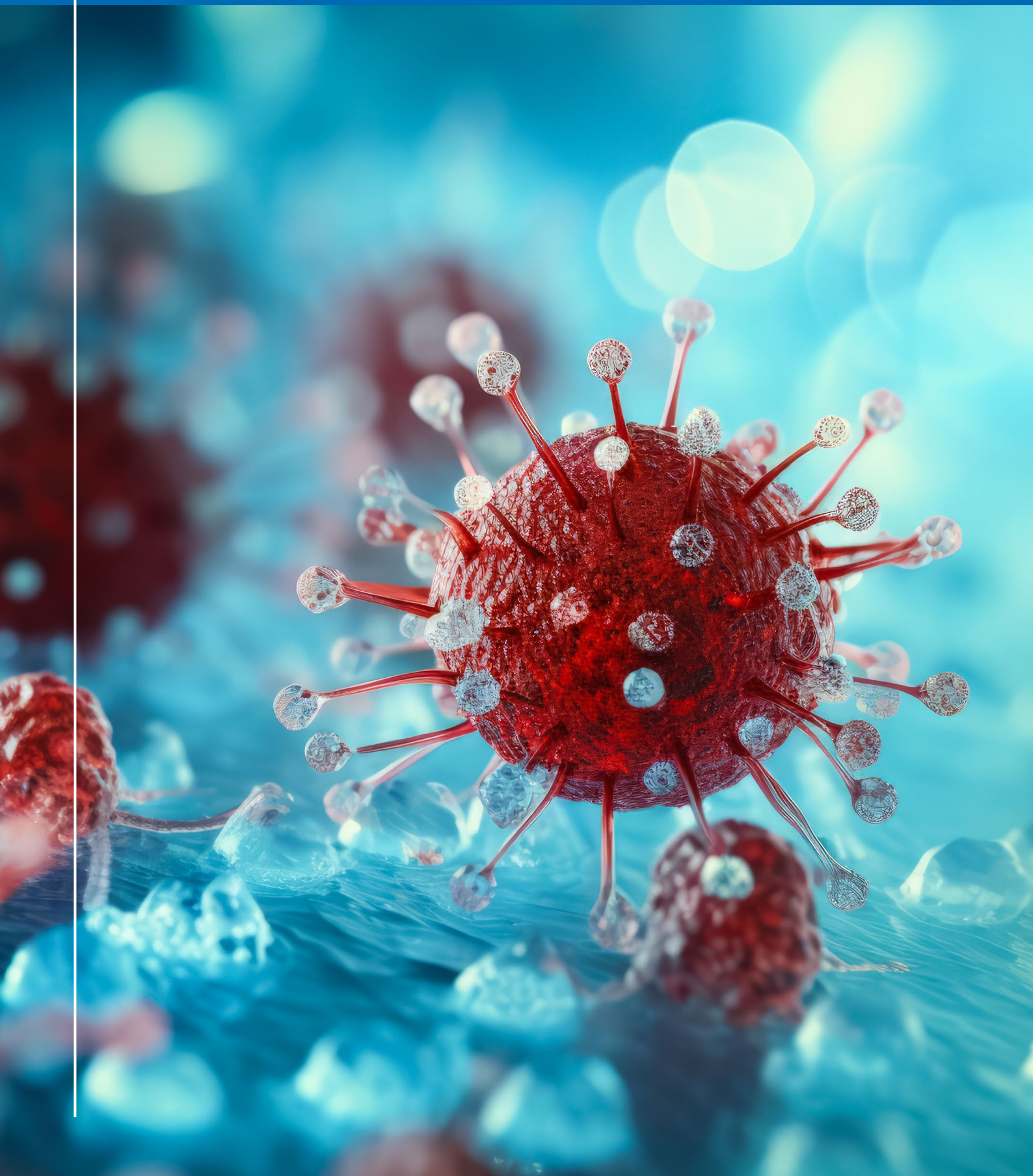
The Waratah Vaccine Trial Alliance was established to attract more vaccine-related clinical trials to NSW and to increase the capability to conduct these rapidly and efficiently. The Alliance, renamed as the 'Waratah Vaccine Trial Network' is a collaboration of clinical vaccine trial researchers, healthcare leaders, consumers, and other key stakeholders for the facilitation and coordination of vaccine research in NSW and across Australia. Approximately $500,000 in funding was provided by NSW Health to support the Network establishment in May 2021.

Waratah Vaccine Trial Network mission is to:

- establish NSW as a premier site in Australia for vaccine trial research
- increase access to clinical vaccine trials for the population of NSW
- provide an efficient, high performing clinical trial network as a platform by which to conduct both industry-sponsored and investigator-initiated vaccine trials
- provide education, training and mentorship of the next generation of vaccine researchers
- engage with consumers to optimise the design conduct and potential benefits of vaccine trials
- facilitate the translation of the results of vaccine trials into policies and programs for our population.

Current trials underway through the Network include *Optimising Q-fever vaccination in Australia: Protecting our rural adolescents* and *Vaccine development for Japanese Encephalitis*.

Clinical Trials



Adaptive Platform Trials Network

The pandemic highlighted that traditional fixed designs for conducting clinical trials do not deliver the level of evidence needed for decision making in such short timeframes. Furthermore, they lack the flexibility necessary to adapt to rapidly changing circumstances and the urgency to respond during a pandemic. An increasingly utilised alternative design is adaptive platform trials, which allow multiple treatments to be evaluated simultaneously with diverse groups of patients. By incorporating pre-specified adaptation mechanisms into the trial design, protocols can be altered as new information becomes available, enabling clinicians to optimise management decisions. The aim of this workstream was to develop a network of adaptive platform trials to enhance NSW's capacity and capability for conducting adaptive clinical trials for the treatment of COVID-19. In total, $3,096,669 in funding has been spent on the Adaptive Platform Trials.

REMAP-CAP

Professor Steve Webb, Monash University

REMAP-CAP is a Randomised, Embedded, Multi-factorial, Adaptive Platform trial for Community-Acquired Pneumonia (CAP). This well-established, Australian-led, international platform evaluates treatments to optimise ICU care for patients with CAP or acute respiratory illness due to COVID-19. The platform allows multiple, time-critical questions about the effectiveness of various treatments for critically ill COVID-19 patients to be answered. Consequently, patients can receive the most promising treatments within a given treatment domain.

The NSW Government contributed $1,380,000 in funding to the REMAP-CAP program. This funding enabled 20 NSW ICUs, including those in regional and remote areas, to contribute to the generation of evidence on the best treatment protocols for patients with severe COVID-19, and provided access to emerging and experimental therapeutics.

The platform allows for multiple treatments across a range of domains of therapeutic care to be evaluated simultaneously. The pandemic ICU domains of REMAP-CAP included antibiotic, macrolide duration, corticosteroid, influenza antiviral, ventilation, statin therapy, anticoagulation and vitamin C.

As of June 2023, some domains of investigation had closed, with the following results:

- COVID-19 Antiviral Domain: among critically ill patients with COVID-19, lopinavir-ritonavir, hydroxychloroquine, or combination therapy worsened outcomes compared to no antiviral therapy. Median organ support-free days among patients in lopinavir-ritonavir, hydroxychloroquine, and combination therapy groups was 4 (-1 to 15), 0 (-1 to 9) and -1 (-1 to 7), respectively, compared to 6 (-1 to 16) in the control group.
- COVID-19 Immune Modulation Domain: treatment with the interleukin-6 receptor antagonists tocilizumab and sarilumab improved outcomes: median number of organ support-free days was 10 (interquartile range, -1 to 16) in the tocilizumab group, 11 (interquartile range, 0 to 16) in the sarilumab group, and 0 (interquartile range, -1 to 15) in the control group.
- COVID-19 Immunoglobulin Domain: posterior probability of futility of 99.4% for the primary outcome of organ support-free days up to day 21.
- COVID-19 Anticoagulation Domain: divergent treatment effect across disease states. In the critically ill population, the trial hit a pre-specified trigger for futility. In non-critically ill patients, therapeutic dose heparin reached the pre-specified statistical threshold for superiority compared with standard of care thromboprophylaxis – posterior probability 98.6% (adjusted odds ratio, 1.27; 95% credible interval, 1.03 to 1.58).
- COVID-19 Antiplatelet Domain: 95.7% posterior probability of futility regarding the odds of improvement in organ support-free days within 21 days.

Importantly the study also demonstrated the ineffectiveness of several treatment options that were consequently removed.

The Australian Clinical Trials Alliance recognised the contribution that REMAP-CAP made to the evidence base of effective COVID-19 treatments by awarding it the Trial of the Year in 2022.

Australasian COVID-19 Trial (ASCOT-ADAPT)

Professor Josh Davis, Hunter Medical Research Institute

The Australasian COVID-19 Trial (ASCOT) ADAptive Platform Trial (ADAPT) is an international, adaptive platform, randomised, controlled trial that evaluates treatments to optimise non-critically ill patients hospitalised with COVID-19. The NSW Government contributed $617,232 in funding to this program.

The study aims to assess clinical, virological and immunological outcomes in patients with COVID-19. The overarching objective is to identify the combination of interventions associated with the highest chance of survival, free of advanced respiratory support or vasopressor/inotropic support at 28 days after randomisation. Only adults hospitalised with COVID-19 but not requiring ICI-level care are included in the research. Treatments investigated include anti-viral therapies (to limit the virus replication) and anticoagulation therapies (to minimise blood clot risk associated with COVID-19).

Critical design features of ASCOT–ADAPT that will contribute to enhanced trial efficiency and rapid implementation of findings include:

- Highly pragmatic and embedded within routine care
- A universal master protocol with several domains. By addressing multiple questions in parallel and evaluating interactions between interventions, the platform will reduce the time, cost and sample size required to reach definitive conclusions on optimal therapy
- Frequent interim analyses are used so that questions are concluded as soon as there is robust statistical confidence instead of when a pre-specified sample size has been recruited. This allows the platform to match the size of the observed treatment effect, including no effect, to conclude superiority and/or non-inferiority as soon as accrued data can support this
- Response adaptive randomisation (RAR). Although treatments will be allocated randomly, patients will preferentially be allocated to treatments that are likely to be the most effective treatments based on statistical models derived from the trial data.

The demographics of patients being admitted to hospital with COVID-19 changed as the pandemic evolved. The adaptive study design of ASCOT-ADAPT allowed for modifications as the patient cohort changed at the different timepoints of the pandemic. This means the study continued to identify effective treatments for patients and remained relevant to the current COVID-19 setting in NSW and Australia.

In September 2022, ASCOT-ADAPT and REMAP-CAP were awarded $3,997,914 from the Australian Government through the MRFF in a joint proposal to combine platforms. Within this joint framework, ASCOT will be able to contribute to global datasets and provide leadership on answering key therapeutic questions for non-critically ill patients. Joining the established infrastructure of both trials to create a Federated Trial will target both moderate and critically ill patients and continue to collect evidence on effective treatments for COVID-19.

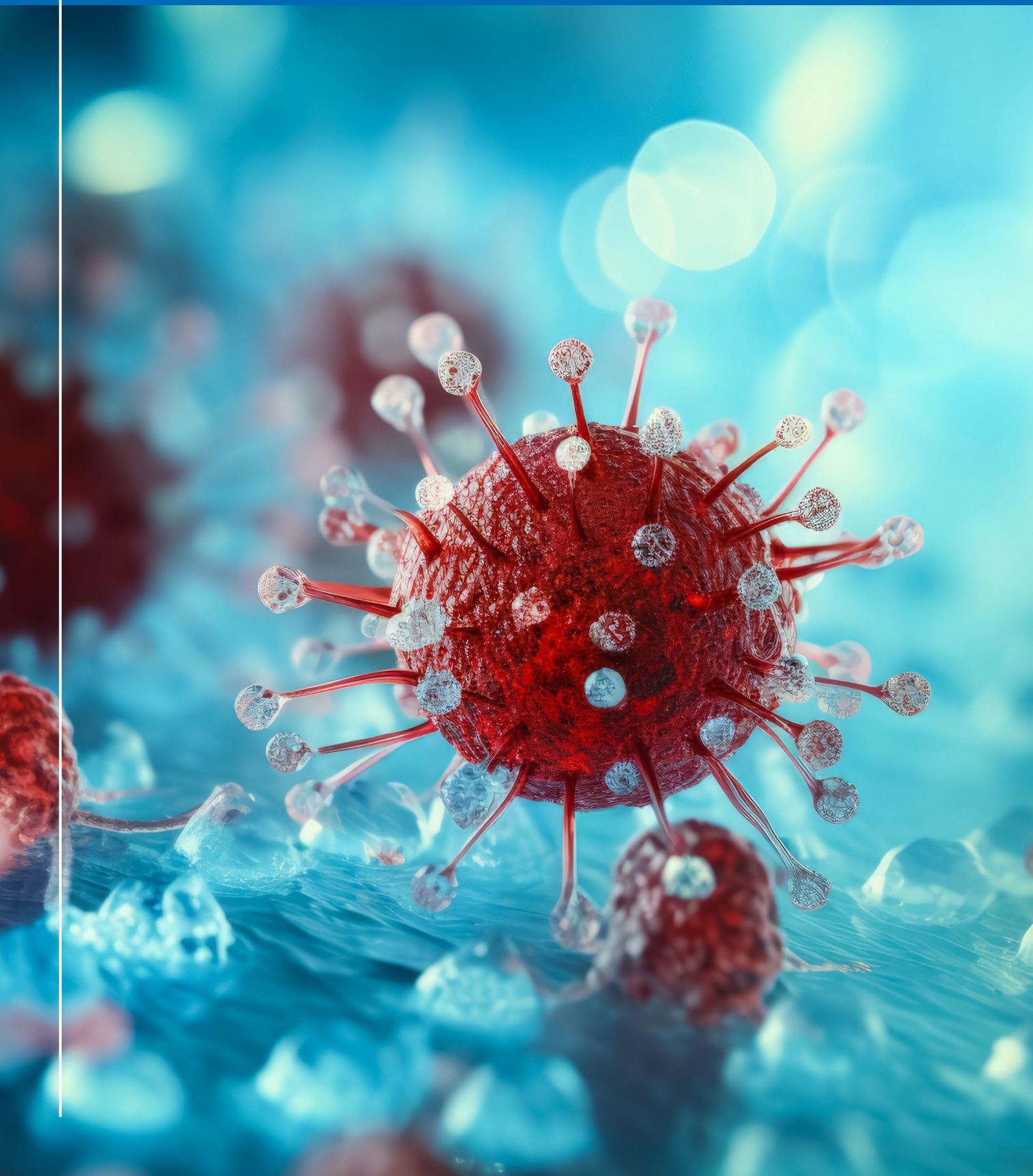
BEAT COVID-19

Professor Guy Marks, NHMRC Clinical Trials Centre, University of Sydney

The BEAT COVID-19 study is a NSW-led, investigator-initiated, randomised clinical trial. It aims to evaluate multiple interventions for the treatment of COVID-19 in high-risk older people who have not been admitted to hospital and are living either in the community or in aged care facilities. The Bayesian adaptive platform trial design will allow testing of multiple treatments for COVID-19, with new treatments allowed to enter and unsuccessful treatments able to leave the platform over time. The first platform domain used Ciclesonide 320mcg (an inhaled corticosteroid) for 14 days. Other potential therapeutic candidates for domains were to be selected using an evidence elicitation framework judged the Beat COVID-19 Candidate Intervention Expert Committee and included interferons, colchicine and other treatments.

As the study focuses on community-based recruitment, it complements the ASCOT-ADAPT and REMAP-CAP, which focus on hospital and ICU settings. Harmonisation of interventions and outcomes, as well as planned sharing of data with the UK PRINCIPLE study meant that smaller patient numbers were needed to detect effect changes. Through the life of the project, multiple strategies for recruitment were used, to ensure that all patients with COVID-19 in NSW had access to the BEAT-COVID trial interventions. The NSW Government provided $1,009,437 in funding to the BEAT-COVID program.

Industry Schemes



The Medical Devices Fund (MDF) supports development and commercialisation of competitive technology in the medical device industry. The MDF also seeks to bring local innovation to market and improve the uptake of cost-effective technology by the health system, boosting economic growth and improving patient outcomes.

Due to the threat COVID-19 presented to small or start-up businesses such as those funded through the MDF, the NSW Medical Devices Fund COVID-19 Relief Package was established.

Four MDF firms left vulnerable from the pandemic received assistance through the COVID-19 Relief Package to ensure viability to support the COVID-19 recovery period ($2.01M). These four firms provide the following technological solutions to care and treatment in NSW:

- Kico Knee Innovations provide a customised total knee replacement technology platform. The platform has software and hardware components that provide orthopaedic surgeons and patients with dynamic, functional and patient-specific solutions. It is primarily aimed at the Australian and US markets
- Tetratherix have developed a novel regenerative biomaterial technology, which can be tuned and adapted for multiple applications in the regeneration of soft tissue & bone as well as the delivery of biologic agents. This water-based polymer solution forms an adhesive hydrogel once administered to the body. The product is fully synthetic, biocompatible and resorbable
- Perx Health is a digital care management company providing condition management and behaviour change services to healthcare providers and health insurers. With these solutions, participants have been shown to engage more regularly and stay motivated as they undergo treatment journeys critical to their health outcomes
- Beyond700 produce a camera system that allows visualisation of the tear film covering the eye, allowing greater precision for diagnostic of conditions that impact on vision and eye comfort.

This funding and other support packages provided by the NSW Government contributed to no MDF recipients permanently closing due to the COVID-19 pandemic.

Triage and referral service

During the COVID-19 pandemic, the Industry Schemes workstream fulfilled a critical triage and referral role between key industry stakeholders with COVID-19 related requests or proposals and relevant policy teams within NSW Health. From January to October 2020, the team processed:

- 47 procurement related requests
- 59 research and development related requests
- 33 other requests.

This included triage and referral of services of a ventilator manufacturer which later became an integral aspect of the NSW Health COVID-19 response. Due to its success, this triage and referral service has developed into a formalised and more general *Health and Medical Research Concierge* accepting requests from organisations globally and providing advice or referrals as appropriate.

The *Health and Medical Research Concierge*, which was redeployed to support triage of COVID-19 related queries during the pandemic, continues to operate as a one-stop-shop for industry, investors, researchers, and governments wanting to learn about or be connected within the NSW health and medical research ecosystem. The International Partnerships team manages the Concierge service and now receive between 10-20 queries per month.

The Concierge supports access to and navigation of the NSW Health system by:

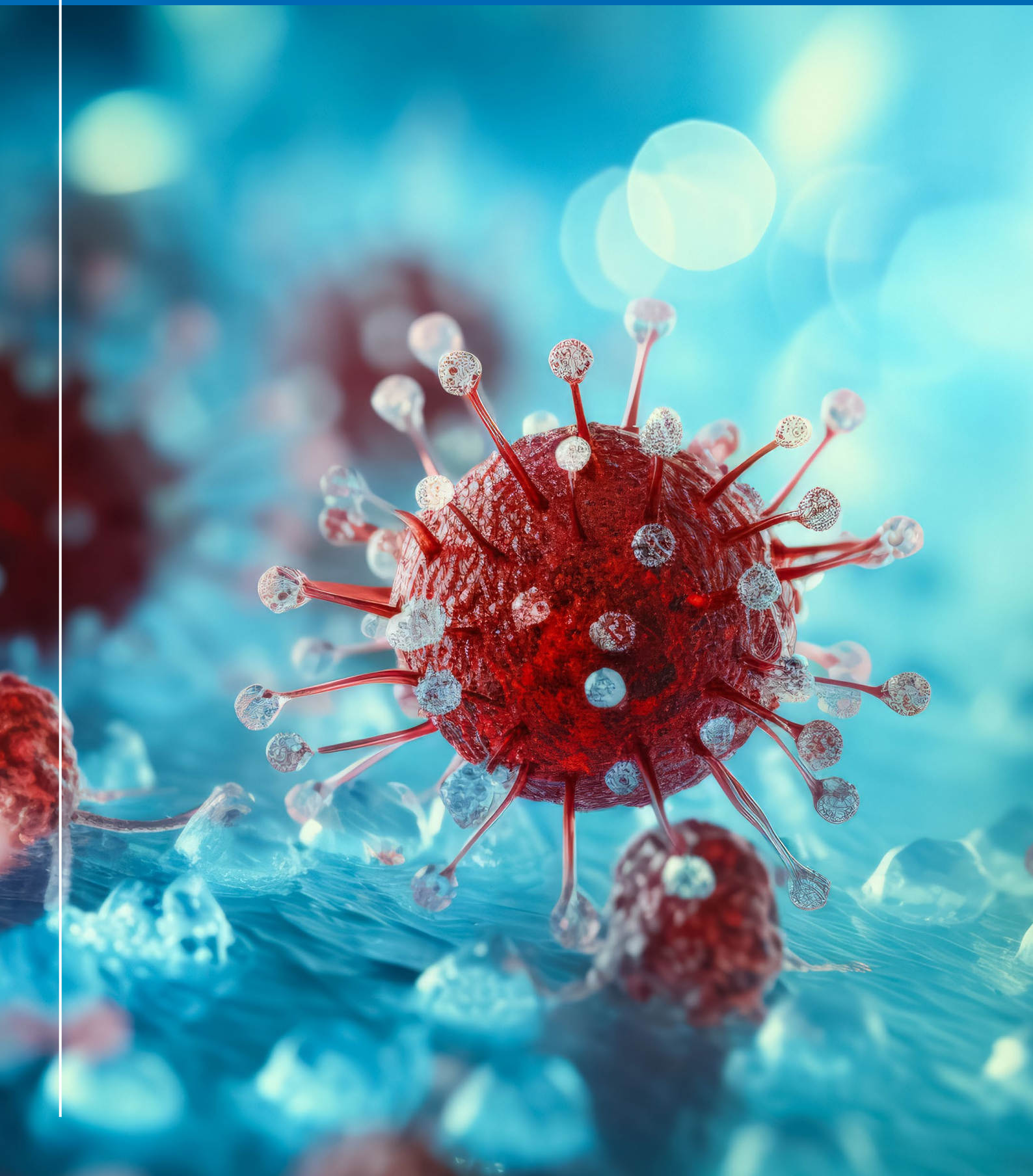
- connecting with experts and resources from within NSW Health
- supporting knowledge sharing
- facilitating research partnerships and collaboration
- helping find and access existing research related services provided by NSW Health
- understanding the health and research environment in NSW
- identifying barriers to information sharing and collaboration.

The Concierge Service demonstrated effectiveness during the pandemic by assisting industry partners to continue development of therapeutic goods in NSW while many Australian jurisdictions stopped doing so. For example, the Concierge Service worked with Allay Therapeutics, a leading San Francisco biotechnology company, to establish clinical trials in NSW during the pandemic. This allowed for development and testing of slow-release pain relief following total knee replacement.

When Allay Therapeutics was unable to visit Australia to oversee the clinical trials during the COVID-19 pandemic, NSW Health facilitated an introduction to local clinical partners, enabling remote oversight and coordination of the trial. NSW Health also worked with trial site, the Prince of Wales Hospital, to minimise the impact of the pause in elective surgery and longer waitlists during the pandemic.

As a result of NSW Health's support, the trial was completed successfully and on time, allowing Allay Therapeutics to progress to a phase 2b trial.

Grant Program Enablers



Grant Program Enablers

The expansion of research grants, clinical trials, research networks and critical infrastructure required supported from the Ministry of Health to strengthen and streamline the NSW research landscape and processes.

The rapid pace of the allocation of research funding through both existing research partnerships and competitive funding streams was one of the key strengths in the NSW approach to the pandemic (PPHD, 2023). Another key element was the integration of government decision makers into processes that identified and approved research priorities, and in the shortlisting of research funding to ensure that research funded met policy and practice needs.

Expediting Statewide Administrative Processes

It was necessary to make changes to the ethics and governance approvals process to facilitate rapid research during the pandemic. The Office for Health and Medical Research's Research Ethics and Governance Unit conducted continuous monitoring to better manage the timely processing of research defined as related to COVID-19 and not related to COVID-19. This monitoring included both ethics applications and applications for Site Specific Assessments (SSAs). Despite the unprecedented influx of applications requiring approval, local heath districts were able to prioritise COVID-19 ethics applications and process them within significantly shorter timeframes. Information presented in the Interim Report shows the mean time to approval for ethics for COVID-related research was 16 days and 7 days for Site Specific Assessments. This was less than half the mean time recorded before than pandemic (32 and 17 days respectively). Since the interim report, this has continued to improve for ethics approvals down to 12 days for COVID-related research and eight days for site approvals.

These efficiencies were achieved through increased capacity across ethics and governance committees, targeted support from the Office for Health and Medical Research, and the change from physical committees to virtual ones. For example, adoption of online meetings was required as face-to-face meetings were not permitted during the pandemic. However, this allowed Human Research Ethics Committees (HRECs) to meet more frequently, speeding up the process. Additionally, most HRECs moved to use of digital signatures, reducing approvals from weeks to a single day.

In terms of developing capacity, the Office for Health and Medical Research worked individually with five sites during September and October 2020 to resolve outstanding governance issues. This support enabled all five research offices to improve their performance in reducing average review times. Because of this strong performance, no applications needed to be re-allocated during 2020. Many of these efficiencies are now business as usual for HRECs across NSW.

Research Translation

An unprecedented challenge facing researchers funded by this Program was how to rapidly make research findings available and accessible to those responsible for acting on them as part of the COVID-19 NSW Health response. In addition to disseminating findings utilising traditional academic channels such as peer-reviewed journal articles and conference presentations, both formal and informal communication channels were established organically as required to facilitate the flow of information.

Leveraging the partnerships and connections fostered prior to the pandemic enabled rapid translation of research evidence in NSW during the pandemic. The close collaboration between highly skilled researchers and policy makers enabled decisions to be informed by locally generated evidence across a broad range of operational areas including transmission in schools, vaccine effectiveness, health workers, wastewater surveillance, COVID-19 outcomes and COVID-19 seroprevalence.

Another key enabler of effective translation was embedding academic partners into the public health response. Working directly alongside policy decision makers and frontline workers within NSW Health, research personnel were key to building the epidemiological capacity of the public health response.

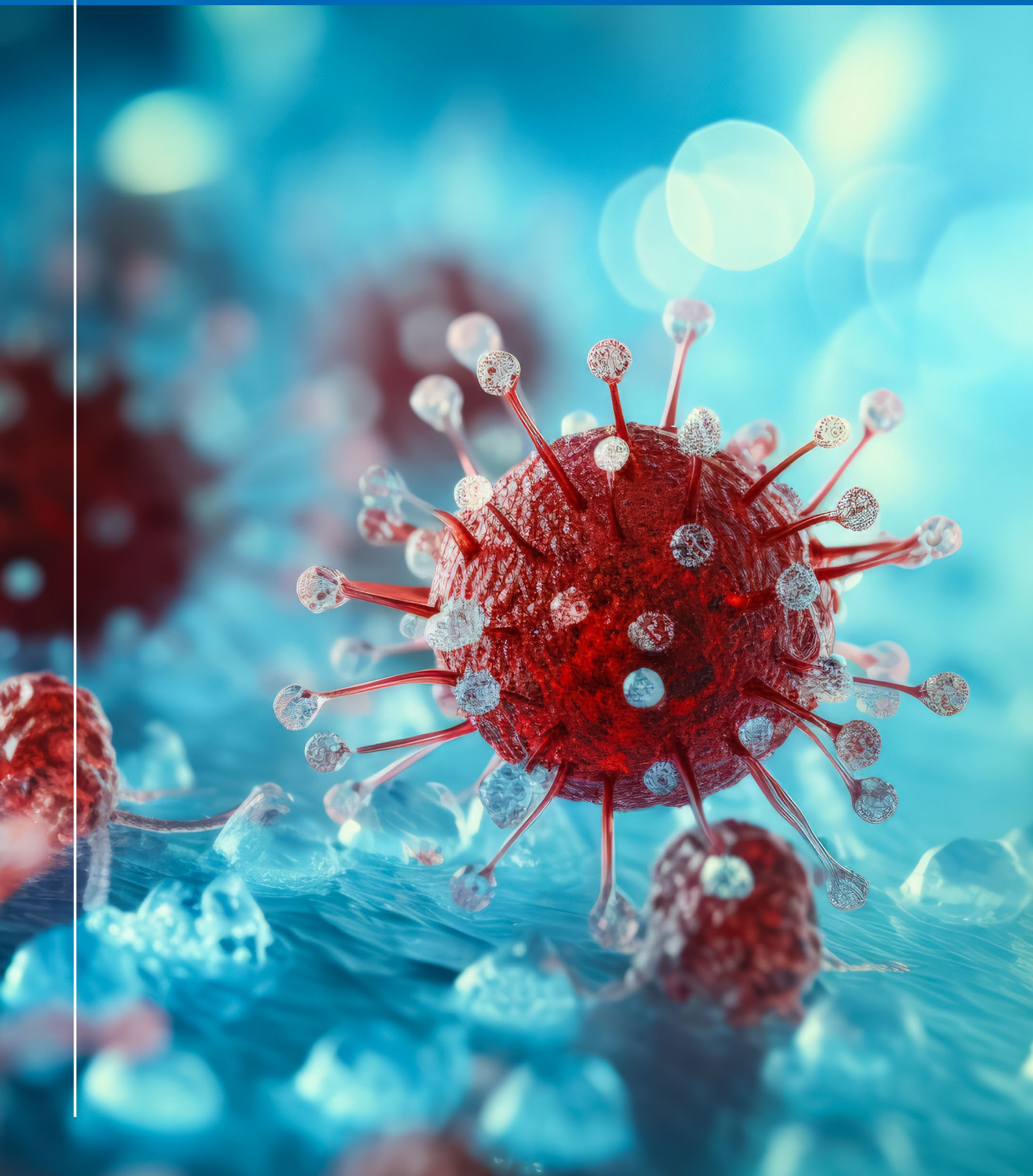
The translation of COVID-19 research into NSW pandemic response decision making was a success by international standards. Hanney et al (2022) collated evidence on research generation and use in pandemic responses in seven countries: Australia, Brazil, Canada, Germany, New Zealand, the United Kingdom and the United States. The study notes significant achievements in research generation and translation in NSW during the pandemic that were built on long-term investment in applied research, research strategy and research-practice partnerships.

Preventive Research Support Program

The Prevention Research Support Program (PRSP) provides funding to NSW research organisations conducting prevention and early intervention research that aligns with NSW Health priorities. PRSP funding supports research infrastructure and strategies to build research capability and translate evidence from research into policy and practice.

In October 2020, the Ministry extended the funding period for the PRSP by 12 months to allow researchers to better contribute to the pandemic research response. For example, the research team at the Centre for Infectious Disease and Microbiology – Public Health (Case Study 1) utilised both PRSP funding and COVID-19 Research Grant funding to redeploy their research program to work on COVID-19. This allowed them to focus on and contribute to preparedness and response, including enhanced genomic tracking of COVID-19 importations and transmissions in NSW. The Kirby Institute similarly pivoted from their PRSP research and engaged in a range of research activities critical to the response, including serosurveillance for SARS-CoV-2 infection, the COVID-19 NSW Outcomes Study, and various modelling and surveillance projects (PPHD, 2023).

Themes
Program-level Impacts



Themes

By evaluating both the principles and processes used in the design and implementation of the NSW Heath COVID-19 Research Program, as well as the resulting outcomes and impacts, four major themes were identified that highlight the key learnings and achievements of the Program:

1. Capitalising on existing research infrastructure
2. Collaboration between researchers and decision makers
3. Enabling new partnerships through targeted and leveraged funding
4. Facilitating future preparedness.

Theme 1: Capitalising on existing research infrastructure supported by NSW Health

An essential element in the rapid development and implementation of the Program was the ability to capitalise on existing relationships between NSW Health and the broader research community in NSW. NSW Health has contributed significantly to research infrastructure and expertise through substantial grant programs provided to NSW researchers. These funds supported the development of academic and medical researchers that were required during the COVID-19 pandemic.

Examples of these grant programs include the Translational Research Grants Scheme, which aims to accelerate evidence translation in the NSW health system, and the Prevention Research Support Program, which provides research infrastructure support. Professor Sintchenko and his team at the Centre for Infectious Disease and Microbiology – Public Health received funding under both these schemes. These funds supported and enabled their work on whole genome sequencing and facilitated a rapid translation of their work to contribute to the NSW Health response.

Another example was the existing 45 and Up Study partnership between the Sax Institute and the NSW Ministry of Health. The 45 and Up Study is Australia's largest ongoing study of ageing, which has been running in NSW for the past 15 years with over 250,000 participants. Due to this close collaboration, there was a shared understanding of the potential for this study to pivot and rapidly collect information from a priority population to support decision makers. Consultations were facilitated between key policy and clinical stakeholders in NSW Health to identify relevant questions and a new research model that leveraged the existing survey platform and participant database. This approach allowed the study to pivot to online surveys and expedite data collection and analysis processes. This model enabled researchers and policy makers to work together to identify and address the challenges that emerged through the pandemic period.

Theme 2: Collaboration between researchers and decision makers

A related theme is the close collaboration forged between NSW Health and the research community to jointly address the challenges of the pandemic. This relationship was demonstrated in several ways. At the outset of the Program, it was anticipated that official pathways would need to be developed to enable the rapid translation of research findings into policy and practice. Templates were developed to facilitate the synthesis of key results for relevant NSW Health policy teams and the NSW Government as evidence for decision making. These tools had limited use and, due to the urgency of the situation, much more direct lines of communication were established that supported regular and on-demand contact between decision makers and researchers.

The *Emergency Response Priority Research* workstream used a targeted approach that allowed NSW Health to rapidly commission specific expertise, drawing on the extensive knowledge and capabilities of researchers to address the gaps in knowledge and understanding faced by those leading the public health response.

Several projects had researchers embedded in roles within NSW Health. This allowed researchers access to assist with answering questions to support the response. Further, it facilitated direct sharing of outcomes and close collaboration with relevant stakeholders within NSW Health. Clinical research was facilitated by ensuring that academic groups and clinical experts could regularly connect to modify existing infrastructure and expertise for optimal outcomes. For example, the partnership between the National Centre for Immunisation Research and Surveillance (NCIRS) and NSW Health to assess vaccine effectiveness used linked surveillance data to conduct the study much more quickly than a traditional collaboration between NSW Health and academics could have.

NSW Health worked closely with independent, external academic groups to build the evidence-base to guide important policy decisions. Academic partners helped to inform the NSW population about the context, risks, impacts and emerging local evidence, providing critical context and scientific credibility for public messages.

Theme 3: Enabling new partnerships through targeted and leveraged funding

The pandemic highlighted the need for established and skilled health researchers. In response to the increased demand for medical and clinical research, greater funding was made available to ensure research could support local and national decision making. Many of the NSW research teams have benefited from this increased funding, including being able to conduct research more quickly or at greater scale than would have otherwise been possible. Groups entered partnerships with diverse organisations to speed the translation of research into action.

An example of this is the partnership between NSW Health Pathology and the Westmead Institute for Medical Research to develop a rapid, sensitive and specific antibody test to diagnose COVID-19, allowing cases to be traced in the community and vaccine effectiveness to be assessed. Ensuring broad eligibility criteria for Program funding enabled this diagnostic service, not typically engaged in research, to apply for and be awarded funding under this scheme. This partnership led to better diagnosis of infection, assessment of vaccine effectiveness and understanding of implications for immune-suppressed patient groups.

Another example was the increased need for modelling data to explore the impacts of various public health measures, including vaccination. The funding provided by NSW Health to Professor Wood at UNSW facilitated a successful NHMRC Partnership grant in collaboration with NSW Health, Queensland Health and ACT Health. This work will further develop the modelling approaches to COVID-19 and adapt these to other respiratory viruses, strengthening current and future surveillance capacity.

The research projects funded under the Program enabled researchers to form new local, national, and international partnerships. Many of the research groups funded by the Program were able to use their findings to support applications for additional grant funding from NSW and national bodies. As of June 2023, these leveraged funds amounted to more than $17 million, including $6.8 million leveraged for *REMAP-CAP* from an initial investment by NSW of $1.4 million, and $5.1 million for *Enhanced genomic tracking of COVID-19 importations and transmissions in NSW*.

Theme 4: Facilitating future preparedness

As well as addressing the immediate needs that arose during the COVID-19 pandemic, the Program has significantly strengthened NSW's preparedness for future infectious disease outbreaks and other public health emergencies. The networks and infrastructure developed during the pandemic will continue to support ongoing and new research into many areas of health. Support provided for commercialisation of many innovations provides a healthy and diverse industry to support government and academic leaders.

Specific examples include the advances in diagnostic capabilities enabled by this Program, such as the increased sensitivity of whole genome sequencing, the development of a template for rapid deployment of new LC-MS assays, and insights from research into the experiences of the community during a pandemic. All these should contribute to better capacity to respond to future pandemics and to develop strategies to better support healthcare workers and the community.

Research into supporting regional and remote hospitals and ICUs, specifically considering the challenges around workforce capacity and services access, has resulted in new models of care, such as 24/7 eICU and the Virtual Rural Generalist Service. Both models of care are aligned with NSW Health's strategy for value-based healthcare and, importantly, can now be rapidly deployed at scale when the need arises.

Beyond the outcomes of the individually funded projects, the lessons from how the health system engaged in close collaboration with the research community should provide future benefits. These processes fostered collaboration and partnership, and rapid translation of evidence into policy, implementation of public health measures, and clinical care. Many of these experiences have informed the development of a more streamlined and effective health research environment across NSW.

References

Campbell D, Edwards B, Milat A et al 2021, 'NSW Health COVID-19 Emergency Response Priority Research program: a case study of rapid translation of research into health decision making', *Public Health Res Pract*, vol. 31, no. 4. https://doi.org/10.17061/phrp3142124

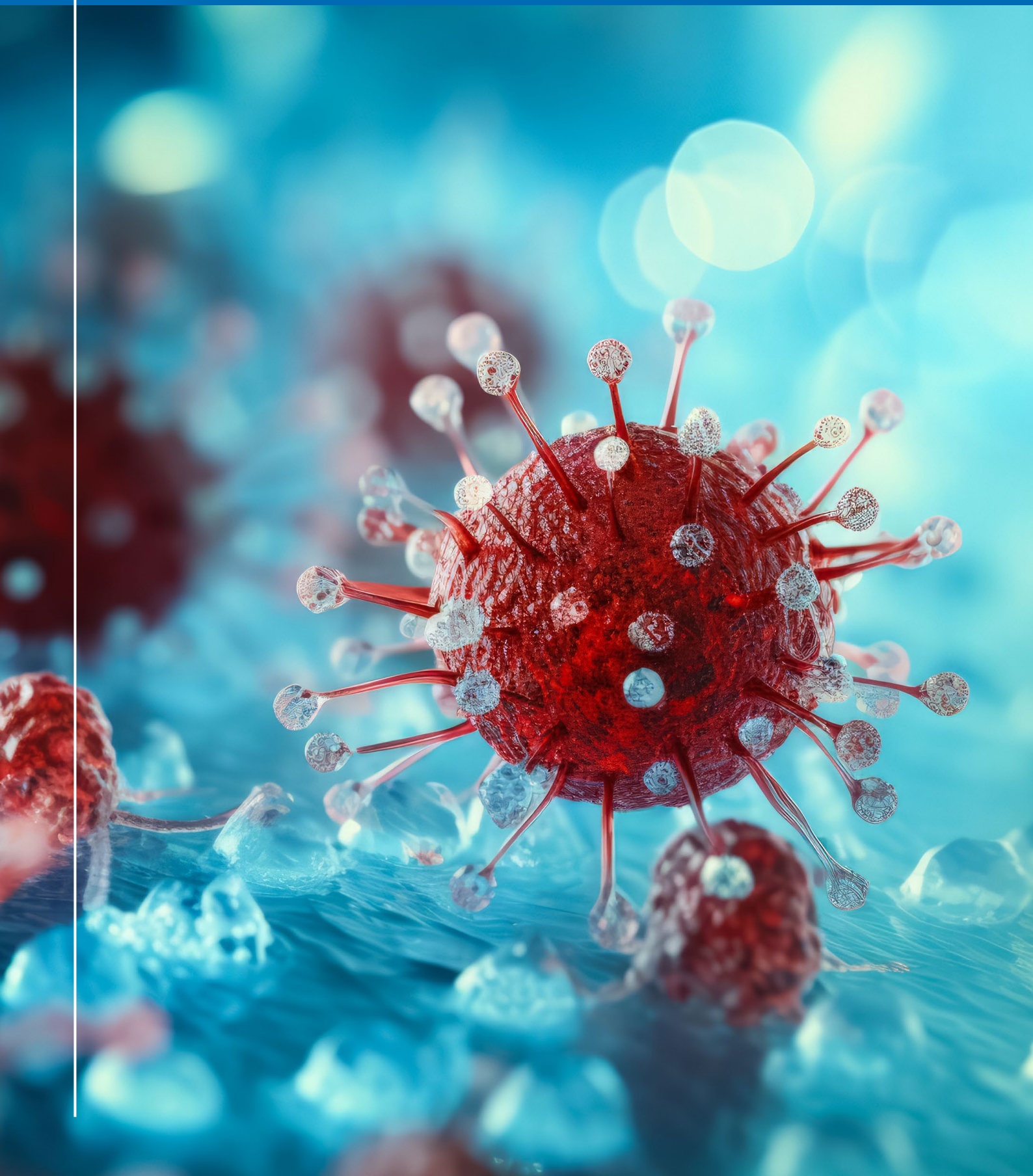
Centre for Epidemiology and Evidence, 2021, NSW Health COVID-19 Research Program Impact Evaluation Report 2021, NSW Ministry of Health, Sydney. https://www.health.nsw.gov.au/research/Pages/covid-impact-evaluation-interim.aspx

Critical Intelligence Unit, 2022, COVID-19 Critical Intelligence Unit website, Agency for Clinical Innovation, NSW Health. https://aci.health.nsw.gov.au/covid-19/critical-intelligence-unit

Hanney SR, Straus SE, Holmes BJ 2022, 'Saving millions of lives but some resources squandered: emerging lessons from health research system pandemic achievements and challenges', *Health Res Policy Syst*, vol. 20, no. 99. https://doi.org/10.1186/s12961-022-00883-6

Population and Public Health Division (PPHD) 2023, Public Health – NSW COVID-19 Response. NSW Ministry of Health, Sydney. https://www.health.nsw.gov.au/Infectious/covid-19/evidence-hub/Pages/phr-report.aspx

Appendices



Appendix A: Program Logic Model

Need		High-level aims	Detailed aims	Activity	Outputs	End user	Impacts: Short term	Impacts: Medium and long term (Note these overlap with short term)
There was a need identified by NSW Health to create research evidence to support the state's response to the COVID-19 pandemic. To address that need a NSW Health COVID-19 Research Program ('the Program') was rapidly designed and implemented to: 1. enhance the NSW research ecosystem 2. fund new research The overarching purpose of the Program is to provide research evidence to guide policy and program development focused on both the NSW COVID-19 response and recovery for the NSW economy.	Research schemes	Workstream 1. COVID-19 Research Grants: to create knowledge and innovations for the pandemic response	Invest in COVID-19 research funding to maximise rapid translation and impact in the short, medium and long term	Develop and administer funded COVID-19 research projects	1. Funded grants and clinical trials by priority and ERPR; recipients report results rapidly using templates. Example metrics for outputs: • # projects funded • # % projects funded by priority area • # % projects by setting • # % projects reporting milestones • $ spent 2. Application of Workstream 6's **Rapid Translation Synthesis** platform to project outputs (i.e. examples of expedited translation from 1-page Evidence Summaries for research findings) 3. Series of new products (application form, reporting template, program logics designed to encourage translation)	**Two broad groups of end users:** 1. **End users for the evaluation:** NSW Health Secretary, Ministry Executive, and NSW Treasury. Other leadership groups across NSW including Public Health Emergency Operations Centre/Public Health Response Branch, State Health Emergency Operations Centre, Critical Intelligence Unit, Senior Executive Forum, and Health System Strategy. 2. **End users for research and infrastructure outputs (use of outputs by these end users facilitate 'impact'):** • Ministry of Health, including the Chief Health Officer and Public Health Emergency Operations Centre • Minister for Health and Medical Research • Researchers and research funders (e.g. NHMRC) • Health services • Other NSW Government departments (e.g. Department of Education, Department of Premier and Cabinet) • Australian Government including advisory committees • Industry (including MDF recipients and biopharmaceutical and devices) • Media • Patients and community	**Contribution to Knowledge Generation** #1: New COVID-19 related research innovations via workstreams 1, 2, 3, 4, 5 and 6 #2: New COVID-19 related research knowledge to the NSW COVID-19 response via workstreams 1, 2, 3, 4, 5 and 6 #3: Rapid translation of findings i.e. direct link between research product and end users – time between discovery and utilisation via workstreams 1, 2, 3, 4, 5 and 7 #4: First analysis of effectiveness from COVID-19 research initiatives, including programs that address equity issues via workstreams 1, 2, 3, 4, 5, 6 and 7 #4a: Key learnings as to what worked/did not work from funded COVID-19 initiatives (including translation). Initial recommendations for health sector preparedness for i) another emergency and/or ii) consideration for post-COVID-19 business as usual via workstreams 1, 2, 3, 4, 5, 6 and 7 **Contributions to Clinical Care** #5: New clinical practice/technologies via workstreams 1, 2, 3, 4, 5 and 6 #6a: Identification of technologies and models of care for COVID-19 via workstream 4 #6b: Informing appropriate immunisation and booter schedule for safety and efficacy in limiting impact of COVID-19, including responding to new variants via workstream 3 **Contribution to Policies and Programs** #7: New, confirmed and/or adapted health and industry policies/programs as a result of research evidence generated by this Program via workstreams 1, 2, 3, 4, 5, 6 and 7 #8: New, confirmed and/or adapted health and industry policies/ programs to support recovery as a result of research evidence generated by this Program via workstreams 1, 2, 3, 4, 5, 6 and 7 #9: New, confirmed and/or adapted HREC and SSA processes to expedite approval processes that are scalable beyond COVID-19 via workstream 5 #10: Safe access to COVID-19 therapeutics for NSW researchers, health care workers and community, and quality data to inform the NSW COVID-19 response via workstreams 3 and 4 **Contributions to the Economy** #11: Viability of MDF recipients (compared to baseline via workstream 5 survey) via workstream 6 #12: Number of MOH funded companies that are pivoting via workstream 6 #13: Number of MOH funded companies that remain viable via workstream 6 #14: Examples of COVID-19 innovations developed by MDF funded companies via workstream 6 #15a: Economic benefit of faster HREC and SSA approval processes (NB: methods of analysis to be determined) via workstreams 5 and 7 #15b: Economic benefit of faster translation due to Rapid Research Synthesis platform (NB: methods of analysis to be determined) via workstream 7 #16: ROI for selected deep-dive research projects and innovations (e.g. Schools Transmission study and impact of opening up schools) via workstream 7 #17: Foster collaboration across and maturity of the clinical trials sector to ensure NSW is a destination of choice for clinical trials Sponsors (COVID-19 and non-COVID-19) via workstream 4 Creation of jobs Higher quality/trained workforce **Contributions to the Community and Health Outcomes** #18a: Greater community knowledge about COVID-19 prevention/treatment/management/new policies via and immunisation policies and other interventions via workstreams 1, 2, 3, 4, 5, 6, 7 and 8 #18b: Reducing risk to the community due to COVID-19 through improved prevention and immunisation policies and other interventions #12: Initial health benefits from technology, treatments and models of care (COVID-19 prevention, treatment, management) via workstreams 1, 2, 3, 4, 5 and 6	*NOTE: Many of these impacts will accrue beyond the life of the evaluation and some may be aspirational. They are provided to: i) document the path to anticipated impacts and demonstrate the long-term view of the COVID-19 Research Program, and ii) list impacts that could be modelled/simulated for anticipated cost/benefits (Note, however, this is currently out of scope for the evaluation).* **Contribution to Knowledge Generation** #1: Analysis of effectiveness from COVID-19 Research Program initiatives, key learnings on programs that demonstrated cost effectiveness; insights on programs that may be suitable for scale-up; insights on programs that addressed equity issues; recommendations for preparedness for the next pandemic/emergency; understanding why/how successful translation occurred via workstreams 1, 2, 3, 4, 5 and 6 but mostly workstream 7 #2: Knowledge about value and affordable research products that did not translate – why they failed to translate and remedies for translation if these products are needed via workstream 7 **Contribution to Clinical Care** #3: Contribution to evidence based, cost effective and affordable research products used in policy and practice (pharma, devices, models of care, immunisation) via workstreams 1, 2, 3, 4, 5, 6 and 7 **Contribution to Policies and Programs** #4: Monitored and evaluated effect of policy including health benefits (i.e. evaluated COVID-19 policies for real world effectiveness – requires simulation modelling) via workstreams 1, 2, 3, 4, 5, 6 and 7 #5: New capability for adaptive platform clinical trials in NSW via workstream 4 #6: Sustained expediting of HREC and SSA approvals due to new innovative processes and policies developed during COVID-19 via workstream 5 **Contribution to the Economy** #7: Growth of devices and therapeutics industry, workforce, and revenues in NSW versus other AU (i.e. economic contribution) workstreams 3 and 6 #8: ROI of sustained acceleration of HREC and SSA processes (as noted methods to be developed) via workstream 5 #9: ROI for selected deep-dive research projects and innovations (establish long-term impacts of projects versus total cost) via workstream 7 #10: Contribution to NSW economy (evidenced in state GDP; employment, device industry growth etc) via workstreams 1, 2, 3, 4, 5, 6 and 7 **Contribution to the Community and Health Outcomes** #11: Health benefits (e.g. quality of life) from technology, treatments and models of care that have been contributed to by the COVID-19 Research Program. Includes prevention, treatment and management via workstreams 1, 2, 3, 4, 5 and 6
	Research schemes	Workstream 2. Emergency Response Priority Research (ERPR): to create evidence for urgent public health management	Facilitate the priority projects focused on public health	Ensure appropriate governance in place, ensure ethics requirements are met, monitor progress, facilitate reporting and dissemination				
	Research infrastructure/ecosystem projects	Workstream 3. Vaccine and RNA research support: enable long-term vaccine research, production, surveillance and accessibility	Establish and fund two research networks and their activities to accelerate NSW-led efforts in developing and delivering safe and effective vaccines and other ENA-based therapies	1. The Vaccine, Infection and Immunology Collaborative Research group will develop and conduct policy-relevant research to support and evaluate COVID-19 vaccines and antivirals, establish appropriate governance and engage and brief stakeholders and policy makers 2. The RNA Production and Research Network will strengthen manufacture, services, research and training across NSW for RNA-based therapeutic research projects relevant to COVID-19, establish governance including an external advisory committee, and organise meetings and conferences	VIM: 1. Patient cohorts 2. Specimen biobank for current and future research 3. Policy briefings 4. Publications, reports and presentations 5. Industry investment and/or clinical trials into NSW RPRN: 1. Services and GLP-products including RNA (siRNA, mRNA), nanoparticles, and RNA-loaded nanoparticles 2. Successful grant applications to other funders 3. Publications, reports and presentations 4. Number of staff and students trained in workforce groups such as GUP, GMP or regulatory affairs 5. Industry investment and/or clinical trials into NSW			
		Workstream 4. Clinical Trials: to increase NSW-based participation in clinical trials in the COVID-19 environment	Clinical trials initiatives to: 1. Implement an adaptive clinical trials platform across NSW for robust and rapid assessment of potential COVID-19 therapeutics 2. Encourage NSW-based participation across multiple sites in high profile industry-sponsored national and international trials 3. Develop statewide accessible clinical trials enabling infrastructure 4. Foster collaboration across, and develop maturity of the sector	1. Establish the Vaccine and Therapeutic Advisory Groups and commence meeting schedule 2. Implement an adaptive clinical trials platform across NSW for robust and rapid assessment of potential COVID-19 therapeutics 3. Encourage NSW-based participation across multiple sites in high profile industry-sponsored national and international trials 4. Develop statewide accessible clinical trials enabling infrastructure	1. Development of adaptive platform clinical trial infrastructure and framework across three settings (ICU, hospital and community) 2. Recommendations from VAG and TAG sent to decisions maker in public or private sector 3. Enabled COVID-19 and non-COVID-19 clinical trials in NSW 4. Establish the Waratah Vaccine Trial Alliance to facilitate clinical trial coordination			
		Workstream 5. Expediting HREC and Site Specific Authorisation (SSA) processes to expedite ethics processes and hardwire innovations into the post-COVID-19 research environment	Speed up approval and site specific authorisation to: 1. Facilitate faster initiation of COVID-19 research 2. Work with LHDs to design framework and processes to monitor and speed up approval for COVID-19 research 3. Investigate opportunities for COVID-19 processes to be retained for general use	Monitor and facilitate LHD/SCHN to expedite ethics and SSA approvals	1. Prioritised HREC approval for COVID-19 research 2. Fortnightly monitoring of HREC and SSA approval times and mechanisms to implement remedies if required. Example metrics for outputs: • time between COVID-19 research ethics/SSA lodgement and approval, by LHD (See REGIS) • process time compared between COVID-19 and non-COVID-19 research ethics process times (See REGIS) 3. Innovative processes and structures to expedite HREC and SSA approval times (e.g. trialled HREC speed interventions, reallocation of ethics applications)			
		Workstream 6. Industry Schemes: to support the medical devices industry during COVID-19 and into the recovery	1. Support commercialisation of therapies and devices for COVID-19 2. Support the medical devices industry during COVID-19 and into the recovery period 3. Assist industry to pivot to address critical supply chain issues	Design and implement the COVID-19 Triage Service, engage across government to support the MediTech sector	1. Operational data from the Triage Service 2. Designed policy to support early stage and vulnerable MDF recipients 3. Pivoting manufacturers			
	Research translation enabling	Workstream 7. Research translation and impact assessment: to expedite the use of research outputs by end users and measure the impact	1. Develop resources for rapid research synthesis and a feedback loop between COVID-19 research findings and key decision makers (i.e. link research outputs to end users) 2. Evaluate the impact of the COVID-19 Research Program	Design architecture of Rapid Translation Synthesis platform, agreed impact framework and methods for evaluating the COVID-19 Program, understand evaluation end user needs for reporting	1. Research translation process established 2. # Evidence Summaries for rapid translation 3. # Research translation processes facilitated			
		Workstream 8. Communication: to communicate and promote the COVID-19 Research Program achievements	1. Communicate the activities and achievements of the Program 2. Promote research findings from the COVID-19 Research Program (i.e. supporting dissemination and translation) 3. Provide a snapshot of all COVID-19 research and assets across NSW (i.e. information and promotion) 4. Assist with communication to LHDs on ethics SSAs (with Workstream 4)	Strategic communication about the Program and wider COVID-19 research across NSW (TBC)	Outputs: 1. Project snapshots 2. Researcher interviews/news articles 3. Project outcome summaries Measures: Reach (webpage visits, impressions, views) Engagement (likes, retweets, comments, shares)			

Appendix B: Table of grant recipients

KEY RESEARCHERS	HOST ORGANISATION	PROJECT TITLE	BUDGET
COVID-19 Research Grants			
Professor William Rawlinson	NSW Health Pathology, The University of Sydney	Improved confirmatory diagnosis of SARS-CoV-2 infection using protein mass spectrometry	$111,318
Professor Vital Sintchenko	NSW Health Pathology, The University of Sydney	Enhanced genomic tracking of COVID-19 importations and transmissions in NSW	$471,583
A/ Professor Fabienne Brilot	Kids Research at Sydney Children's Hospitals Network	Ultra-sensitive PC2 serology and rapid viral outgrowth assays	$567,130
Dr Linda Hueston	NSW Health Pathology, Westmead Institute for Medical Research	Development, evaluation and validation of enzyme linked immunosorbent assay (ELISA) assays for both the diagnosis of COVID-19 and utility in seroprevalence in communities	$389,411
Professor Anthony Cunningham	Westmead Institute for Medical Research	Novel diagnostics for evaluating duration of immunity after COVID-19 and for Phase I/II vaccine trials	$540,384
Dr Martin McNamara	Sax Institute	45 and up COVID Insights	$983,920
Professor Kim Usher	University of New England	Impact of COVID-19 on Indigenous Australians' preventive health behaviours: A mixed methods study	$335,680
Professor Kathy Clapham	University of Wollongong	A place-based pandemic response to the strengths and vulnerabilities of Aboriginal communities in south-eastern NSW	$793,125
Associate Professor Joanne Bryant	UNSW Sydney	A rapid qualitative assessment of COVID-19 health needs in three Aboriginal communities	$152,092
Professor Kristine Macartney	NCIRS and Sydney Children's Hospitals Network	Designing and testing COVID-19 vaccine public health messages	$297,200
A/Professor Deepak Bhonagiri	South Western Sydney Local Health District	24/7 eICU model of care for Level 4 ICUs in rural NSW	$499,696
Dr Shannon Nott Professor Andrew Wilson	Western NSW Local Health District and University of Sydney	Evaluation of the virtual rural generalist service (VRGS) as an effective, "COVID-19 resilient" model of care	$500,000
Scientia Professor Richard Bryant	UNSW Sydney	Rapid evaluation of a scalable program for reducing common mental disorders during COVID-19	$496,624
Dr Milena Heinsch	The University of Newcastle	The eCliPSE COVID-19 project: an electronic pathway to care for NSW residents to reduce depression, anxiety, and alcohol use problems in the face of COVID-19	$459,046
Dr Valsamma Eapen	South Western Sydney Local Health District	A digital solution to address the mental health and financial impacts of the pandemic for children and their parents in the first 2000 days	$495,000
Ms Sandra Bailey	Sax Institute	Supporting the mental health of health workers at Aboriginal Community Controlled Health Services in NSW during the COVID-19 pandemic and beyond	$498,010
A/Professor Emily Blyth	The University of Sydney	Manufacture of banked SARS-CoV-2 specific T lymphocytes derived from recovered COVID-19 patients to prevent progression to severe COVID-19 in vulnerable individuals	$423,768
		Sub-Total	**$8,013,987**

KEY RESEARCHERS	HOST ORGANISATION	PROJECT TITLE	BUDGET
Emergency Response Priority Research			
Professor Kristine Macartney	NCIRS	Monitoring and investigating the safety and effectiveness of the COVID-19 vaccination program	$610,629
Professor Kristine Macartney Scientia Professor John Kaldor	NCIRS	Serosurveillance for SARS-CoV-2 infection	$476,567
Professor Kristine Macartney Dr Lucy Deng	NCIRS	The Australian First Few 'X' (FFX) Project for COVID-19	**Budget supplement**
Dr Louise Causer	UNSW	Retrospective infected health care worker study	$88,585
Professor Kristine Macartney	NCIRS	NSW Health COVID-19 schools transmission investigation projects	$1,014,041
Professor Robert Booy Dr Shopna Bag	University of Sydney, Western Sydney LHD	Burden of ILI disease in adults ≥65 yrs in aged care facilities	**Budget supplement**
Scientia Professor John Kaldor A/Professor Bette Liu	UNSW	COVID-19 NSW Outcomes Study	$66,778
Dr Philip Britton	Sydney Children's Hospitals Network	Surveillance of paediatric COVID-19, Kawasaki disease and PIMS-TS via PAEDS	$100,000
Dr Kaye Power	Sydney Water	Wastewater-based epidemiology for COVID-19 (Phase 1)	$46,000
Professor James Wood	UNSW	NSW COVID-19 modelling and epidemiological analysis	$823,260
Professor Kristine Macartney	NCIRS	Vaccine effectiveness	$325,689
Professor Margaret Hellard	Burnet Institute	NSW Covasim analysis	$202,650
		Sub-Total	**$3,754,199**
Vaccine Research Support			
Professor Pall Thordarson	UNSW	NSW-RPRN	$4,898,951
Professor Anthony Cunningham	The Westmead Institute for Medical Research	VIIM	$4,696,272
		Sub-Total	**$9,595,223**
Additional vaccine support activities			
	Sydney Children's Hospital Network	Waratah Vaccine Trial Alliance	$498,274
Professor Warwick Britton Professor Christopher Goodnow	Centenary Institute Garvan Institute of Medical Research	COVID-19 Vaccine Acceleration Program	$1,995,867
		Sub-Total	**$2,494,141**

KEY RESEARCHERS	HOST ORGANISATION	PROJECT TITLE	BUDGET
Clinical Trials			
Professor Steve Webb	Monash University	REMAP-CAP	$1,380,000
Professor Josh Davis	Hunter Medical Research Institute	ASCOT-ADAPT	$617,232
Professor Guy Marks	NHMRC Clinical Trials Centre, University of Sydney	BEAT COVID	$1,099,437
		Sub-Total	**$3,096,669**
Industry Schemes			
	Kico Knee Innovations Pty Ltd		$1,000,000
	Tetratherix Pty Ltd		$481,381
	Perx Health Pty Ltd		$380,000
	Beyond700 Pty Ltd		$151,000
		Sub-Total	**$2,012,381**
		TOTAL	**$29,327,396**

Appendix C: List of publications

The following publications were significantly supported through funding from the NSW Government during the COVID-19 pandemic. This is not an exhaustive list but rather those most relevant to the COVID-19 Research Program.

Aggarwal, A., Stella, A.O., Walker, G., Akerman, A., Esneau, C., Milogiannakis, V., Burnett, D. L., McAllery, S., Silva, M.R., Lu, Y., Foster, C.S.P., Brilot, F., Pillay, A., Van Hal, S., Mathivanan, V., Fichter, C., Kindinger, A., Hoppe, A.C., Munier, M.L., Amatayakul-Chantler, S., ... Turville, S. G. (2022). Platform for isolation and characterization of COVID-19variants enables rapid characterization of Omicron in Australia. *Nature Microbiology*, *7*, 896–908. https://doi.org/10.1038/s41564-022-01135-7

Akerman, A., Milogiannakis, V., et al. (2023). Emergence and antibody evasion of BQ, BA.2.75 and SARS-CoV-2 recombinant sub-lineages in the face of maturing antibody breadth at the population level. *Lancet eBioMedicine*, 90:104545. https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(23)00110-X/fulltext

Arabi, Y.M., Gordon, A.C., Derde, L.P.G., Nichol, A.D., Murthy, S., Beidh, F.A., Annane, D., Swaidan, L.A., Beane, A., Beasley, R., Berry, L.R., Bhimani, Z., Bonten, M.J.M., Bradbury, C.A., Brunkhorst, F.M., Buxton, M., Buzgau, A., Cheng, A., De Jong, M., Detry, M.A., ... REMAP-CAP Investigators (2021). Lopinavir-ritonavir and hydroxychloroquine for critically ill patients with COVID-19: REMAP-CAP randomized controlled trial. *Intensive Care Medicine*, *47*(8), 867–886. https://doi.org/10.1007/s00134-021-06448-5

Arnott, A., Draper, J., Rockett, R. ., Lam, C., Sadsad, R., Gall, M., Martinez, E., Byun, R., Musto, J., Marais, B., Chen, S. C., Kok, J., Dwyer, D. E., & Sintchenko, V. (2021). Documenting elimination of co-circulating COVID-19 clusters using genomics in New South Wales, Australia. *BMC research notes*, *14*(1), 415. https://doi.org/10.1186/s13104-021-05827-x

ATTACC Investigators, ACTIV-4a Investigators, REMAP-CAP Investigators, Lawler, P. R., Goligher, E.C., Berger, J.S., Neal, M.D., McVerry, B.J., Nicolau, J.C., Gong, M.N., Carrier, M., Rosenson, R.S., Reynolds, H.R., Turgeon, A.F., Escobedo, J., Huang, D.T., Bradbury, C.A., Houston, B.L., Kornblith, L.Z., Kumar, A., ... Zarychanski, R. (2021). Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19. *The New England Journal of Medicine*, *385*(9), 790–802. https://doi.org/10.1056/NEJMoa2105911

Axfors, C., Janiaud, P., Schmitt, A.M., Van't Hooft, J., Smith, E.R., Haber, N.A., Abayomi, A., Abduljalil, M., Abdulrahman, A., Acosta-Ampudia, Y., Aguilar-Guisado, M., Al-Beidh, F., Alejandria, M.M., Alfonso, R.N., Ali, M., AlQahtani, M., Al Zamrooni, A., Anaya, J.M., Ang, M.A.C., Aomar, I.F., ... Hemkens, L.G. (2021). Association between convalescent plasma treatment and mortality in COVID-19: a collaborative systematic review and meta-analysis of randomized clinical trials. *BMC Infectious Diseases*, *21*(1), 1170. https://doi.org/10.1186/s12879-021-06829-7

Baldelli, A., Boraey, M.A., Oguzlu, H., Cidem, A., Rodriguez, A.P., Ong, H.X., Jiang, F., Bacca, M., Thamboo, A., Traini, D., & Pratap-Singh, A. (2022). Engineered nasal dry powder for the encapsulation of bioactive compounds. *Drug Discovery Today*, *27*(8), 2300–2308. https://doi.org/10.1016/j.drudis.2022.04.012

Basile, K., Rockett, R.J., McPhie, K., Fennell, M., Johnson-Mackinnon, J., Agius, J.E., Fong, W., Rahman, H., Ko, D., Donavan, L., Hueston, L., Lam, C., Arnott, A., Chen, S.C., Maddocks, S., O'Sullivan, M.V., Dwyer, D.E., Sintchenko, V., & Kok, J. (2022). Improved Neutralisation of the COVID-19Omicron Variant following a Booster Dose of Pfizer-BioNTech (BNT162b2) COVID-19 Vaccine. *Viruses*, *14*(9), 2023. https://doi.org/10.3390/v14092023

Bolsewicz, K.T., Steffens, M.S., Bullivant, B., King, C., & Beard, F. (2021). "To Protect Myself, My Friends, Family, Workmates and Patients ...and to Play My Part": COVID-19 Vaccination Perceptions among Health and Aged Care Workers in New South Wales, Australia. *International journal of environmental research and public health*, *18*(17), 8954. https://doi.org/10.3390/ijerph18178954

Bryant, R.A., Dawson, K.S., Keyan, D., Azevedo, S., Yadav, S., Tran, J., Rawson, N., & Harvey, S. (2022). Effectiveness of a Videoconferencing-Delivered Psychological Intervention for Mental Health Problems during COVID-19: A Proof-of-Concept Randomized Clinical Trial. *Psychotherapy and psychosomatics*, *91*(1), 63–72. https://doi.org/10.1159/000520283

Camphor, H.S., Nielsen, S., Bradford-Hartke, Z., Wall, K., & Broome, R. (2022). Retrospective epidemiological analysis of COVID-19 wastewater surveillance and case notifications data – New South Wales, Australia, 2020. *Journal of water and health*, *20*(1), 103–113. https://doi.org/10.2166/wh.2021.275

Capon, A., Houston, J., Rockett, R., Sheppeard, V., Chaverot, S., Arnott, A., Parashko, T., Ferson, M. (2021). Risk factors leading to COVID 19 cases in a Sydney restaurant. *Australian and New Zealand Journal of Public Health, 45*(5), 512-516. https://doi.org/10.1111/1753-6405.13135

Capon, A., Sheppeard, V., Gonzalez, N., Draper, J., Zhu, A., Browne, M., Sullivan, E., Mihajlovic, M., Rockett, R., & Ferson, M. J. (2021) Bondi and beyond. Lessons from three waves of COVID-19 from 2020. *Public Health Research & Practice*, *31*(3), 3132112. https://doi.org/10.17061/phrp3132112

Dawson, G., Bleicher, K., Baynes, S., D'Este, C., Steinberg, J., Weber, M.F., Newby, J., Ding, D., Liu, B., Edwards, B., Milat, A., & McNamara, M. (2022). 45 and Up COVID Insights: a dynamic and collaborative approach to evidence-making during the COVID-19 pandemic. *Public health research & practice*, *32*(4), 32232214. https://doi.org/10.17061/phrp32232214

Eapen, V., Woolfenden, S., Schmied, V., Jalaludin, B., Lawson, K., Liaw, S.T., Lingam, R., Page, A., Cibralic, S., Winata, T., Mendoza Diaz, A., Lam-Cassettari, C., Burley, J., Boydell, K., Lin, P., Masi, A., Katz, I., Dadich, A., Preddy, J., Bruce, J., … Raine, K. H. (2021). "Watch Me Grow- Electronic (WMG-E)" surveillance approach to identify and address child development, parental mental health, and psychosocial needs: study protocol. *BMC Health Services Research*, *21*(1240). https://doi.org/10.1186/s12913-021-07243-0

Escarate E., Jones C.G., Clarke E., Clark P., Norton S., Bag S., Kok J., Dwyer D.E., Lindley R.I., Booy R. Rapid on-site molecular Point of Care Testing during influenza outbreaks in aged care facilities improves antiviral use and reduces hospitalisation. *Aust N Z J Public Health*. 2022 Dec;46(6):884-888. https://www.sciencedirect.com/science/article/pii/S1326020023000389?via%3Dihub doi: 10.1111/1753-6405.13307. Epub 2022 Oct 3. PMID: 36190193.

Gidding, H.F., Machalek, D.A., Hendry, A.J., Quinn, H.E., Vette, K., Beard, F.H., Shilling, H.S., Hirani, R., Gosbell, I.B., Irving, D.O., Hueston, L., Downes, M., Carlin, J.B., O'Sullivan, M.V., Dwyer, D.E., Kaldor, J.M., & Macartney, K. (2021). Seroprevalence of SARS-CoV-2-specific antibodies in Sydney after the first epidemic wave of 2020. *The Medical journal of Australia*, *214*(4), 179–185. https://doi.org/10.5694/mja2.50940

Hasan, T., Lim, H.L., Case, J., Hueston, L., Bag, S., Dwyer, D.E., & O'Sullivan, M.V.N. (2021). The utility of SARS-CoV-2-specific serology in COVID-19 diagnosis. *Australian and New Zealand Journal of Public Health*, *45*(6), 616-621. https://doi.org/10.1111/1753-6405.13155

Hasan, T., Lim, H.L., Hueston, L., Dwyer, D.E., & O'Sullivan, M. (2021). SARS-CoV-2-specific IgM screening has low sensitivity for identifying potentially infectious travellers. *Pathology*, *53*(7), 917-919. https://doi.org/10.1016/j.pathol.2021.08.002

Heinsch, M., Tickner, C., & Kay-Lambkin, F. (2022). Placing equity at the heart of eHealth implementation: a qualitative pilot study. *International Journal for Equity in Healt*h, *21*, 38. https://doi.org/10.1186/s12939-022-01640-5

Heinsch, M., Wyllie, J., Carlson, J., Wells, H., Tickner, C., & Kay-Lambkin, F. (2021). Theories Informing eHealth Implementation: Systematic Review and Typology Classification. *Journal of Medical Internet Research*, *23*(5), e18500. https://doi.org/10.2196/18500

Hueston L. (2022). Immunofluorescent Antibody Techniques in the Diagnosis of COVID-19 Infection in Humans. *Methods in molecular biology (Clifton, N.J.)*, *2452*, 99–107. https://doi.org/10.1007/978-1-0716-2111-0_7

Hueston, L., Kok, J., Guibone, A., McDonald, D., Hone, G., Goodwin, J., Carter, I., Basile, K., Sandaradura, I., Maddocks, S., Sintchenko, V., Gilroy, N., Chen, S., Dwyer, D.E., & O'Sullivan, M.V.N. (2020). The Antibody Response to COVID-19Infection. *Open Forum Infectious Diseases*, *7*(9), ofaa387. https://doi.org/10.1093/ofid/ofaa387

Jones C.G., Escarate E., Clarke E., Clarke P., Norton S., Bag S., Kok J., Dwyer D., Lindley R.I., Booy R. Outbreaks of Human Metapneumovirus in Western Sydney Aged-Care Facilities in 2018. Commun Dis Intell (2018). 2022 Aug 18;46 https://www1.health.gov.au/internet/main/publishing.nsf/Content/2A15CD097063EF40CA2587CE008354F1/$File/outbreaks_of_human_metapneumovirus_in_western_sydney_aged_care_facilities_in_2018.pdf doi: 10.33321/cdi.2022.46.54. PMID: 35981816.

Katelaris, A.L., Wells, J., Clark, P., Norton, S., Rockett, R., Arnott, A., Sintchenko, V., Corbett, S., & Bag, S.K. (2021). Epidemiologic Evidence for Airborne Transmission of SARS-CoV-2 during Church Singing, Australia, 2020. *Emerging Infectious Diseases*, *27*(6), 1677-1680. https://doi.org/10.3201/eid2706.210465

Koirala, A., Gidding, H.F., Vette, K., Macartney K. on behalf of the PAEDS Serosurvey Group. (2022). The seroprevalence of SARS-CoV-2-specific antibodies in children, Australia, November 2020 – March 2021. *Med J Aust*, 217 (1), pp. 43-45.

Koirala, A., Winkler, N.E., Quinn, H.E., Gardiner, E., Liu, B., Forbes, J., Sharpe, C., van Tussenbroek, T., Wood, N., & Macartney, K. (2023). Understanding COVID-19 Delta and Omicron variant transmission and vaccine impact in schools and child-care settings in Australia: a population-based study. *Lancet Regional Health – Western Pacific*. https://doi.org/10.1016/j.lanwpc.2023.100736

Lam, C., Gray, K., Gall, M., Sadsad, R., Arnott, A., Johnson-Mackinnon, J., Fong, W., Basile, K., Kok, J., Dwyer, D. E., Sintchenko, V., & Rockett, R. J. (2021). COVID-19 Genome Sequencing Methods Differ in their

Abilities to Detect Variants from Low-Viral-Load Samples. *Journal of clinical microbiology*, *59*(11), e0104621. https://doi.org/10.1128/JCM.01046-21

Lane, C.R., Sherry, N.L., Porter, A.F., Duchene, S., Horan, K., Andersson, P., Wilmot, M., Turner, A., Dougall, S., Johnson, S.A., Sait, M., Gonçalves da Silva, A., Ballard, S.A., Hoang, T., Stinear, T.P., Caly, L., Sintchenko, V., Graham, R., McMahon, J., … Howden, B.P. (2021). Genomics-informed responses in the elimination of COVID-19 in Victoria, Australia: an observational, genomic epidemiological study. *Lancet Public Health*, *6*(8): e547-e556. https://doi.org/10.1016/S2468-2667(21)00133-X

Lee, E., Sandgren, K., Duette, G., Stylianou, V.V., Khanna, R., Eden, J.S., Blyth, E., Gottlieb, D., Cunningham, A.L., & Palmer, S. (2021). Identification of COVID-19 nucleocapsid and spike T-cell epitopes for assessing T-cell immunity. *Journal of Virology*, *95*(6), e02002-20. https://doi.org/10.1128/JVI.02002-20

Liu, B., Gidding, H., Stepien, S., Cretikos, M., & Macartney, K. (2022). Relative effectiveness of COVID-19 vaccination with 3 compared to 2 doses against COVID-19B.1.1.529 (Omicron) among an Australian population with low prior rates of COVID-19infection. *Vaccine*, *40*(43), 6288–6294. https://doi.org/10.1016/j.vaccine.2022.09.029

Liu, B., Jayasundara, D., Pye, V., Dobbins, T., Dore, G.J., Matthews, G., Kaldor, J., & Spokes, P. (2021). Whole of population-based cohort study of recovery time from COVID-19 in New South Wales Australia. *The Lancet regional health. Western Pacific*, *12*, 100193. https://doi.org/10.1016/j.lanwpc.2021.100193

Liu, B., Spokes, P., Alfaro-Ramirez, M., Ward, K., & Kaldor, J. (2020). Hospital outcomes after a COVID-19 diagnosis from January to May 2020 in New South Wales Australia. *Communicable diseases intelligence (2018)*, *44*, 10.33321/cdi.2020.44.97. https://doi.org/10.33321/cdi.2020.44.97

Liu, B., Spokes, P., He, W., & Kaldor, J. (2021). High risk groups for severe COVID-19 in a whole of population cohort in Australia. *BMC infectious diseases*, *21*(1), 685. https://doi.org/10.1186/s12879-021-06378-z

Macartney, K., Quinn, H. E., Pillsbury, A.J., Koirala, A., Deng, L., Winkler, N., Katelaris, A.L., O'Sullivan, M. V. N., Dalton, C., Wood, N., & NSW COVID-19 Schools Study Team. (2020). Transmission of COVID-19in Australian educational settings: a prospective cohort study. *The Lancet. Child & adolescent health*, *4*(11), 807–816. https://doi.org/10.1016/S2352-4642(20)30251-0

Marcato, A.J., Black, A.J., Walker, C.R., Morris, D., Meagher, N., Price, D. J., McVernon, J., & Australian FFX Household Transmission Project Group (2022). Learnings from the Australian first few X household transmission project for COVID-19. *The Lancet regional health. Western Pacific*, *28*, 100573. https://doi.org/10.1016/j.lanwpc.2022.100573

Nguyen, T.T., Nguyen, D.T.N., Le, H.N.M., Eden, J-S. Rockett, R.J., Nguyen, T.T.H., Vu, B. T.N., Tran, G.V., Le, T.V., Dwyer, D.E., & van Doorn, H.R. (2020) Genetic diversity of COVID-19and clinical, epidemiological characteristics of COVID-19 patients in Hanoi, Vietnam. *PLoS ONE*, *15*(11), e0242537. https://doi.org/10.1371/journal.pone.0242537

Nott S. The Virtual Rural Generalist Service – a COVID-19 resilient support service for rural and remote communities. Rural Remote Health. 2023 Jan;23(1):8131. doi:10.22605/RRH8131. Epub 2023 Jan 10. PMID: 36802813.

Rafferty, A.C., Hewitt, M.C., Wright, R., Hogarth, F., Coatsworth, N., Ampt, F., Dougall, S., Alpren, C., Causer, L., Coffey, C., Wakefield, A., Campbell, S., Pingault, N., Harlock, M., Smith, K.J., & Kirk, M. D. (2021). COVID-19 in health care workers, Australia 2020. *Communicable diseases intelligence (2018)*, *45*, 10.33321//cdi.2021.45.57. https://doi.org/10.33321//cdi.2021.45.57

REMAP-CAP Investigators, ACTIV-4a Investigators, ATTACC Investigators, Goligher, E.C., Bradbury, C.A., McVerry, B.J., Lawler, P.R., Berger, J.S., Gong, M.N., Carrier, M., Reynolds, H.R., Kumar, A., Turgeon, A.F., Kornblith, L.Z., Kahn, S.R., Marshall, J.C., Kim, K.S., Houston, B.L., Derde, L.P.G., Cushman, M., … Zarychanski, R. (2021). Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19. *The New England Journal of Medicine*, *385*(9), 777–789. https://doi.org/10.1056/NEJMoa2103417

REMAP-CAP Investigators, Gordon, A.C., Mouncey, P.R., Al-Beidh, F., Rowan, K.M., Nichol, A.D., Arabi, Y.M., Annane, D., Beane, A., van Bentum-Puijk, W., Berry, L.R., Bhimani, Z., Bonten, M.J.M., Bradbury, C.A., Brunkhorst, F.M., Buzgau, A., Cheng, A.C., Detry, M.A., Duffy, E.J., Estcourt, L.J., … Derde, L.P.G. (2021). Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19. *The New England Journal of Medicine*, *384*(16), 1491–1502. https://doi.org/10.1056/NEJMoa2100433

REMAP-CAP Writing Committee for the REMAP-CAP Investigators, Bradbury, C.A., Lawler, P.R., Stanworth, S.J., McVerry, B.J., McQuilten, Z., Higgins, A.M., Mouncey, P.R., Al-Beidh, F., Rowan, K.M., Berry, L.R., Lorenzi, E., Zarychanski, R., Arabi, Y.M., Annane, D., Beane, A., van Bentum-Puijk, W., Bhimani, Z., Bihari, S., Bonten, M.J.M., … Gordon, A. C. (2022). Effect of Antiplatelet Therapy on Survival and Organ Support-Free Days in Critically Ill Patients With COVID-19: A Randomized Clinical Trial. *JAMA*, *327*(13), 1247–1259. https://doi.org/10.1001/jama.2022.2910

REMAP-CAP Writing Committee for the REMAP-CAP Investigators, Estcourt, L.J., Turgeon, A.F., McQuilten, Z.K., McVerry, B.J., Al-Beidh, F., Annane, D., Arabi, Y.M., Arnold, D.M., Beane, A., Bégin, P., van Bentum-Puijk, W., Berry, L.R., Bhimani, Z., Birchall, J.E., Bonten, M.J.M., Bradbury, C.A., Brunkhorst, F.M., Buxton, M., Callum, J.L., … Shankar-Hari, M. (2021). Effect of Convalescent Plasma on Organ Support-Free Days in Critically Ill Patients With COVID-19: A Randomized Clinical Trial. *JAMA*, *326*(17), 1690–1702. https://doi.org/10.1001/jama.2021.18178

Rockett, R.J., Draper, J., Gall, M., Sim, E.M., Arnott, A., Agius, J.E., Johnson-Mackinnon, J., Fong, W., Martinez, E., Drew, A.P., Lee, C., Ngo, C., Ramsperger, M., Ginn, A. N., Wang, Q., Fennell, M., Ko, D., Hueston, L., Kairaitis, L., Holmes, E.C., … Sintchenko, V. Co-infection with COVID-19Omicron and Delta variants revealed by genomic surveillance. *Nature Communications*, *13*(1), 2745. https://doi.org/ 10.1038/s41467-022-30518-x.

Shen, Y., Freeman, J.A., Holland, J., Naidu, K., Solterbeck, A., Van Bilsen, N., Downe, P., Kerridge, I., Wallman, L., Akerman, A., Aggarwal, A., Milogiannakis, V., Martins Costa Gomes, G., Doyle, C.M., Sandgren, K. J., Turville, S., Cunningham, A. L., & Mulligan, S.P. (2022). Multiple COVID-19 vaccine doses in CLL and MBL improve immune responses with progressive and high seroconversion. *Blood*, *140*(25), 2709–2721. https://doi.org/10.1182/blood.2022017814

Shen, Y., Freeman, J.A., Holland, J., Naidu, K., Solterbeck, A., Van Bilsen, N., Downe, P., Kerridge, I., Wallman, L., Akerman, A., Aggarwal, A., Milogiannakis, V., Martins Costa Gomes, G., Doyle, C.M., Sandgren, K.J., Turville, S., Cunningham, A. L., & Mulligan, S. P. (2022). Multiple COVID-19 vaccine doses in CLL and MBL improve immune responses with progressive and high seroconversion. *Blood*, *140*(25), 2709–2721. https://doi.org/10.1182/blood.2022017814

Shen, Y., Freeman, J.A., Holland, J., Solterbeck, A., Naidu, K., Soosapilla, A., Downe, P., Tang, C., Kerridge, I., Wallman, L., Van Bilsen, N., Milogiannakis, V., Akerman, A., Martins Costa Gomes, G., Sandgren, K., Cunningham, A.L., Turville, S., & Mulligan, S.P. (2022). COVID-19 vaccine failure in chronic lymphocytic leukaemia and monoclonal B-lymphocytosis; humoural and cellular immunity. *British Journal of Haematology*, *197*(1), 41-51. https://doi.org/10.1111/bjh.18014

Steffens, M.S., Bullivant, B., Bolsewicz, K., King, C., & Beard, F. (2022). Factors Influencing COVID-19 Vaccine Acceptance in High Income Countries Prior to Vaccine Approval and Rollout: A Narrative Review. *International journal of public health*, *67*, 1604221. https://doi.org/10.3389/ijph.2022.1604221

Tea, F., Ospina Stella, A., Aggarwal, A., Ross Darley, D., Pilli, D., Vitale, D., Merheb, V., Lee, F.X.Z., Cunningham, P., Walker, G.J., Fichter, C., Brown, D.A., Rawlinson, W.D., Isaacs, S.R., Mathivanan, V., Hoffmann, M., Pöhlman, S., Mazigi, O., Christ, D., Dwyer, D.E., … Turville, S.G. (2021). COVID-19 neutralizing antibodies: Longevity, breadth, and evasion by emerging viral variants. *PLoS Medicine, 18*(7), e1003656. https://doi.org/10.1371/journal.pmed.1003656

Tobin, R.J., Wood, J.G., Jayasundara, D., Sara, G., Walker, C.R., Martin, G.E., McCaw, J.M., Shearer, F.M., & Price, D.J. (2023). Real-time analysis of hospital length of stay in a mixed COVID-19 Omicron and Delta epidemic in New South Wales, Australia. *BMC infectious diseases*, *23*(1), 28. https://doi.org/10.1186/s12879-022-07971-6

Usher, K., Jackson, D., Peng, W., Amarasena, S., Porter, C., McCowan, D., Miller, J., Peake, R., & Sibbritt, D. (2022). Australian Aboriginal and Torres Strait Islander people at risk of declining mental health due to failure to attend for referred follow-up mental health appointments during COVID-19. *International journal of mental health nursing*, *31*(6), 1279–1281. https://doi.org/10.1111/inm.13060

Williams, P., Koirala, A., Saravanos, G.L., Lopez, L.K., Glover, C., Sharma, K., Williams, T., Carey, E., Shaw, N., Dickens, E., Sitaram, N., Ging, J., Bray, P., Crawford, N.W., McMullan, B., Macartney, K., Wood, N., Fulton, E.L., Lau, C., & Britton, P.N. (2022). COVID-19 in New South Wales children during 2021: severity and clinical spectrum. *The Medical Journal of Australia*, *217*(6), 303–310. https://doi.org/10.5694/mja2.51661

Wurzel, D., McMinn, A., Hoq, M., Blyth, C.C., Burgner, D., Tosif, S., Buttery, J., Carr, J., Clark, J.E., Cheng, A.C., Dinsmore, N., Francis, J.R., Kynaston, A., Lucas, R., Marshall, H., McMullan, B., Singh-Grewal, D., Wood, N., Macartney, K., Britton, P.N., … Crawford, N.W. (2021). Prospective characterisation of COVID-19infections among children presenting to tertiary paediatric hospitals across Australia in 2020: a national cohort study. *BMJ open*, *11*(11), e054510. https://doi.org/10.1136/bmjopen-2021-054510

Wyllie, J., Carlson, J., Heinsch, M., Kay-Lambkin, F., & McCoy, A. (2022). eHealth Services and SDG3: Increasing the Capacity of Care. *Australasian Marketing Journal*, *30*(2), 131–141. https://doi.org/10.1177/18393349211069114

Zhang, Y., Almazi, J.G., Ong, H.X., Johansen, M.D., Ledger, S., Traini, D., Hansbro, P.M., Kelleher, A.D., & Ahlenstiel, C.L. (2022). Nanoparticle Delivery Platforms for RNAi Therapeutics Targeting COVID-19 Disease in the Respiratory Tract. *International Journal of Molecular Sciences*, *23*(5), 2408. https://doi.org/10.3390/ijms23052408

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