WA COVID-19 RESEARCH COLLABORATION

Executive Summary

The Western Australian Health Translation Network (WAHTN) is a partnership of 20 state-wide contributing member organisations, and eight associate partners. Our membership includes: Western Australia's Area Health Services and major hospitals; PathWest; the WA Department of Health; WA's five universities (University of Western Australia, Murdoch, Curtin, Edith Cowan University and the University of Notre Dame Australia); WA's major medical research institutes (Telethon Kids Institute, Harry Perkins Institute of Medical Research, Institute for Respiratory Health, Perron Institute, Ear Science Institute and Lions Eyes Institute); St John of God Health Care; and Ramsay Health Care (https://www.wahtn.org/about-us/our-partners/).

WAHTN was tasked by the WA Minister for Health, the Hon. Roger Cook MLA and the WA Department of Health, with coordinating a medical research sector wide response to the COVID-19 threat. The need for WA to act swiftly and decisively was crucial, as the global impact of COVID-19 was considered profound with severe implications for the health of Western Australians, the economy and possibly even public order.

The WA COVID-19 Research Collaboration is a state-wide collaborative response brought together under the WAHTN. The group is comprised of senior clinicians, researchers, administrators and consumer groups working together to develop workable, ready solutions to the pandemic and to examine community and mental health impacts of COVID-19.

The group worked together quickly and cooperatively to identify existing clinical trials that, with an immediate injection of resources, could be accelerated to deliver solutions in existing hospital sites and, as a matter of equity, expanded to other hospitals. The successful "flattening of the curve" in WA has as of July 2020 rendered those trials superfluous for the moment.

The collaboration improved existing support platforms and created new ones to support both existing clinical trials and also new and emerging research made possible by increased funding in response to the crisis.

As of July 2020 there is still no specific treatment for COVID-19. While there is no effective vaccine as yet or "silver bullet", clinical trials in jurisdictions with high infection rates have produced some treatments that partially reduce severity and reduce deaths in the very sickest patients.

An early goal of this collaboration in WA was to rapidly provide the infrastructure and research needed to ensure all Western Australians had the opportunity to participate in world-leading research and clinical trials targeted at combating COVID-19, giving them the best chance of recovery. With no current cases in WA this approach is academic. Over time however, as WA responds to COVID-19 with social, commercial and economic changes, new research priorities are presenting around mental health and how best to safely reverse societal restrictions.

Along with providing vital information and infrastructure for current research strategies, this work will also inform and support our approach to future pandemics.

As the only body engaging with all research sectors, the WAHTN has been the best placed to coordinate the various research streams, coordinate funding from government, other agencies

and philanthropy, and ensure that funded research is relevant, timely and coordinated. On the 23rd of March 2020 the WAHTN called an online one off meeting of WA researchers to address the challenge of COVID-19. Such was the success of the meeting that weekly meetings were held of over 40 researchers for the next few months. A dedicated web page on the WAHTN website was created as a resource for the WA research community https://wahtn.org/wa-covid-19-research-collaboration/. These meetings continue on a monthly basis as of July 2020. A smaller advisory group also met weekly for much of this period. The minutes of these meetings can be found on the web page.

Introduction

The Western Australian Health Translation Network (WAHTN) https://wahtn.org/ comprises researchers from WA's five Area Health Services, private hospitals, the Department of Health, PathWest, six Medical Research Institutes and five universities. It is a member of the nationwide Australian Health Research Alliance (AHRA), a grouping of WAHTN and nine other similar entities facilitating coordination of research and its translation across Australia. https://ahra.org.au/

The global impact of COVID-19 is profound with health threats complicated by the closely linked economic fragility and volatility that uncertainty brings. Given WAHTN's wide membership and role, the Minister for Health Roger Cook along with the WA Department of Health tasked WAHTN with coordinating the WA research community's response to the COVID-19 threat.

This public health threat is the most serious seen since the 1918 H1N1 influenza pandemic which killed 50 million of the 500 million people infected worldwide.

COVID-19 virus poses a singular threat to society with many health systems already overwhelmed. The virus is new and there is much to learn about infectivity and both individual and population risk in a very short time. Understanding the pathways to infection and the biological consequences may enable the development of effective treatments and vaccines to mitigate the current threat.

An immediate problem was that there were no specific therapeutic agents approved as effective for coronavirus infections. All the promising treatments are "off-label". Some of these treatment options included antiviral (Remdesivir); antimalarial (chloroquine/ hydroxychloroquine); combination of two HIV drugs Lopinavir/ ritonavir and the same two HIV drugs along with anti-inflammatory interferon beta. Other potential drug treatments included antibiotics/antiparasitics, nonspecific anti-inflammatory and immunosuppressive drugs and monoclonal antibodies. There was a need to appropriately test these and other emerging therapies. Many of these candidates were part of, or were considered for, trials by WAHTN researchers.

The WA COVID-19 Research Collaboration brought together researchers, scientists and clinical trial teams under the WAHTN as 'one voice' in collaboration, building a coordinated response for WA. Through distinct streams of work, researchers across WA contributed to this collaboration.

Stream 1: Hospital Collaboration
The immediate core objective was to build a platform for real-time accurate patient data supported by biological samples that could be relayed in a de-identified manner for all WA and other researchers and scientists. This collaboration would enable all researchers' access to high quality data, samples and analysis minimising duplication, reducing costs and maximising output for patient care. Different approaches to understanding the infection that are relevant to both individual patients and the general population were to be examined to triangulate treatment and outcome effects. This collaboration was a genuinely targeted, efficient, WA-driven, response to the viral threat and thought to be a critical part of the clinical trials conducted in WA now and into the future. This body of work was led by South Metropolitan Health Service (SMHS), and embedded across several of the metropolitan hospitals and with the input of all partners.

Stream 2: Community
WAHTN developed a community based research program (CIVIC Study) in collaboration with health outcomes researchers across the State to prospectively determine the long-term impact

of exposure to COVID-19 and the health implications of infection prevention control strategies. Ethics approval was obtained and the recruitment module tested. CIVIC includes the collection of details about lifestyle, cardiac and respiratory risk factors as well as mental health and wellbeing. These are delivered by online systems. The plan was for this to be the framework from which focussed community and longitudinal research could be targeted to specific groups or to the broader cohort. While the immediate focus was on existing and imminent clinical trials, and underlying supports, it was thought just as important to immediately set a framework to examine the broader questions on the social and mental health impacts of the CORVID -19 crisis. While the lack of COVID-19 patients has stalled most clinical trials the CIVIC studies that also examine the health and mental health implications and of the societal lockdown have continued.

Stream 3: Clinical Trials

There is no known treatment for COVID-19, however there were thought to be several good treatment candidates that could be tested through urgent clinical trials assuming large numbers of infected patients. WA scientists and clinicians were well placed to contribute to a number of these trials, some of which were part of a larger international collaboration. The WA COVID-19 Research Collaboration identified several promising trials which had the ability to be implemented immediately:

- ASCOT trial - a randomised controlled trial for adults who are hospitalised with COVID-19 to determine if any of the treatments will prevent admission to the Intensive Care Unit, thus improving outcomes and reducing deaths.
- REMAP-CAP trial – a platform trial for ICU patients designed by a global network of clinicians during the 2009 H1N1 pandemic.
- BRACE trial – repurposing a vaccine used for tuberculosis (BCG) to prevent infections in our health care workers.

The first two are at present redundant in WA. The BRACE study has been successful in recruiting many hundreds of health care workers and may yet prove invaluable if a "second wave" occurs.

Funding

Rapid Funding Process

WA has an international reputation for the quality of its infectious diseases and respiratory research, tangible examples of this include: the Telethon Kids Institute which has recently recruited additional international talent in Professors Tobias Kollmann (International Human Vaccines Project) and Peter Gething (Oxford University); the Harry Perkins Institute for Medical Research which runs international clinical trials and has high through-put laboratory capacity; and the Australian National Phenome Centre which is one of the largest and best-equipped metabolic laboratories in the world and has advanced data modelling capability.

From March 2020, WA's medical research community is working together as "Team WA". Facilitated by WAHTN, it identified the major research projects and programs that were the most urgent, that is those that could save lives in the first few months of an uncontrolled epidemic. Additionally, it has built capacity that will allow for new ideas to emerge and be supported quickly in this rapidly evolving landscape, as well as research post COVID-19.

To this end, WAHTN sought to develop a nimble and rigorous process for allocation of research funds for trials and infrastructure that would reduce the lengthy time delays and red tape that are integral to the usual funding application process. An expert scientific panel was assembled under the Chair of the WA Chief Scientist, Professor Peter Klinken. This panel assisted and guided the WAHTN in distributing funds quickly, where needed.

While a collaborative approach to funding was sought, silo funding for particular aspects of the research plan were respected, for example, some research Foundations were only able to fund projects or infrastructure within their area health service or organisation. This was accommodated as the collaborative plan incorporated agreed research priorities that stretched across all area health services and health research sectors in WA.

Committed Funds

The State government committed $3M from the WA Department of Health. Additional funding was pledged from a number of hospital based Foundations.

In addition to government and Foundation funding, key WAHTN partners have committed significant in kind resources and personnel to bring the proposal together and progress this work. An example of this is the Australian National Phenome Centre (ANPC), which has deployed 90% of its staff onto COVID-19 research and key members of the SMHS COVID-19 Research Response (CRR) Team who reacted early and have written the protocol underpinning the hospital collaboration studies.

Originally, committed funds were used primarily for:

- Expanding relevant (respiratory) clinical trials;
- Ensuring there was sufficient infrastructure to cope with the expansion;
- Engaging people to manage the additional work; and
- Establishing a centralised data and biobanking system to ensure a collaborative approach.

Of the $3M committed by the WA Department of Health, a third was used immediately to support infrastructure (including workforce) which was needed by the broader research community before the projected COVID-19 cases ramped up. This included funds to progress standardised, uniform collection and storage of samples across the metropolitan area health services, and the purchase of OpenSpecimen biobanking software along with -80C freezers.

The remaining two thirds of funds from the WA Department of Health plus expected additional funds from other sources were be allocated through a competitive research process.

Further funds were raised through philanthropic sources to support specific trials.

Flexible Emerging Priorities Fund

Early in the pandemic, it was realised that some of the most important research question may not be apparent and there was a need to build a flexible funding source to support innovative research in a timely manner, as novel opportunities arise.

It would enable a responsive approach to emerging issues such as:

- The short and long term effects of social isolation on different communities;
- Social and emotional legacies of COVID-19;
- Impact on regional and remote communities;
- Specific strategies for Aboriginal and vulnerable communities; and
- Education interruption and its consequences for children.

Governance

WAHTN received formal accreditation as an Advanced Health Research and Translation Centre (AHRTC) by the National Health and Medical Research Council (NHMRC) in June 2017. The NHMRC accreditation recognises WAHTN as a network of world-class academic, research and health care delivery partner organisations prepared to embrace and accelerate research translation.

Along with being a network of 20 partners capturing the broad research community of WA, WAHTN has within its structure, the Consumer and Community Health Research Network (CCHRN) which facilitates consumer and community involvement (CCI) in health research and will lead the consumer involvement across the three Streams of work.

Committees

A number of committees were established to provide oversight and guidance of the various work streams and interest areas across the WA COVID-19 Research Collaboration. They include:

- WA COVID-19 Research Collaboration meetings: This group is comprised of over 40 key members of WA's health and medical research sector. The group includes scientists, clinicians, educators, administrators, and government and consumer representation.
- Advisory group: A smaller subgroup of the WA COVID-19 Research Collaboration.
- COVID Research Response (CRR) Team: Based across SMHS, EMHS, NMHS and the ANPC.
- CIVIC Study: Lead by Chris Read and supported by the Clinical Trials and Data Management Centre (CTDMC) and Curtin University.
- WA Biobank Steering Committee: Lead by Aron Chakera and supported by Jennie Hui and Pathwest.

Further information, including minutes and contact details, can be found at https://www.wahtn.org/wa-covid-19-research-collaboration/

Work Flow

The WA COVID-19 Collaboration has agreed to three primary work streams:

- Stream 1: Hospital Collaboration
- Stream 2: Community
- Stream 3: Clinical Trials

Details of each stream are captured in the following pages, and diagrammatically in Figure 1.

WA COVID-19 Research Collaboration

WAHTN
Western Australian Health Translation Network

Lead Groups & Organisations

- PATHWEST *Sample processing*
- CCHRN *Consumer & Community*
- SMHS *ISARIC protocol*
- NMHS *Biobanking*
- Telethon Kids Institute *BRACE trial*
- EMHS *ASCOT trial*
- SJOG *REMAP-CAP trial*
- CTDMC & Curtin *CIVIC trial*

WAHTN
Central Coordination

Minister for Health

Department of Health

HOSPITAL
ISARIC protocol

- CRR Hospital Collaboration
- Sample collection
- Data collection
- Biobanking
- ANPC

COMMUNITY

- CIVIC study CTDMC
- Mental Health
- Chronic Disease
- Aboriginal Health

CLINICAL TRIALS

- ASCOT
- REMAP-CAP
- BRACE
- *Emerging Trials and Research Projects*

Stream 1: Hospital Collaboration

1. CRR Project (ISARIC protocol)

The COVID Research Response (CRR) team brought together researchers, scientists and clinical trial teams under the WAHTN as 'one voice' in collaboration, building a coordinated response for WA. The immediate core objective was to build a platform for real-time accurate patient data supported by biological samples that can be relayed in a de-identified manner for all WA and other researchers and scientists.

In anticipation of a global pandemic, the World Health Organisation (WHO) supported the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC), to develop a rapid response platform for clinical trials for Severe Acute Respiratory Infection (SARI). The protocol enables and outlines accurate protocols for data and biological samples to be collected in a globally harmonised manner. The benefits include; improved data quality, reduced error of measurement and increased statistical power through the ability to combine, compare treatments and outcomes on a grand scale by statistical means. This standardised protocol was approved by the WHO and designed to be used for coordinated clinical investigation of suspected or confirmed cases of COVID-19.

The COVID Research Response (CRR) team is leading this WHO ISARIC platform in a state-wide collaboration. The CRR reflects a large team that includes input from the directors of the metropolitan area health services, Murdoch University, the Australian National Phenome Centre (ANPC), the University of Western Australia (UWA), a core trial team and links across all the hospitals in the state. Work to date has been supported and funded by UWA and Murdoch University and includes:

- CRR has helped set up of the WA Department of Health REDCap database to record details of all patients presenting with SARI in a standardised clinical pathway. This REDCap system has been coordinated to 'handshake' established data systems with all metropolitan Area Health Services as well as the Western Australia Country Health Service (WACHS). This will enable a streamlined coordinated platform. Data will provide clinical uploads for patient care and simultaneous data warehousing. Though children are not primarily targeted by COVID-19 the Child and Adolescent Health Service (CAHS) will be invited to participate.
- CRR has enabled ethics and governance approvals for an integrated combined biobank of laboratory samples as part of routine care incorporating; storage of excess from daily clinical samples and additional specific samples for experimental, laboratory and genetic analysis. This is particularly relevant in WA research projects, as we can work in collaboration with the ANPC, which have made available their considerable resource to help. There are many groups who are interested and will have access to the biosamples to search for biomarkers and potential therapeutic targets.
- CRR will provide coordinated high-quality data in patient data and biological samples to all WA researchers through the WAHTN. This platform provides a template for all research analytics and will coordinate the data interrogation and interpretation at a State, National and International level.

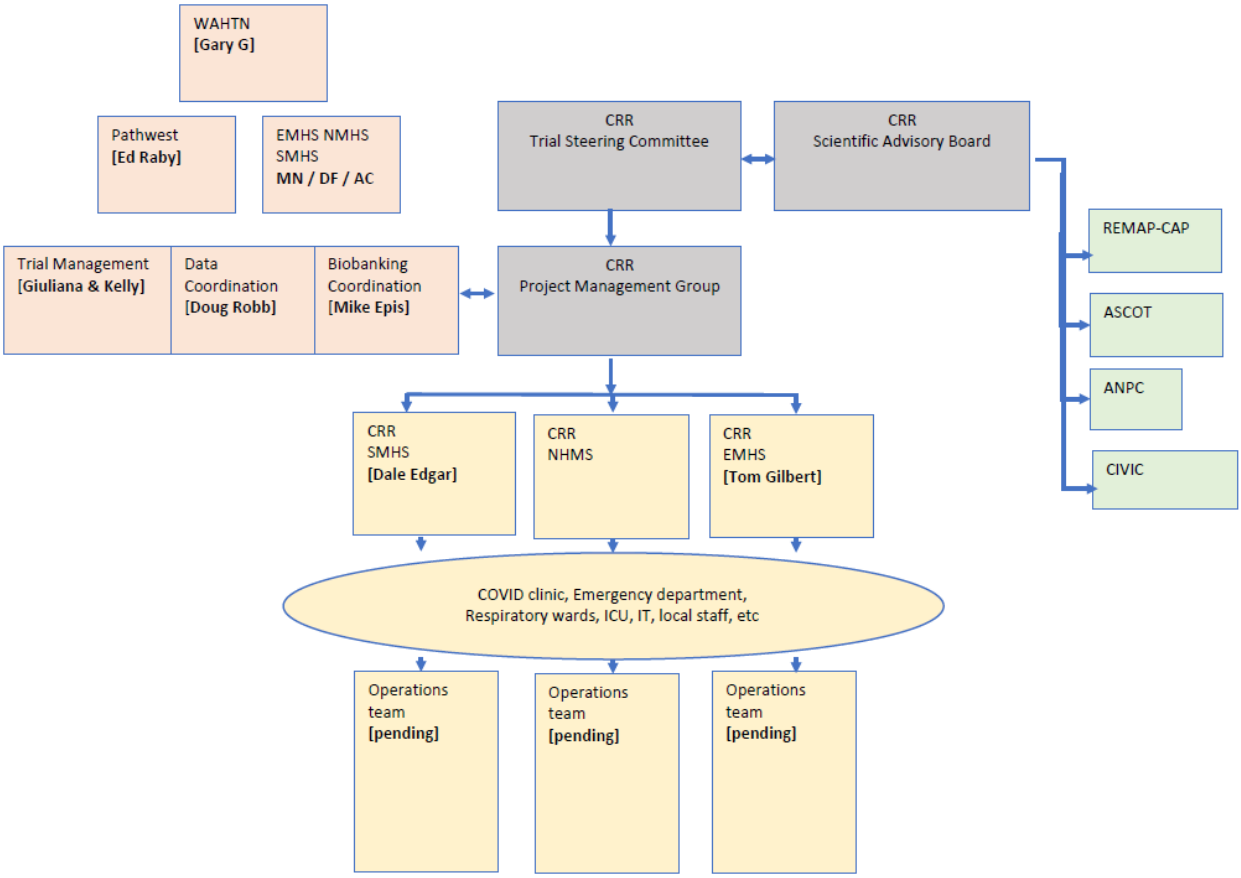
As a team, the entities are uniquely placed to facilitate the WA state-wide research strategy with coordination through WAHTN. CRR is building an integrated data and sample platform for all health systems to copy and collaborate to deliver hard science about the COVID-19 infection. The physical colocation of key units place WA in an ideal position for this project, for instance; emergency departments, critical care and now COVID-19 clinics providing high-fidelity acute patient management with embedded research practices, at all tertiary hospital sites; and the ANPC is situated in the Harry Perkins (South) building adjacent to the Fiona Stanley Hospital and Murdoch University. This is co-located with the CRR, the Biobank and is proximal to PathWest Laboratories and clinical activity. In the north the grouping of the Sir Charles Gairdner Hospital, the Perth Children's Hospital with The Harry Perkins (North) building and the Telethon Kids Institute provides another important focus. All of these institutions are partners in the WAHTN.

The CRR aims to capture high quality patient data and biological samples that are available to all researchers in WA. WAHTN will ensure that researchers will be made aware they can access biological specimens through software OpenSpecimen. All studies can approach the working group for access to samples and data. The CRR will help coordinate ethics, MOU, MTA's etc and facilitate open communication and collaboration between groups to avoid duplication and data sharing

This collaboration will enable access for all researchers to high quality data, samples and analysis, thus minimising duplication, reducing costs and maximising output for patient care.

The Governance of CRR is illustrated in the diagram below. Additional information, including work flow charts, key personnel, sample collection protocols and procedures can be found in detail on the WAHTN website: https://www.wahtn.org/wa-covid-19-research-collaboration/

While the CRR was created in a short space of time and was well placed to capture the data and samples of early WA COVID-19 patients it is now on hold given there are no new COVID-19 patients. The model however is suitable of course for other clinical trials and is a welcome addition to the WA research environment.



2. Australian National Phenome Centre

World-leading researchers at the ANPC are working to revolutionize the diagnosis, prevention and treatment of serious health challenges like Cancer, Alzheimer's, Autism, Obesity and Type 2 Diabetes.

By analysing the molecular, physical and biochemical characteristics of biological tissue and fluids such as blood and urine, researchers at the ANPC aim to predict the complex genetic, environmental and lifestyle interactions causing disease.

The work of the ANPC supports almost every area of bioscience. It reaches across traditional research silos and fosters a new, more collaborative approach to science. Long-term, the ANPC working with State, National and International partners will build 'global atlases' of human disease, providing insights into future health risks, which everyone on the planet can benefit from.

The ANPC uses the largest collection of mass spectrometers in the Southern Hemisphere, combined with nuclear magnetic resonance spectroscopy and advanced data modelling, to identify the unique metabolic 'signature' of individuals and communities.

One of the great strengths of the ANPC is its broad and deep metabolic analysis capacity- designed for clinical diagnostic and prognostic biomarker discovery together with capacity for large scale epidemiological studies.

The recent emergent global threat of COVID-19 underpins the need for facilities like the ANPC that can perform high quality biomarker discovery on infectious samples at large scale. This is a problem that spans population health and disease prevention plus acute patient care and optimisation of clinical trials. There has never been anything quite like this in modern times and the ANPC is well placed to address many of these complex interactions.

The ANPC is able to profile and model thousands of metabolites that create the distinctive signatures of disease and to use these for stratifying patients with mild and severe disease and potentially predict outcomes of infections as well as actively monitoring clinical trial interventions to understand the molecular basis for differential responses to therapy.

Throughout this pandemic, ANPC will be able to provide real time analytics to the front line carers of COVID-19 patients. The ability to deliver a rapid prognostic metric of clinical condition is important, particularly within the emergency or critical care setting, where a gain in minutes or hours with respect to choosing and implementing a therapeutic strategy can mean the difference between life and death. With its ability to work with smaller sets of WA samples plus collaboration with other centres with large numbers of cases of COVID-19 the ANPC is producing novel insights into COVID-19 and have justified the great investment WAHTN partners have made in creating the ANPC.

3. Biobanking

In 2018, WAHTN commissioned a scoping project utilising Medical Research Future Funds (MRFF) to develop recommendations for national guidelines and piloting infrastructure for a scalable, shared, and standardised data repository of clinical and research genomics resource facility in WA. The project, overseen by Dr Aron Chakera as Chair of the WAHTN Biobank Steering Committee, has the potential to be scaled to national activity and has produced an international scan of Biobank resources, facility ethics and economics across Australia, the UK and Japan. Currently, a database of all existing capacity has been compiled from WA stakeholders to support the immediate CRR project.

Focus is now urgently turning to the establishment of a centralised biobank in WA.

WAHTN has invested in the biobank cataloguing system OpenSpecimen. Upscaling on this software, which has been piloted by Telethon Kids Institute through the Origins Study, will provide researchers throughout WA access to see what samples are being stored in real time, the availability of samples and those tests already performed. Consequently, this will avoid duplication of investigations, minimise waste and maximise collaborations with significant cohesive data output.

The current setup of the Biobanking platform includes the appointment of a Biobank manager and procurement of -80'C freezers, which are now operational in the Harry Perkins South building. Additional freezers are being procured for NMHS.

Discussions have been held between all parties to establish sample types and consumables required for collection sites, labelling and banking protocols. Communications with OpenSpecimen have commenced to set up the WA online repository.

Funding will be required for the next steps to occur, these include:

- The purchase of consumables and equipment across sites;
- Establishment of data extraction protocols from OpenSpecimen for samples retrieval and replacement;
- Establishment of collection protocols for all samples from receipt to storing at offsite locations;
- Set up Royal Perth Hospital, Sir Charles Gairdner Hospital and Fiona Stanley Hospital PathWest centres; and
- Staffing of sites for sample collection.

4. Computing & Bioinformatics

The National Computational Infrastructure (NCI) and Pawsey Supercomputing Centre (Pawsey) are joining efforts to offer additional computation and data resources to support the national and international research community to acquire, process, analyse, store and share data supporting COVID-19 research. https://pawsey.org.au/covid19-accelerated-access/

Stream 2: Community

Cardiopulmonary and health implications of coronavirus (COVID-19) exposure in the community (CIVIC)

COVID-19 infection shows no signs of abating soon. Like other diseases associated with the coronavirus family such as Severe Acute Respiratory Syndrome (SARS), COVID-19 is a disease of the respiratory system. However, those with hypertension and cardiovascular disease (CVD) appear to be highly susceptible to its more severe effects, with mortality rates 2-3-fold higher, respectively than the general population (WHO-China Joint Mission report).

Recent reports of profound myocarditis and fatal arrhythmias suggest potential critical influence of COVID-19 on the cardiovascular systems. Patients presenting with COVID-19 and pre-existing CVD have an increased risk of severe disease and death. COVID-19 infection has also been associated with multiple direct and indirect cardiovascular complications including myocardial injury, myocarditis, arrhythmias and venous thromboembolism.

However, true COVID-19 exposure in the Australian community and its potentially significant cardiovascular implications is currently unclear as testing is not freely available for everyone, including those presenting with symptoms who do not meet current guidelines for testing. Therefore there is a high unmet need to collect data from patients in the community in order to understand the long-term impact of COVID-19 infection.

The Australian Government has taken a staggered approach to slow down the spread of COVID-19 in order not to overwhelm the hospitals and other public health services. People who have been exposed to COVID-19 or tested positive have been advised to either quarantine or self-isolate for 14 days. This containment strategy has resulted in increased cases of anxiety and depression.

Psychosocial risk factors, particularly anxiety and depression, can exacerbate cardiovascular risk and increase morbidity and mortality. These otherwise modifiable CVD risk factors can be intensified by the effects of COVID-19 in isolation.

When Australia was on the cusp of COVID-19 infection explosion, there was a need for community data on anxiety and depression to be collected concurrently to lower the long-term risk of CVD. This will assist in decision-making so that public mental health interventions can be formally integrated into public health preparedness and emergency response plans.

The Cardiopulmonary and health implications of coronavirus (COVID-19) exposure in the community (CIVIC) Study has been established to provide the framework for a modular distribution of surveys and targeted interventions across a number of health and social welfare domains. Along with Cardiovascular Health, working groups are being established in:

- Mental Health: currently led by Sean Hood (UWA) and Peter McEvoy;
- Sub-groups focussing on anxiety, depression, isolation;
- Child Health: currently led by Graham Hall (Telethon Kids Institute) and others;
- Workforce: led by Suzanne Robinson (Curtin University) and Justin Manual (WACHS);
- Aged Care;
- Respiratory: led by Fraser Brims and others; and
- Others to be developed, as required.

Links are being established with WA Cohort studies, including:

- Busselton Study – Alan James and Jennie Hui;
- Raine Study – Leon Straker;
- Mens Health Study – Bu Yeap;
- Origins Study – Telethon Kids Institute; and
- Others, as required.

CIVIC Study data will incorporate some of the platforms established in Stream 1, including:

- The REDCap software application (baseline module in testing phase) on multiple platforms (PC/tablet/phone);
- The ISARIC risk factor and symptom data; and
- E-Consent for data linkage and follow-up.

CIVIC Study ethics approval has been fast-tracked and received through Curtin University Ethics Committee. The roll-out of the base module commenced on 20 April 2020. Information pamphlets and videos have been produced, along with documentation relating to study protocols and procedures. These are available on the WAHTN website: https://www.wahtn.org/wa-covid-19-research-collaboration/

Subsequent modules will be developed by workgroups established from WA clinical expert groups and coordinated through the CIVIC platform. Though no new cases of COVID-19 are currently present these studies are important both for the focus on the secondary effects of the pandemic, namely social lockdown and isolation, as well as being in place for a possible "second wave"

Stream 3: Clinical Trials

Given the experience in other jurisdictions it was feared that Australia would be faced with overwhelming numbers that would tax our health system, especially our intensive care units. An early focus on the WAHTN was to ensure that existing trials set up for such a pandemic would be available in WA and for as many patients as possible. To this end WAHTN worked to ensure adequate funding through Government or philanthropy was made available and also lobbied with many others to have the revision of the Guardianship and Administration Act passed by parliament allowing for the recruitment of those who could not consent into appropriate trials. Given the lack of definitive treatment for COVID-19 it was argued that these trials were the only way West Australians could access possibly helpful therapies. Many WA researchers were already a part of international trials and collaboration that could change the course of the disease. With the relatively slower rate of infection here in WA however these trials are now not recruiting but remain open if needed. The trials considered under Stream 3 include the following.

1. ASCOT Trial

Treating established COVID infection to reduce deaths and improve outcomes.

The ASCOT trial is a randomised controlled trial for adults who are hospitalised with COVID-19 to determine if any of the treatments will prevent admission to the Intensive Care Unit. The original treatments included kaletra (a HIV medicine), hydroxychloroquine (a malaria medicine), both kaletra and hydroxychloroquine or nothing. These treatments have been shown to kill the virus in the lab, but it is unclear yet whether they will be of benefit in COVID-19. ASCOT runs at 65 hospitals in Australia and it is harmonised with the WHO trials happening globally. In WA, there are 6 hospitals involved so far: Sir Charles Gairdner Hospital (SCGH), Fiona Stanley Hospital (FSH), Armadale Hospital, Royal Perth Hospital (RPH), St John of God (SJOG) Midland and SJOG Subiaco.

2. REMAP-CAP

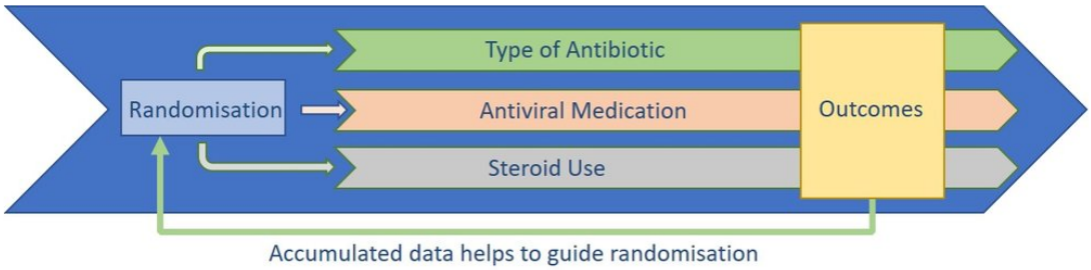
A platform trial for ICU patients with COVID-19.

The trial has been designed by a global network of clinicians who cared for patients and conducted research during the 2009 H1N1 pandemic. The objective is to generate evidence that can be applied to clinical practice during the pandemic to reduce deaths or reduce the length of ICU admission or both in critically ill patients with COVID-19 infection. The trial has been recruiting during the inter-pandemic period and was 'pre-designed' to adapt when a pandemic occurred. Sites, with ethics and other approvals, exist. The platform recruits currently in more than 50 ICUs in 13 countries on 3 continents.

The platform will evaluate, on an open-label basis:

- Antiviral therapy (no antiviral / kaletra, hydroxychloroquine being added);
- Corticosteroid strategy (no steroid, fixed 7 days, only while in septic shock); and
- Immune modulation (no modulator / interferon-beta / anakinra).

Patients who are eligible for participation in REMAP-CAP are randomised to receive one intervention in each of one or more categories of treatment ("domains"). These interventions can be tested simultaneously. Information from patients already participating in the study can also be used to help guide the treatment of new patients joining the study. Most trials are not able to do this.



3. THE BRACE Trial

Preventing infections in our treasured health care workers.

With no vaccine and no preventative medical intervention anywhere close to providing protection for our health care workers, we need to consider alternatives. The BRACE trial is testing a BCG vaccine used for tuberculosis that has effects on the immune system which provide protection against a diverse range of pathogens, including viral infections. It is not a vaccine specific to Coronavirus rather a vehicle to reduce severity of the virus and keep our health care workers safer, faster. Four thousand front line health care workers in our hospitals were invited to participate in the trial: 2,000 in Perth and 2,000 in Melbourne. Health care workers have been successfully recruited.

4. Funded Project Grants

The Health Department made available $3M to the WAHTN to help the COVID-19 Research Response. A Grant Review Panel formed by WAHTN with WA's Chief Scientist chairing met on 16 April 2020 to allocate $2M of funding from the WA Department of Health to a number of project grants spanning the categories of: testing, outcomes, clinical trials and community based studies.

Successful projects were strongly encouraged to make use of the platforms and infrastructure supports that are being established through Stream 1 and 2 of the WA COVID-19 Research Collaboration.

Further funding was sought from Philanthropic and other sources. It is hoped that strong projects that missed out on funding in this round will be supported through subsequent funding rounds, when available. A further $1M was allocated for research infrastructure with the largest portion allocated to biobanking.

Summary

Having formed in 2015 and with the support of the Health Minister in 2020 the WAHTN has greatly enhanced the ability of WA medical researchers to come together in a unified neutral fashion to best meet the challenges of the global COVID-19 pandemic. The recognition of this central and vital role was underscored by the Department of Health's decision to partner with the WAHTN to distribute funds for both clinical research and much needed infrastructure support. This important role has also been recognised by the enthusiastic response to weekly meetings of WA researchers over the last four months. While in July 2020 WA exists in a protective bubble with no communal transmission it is recognised that the inevitable opening of borders will require the best of both our clinical services and supportive research efforts.

Appendix A: Indicative Budget

FUNDING REQUEST	DOH
CLINICAL TRIALS & PROJECTS	
sub-total	*$1,895,377*
CIVIC (Prof Chris Reid, Curtin University)	
CORE Staff	
Consumables, fees	
sub-total	*$300,000*
CRR (administered by Prof Jon Watson, UWA)	
Core Trial Management Team (CRR)	$100,223
Local Site Set Up (SMHS)	$109,000
Local Site Set Up (EMHS)	$55,400
Local Site Set Up (NMHS)	
Consumables, sample testing	$40,000
sub-total	*$304,623*
BIOBANKING - 12mths (administered by Prof Jon Watson, UWA)	
Infrastructure	
Staff	
sub-total	*$500,000*
TOTAL	**$3,000,000**

Appendix B: Key Personnel

WAHTN leadership	Gary.Geelhoed@uwa.edu.au
CRR Directors (Stream 1)	Toby.Richards@uwa.edu.au Merrilee.Needham@health.wa.gov.au
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Post Graduates	Jay.Jay@uwa.edu.au
Medical Students	STRIVEWA@uwa.edu.au
Mental Health	Sean.Hood@health.wa.gov.au

Researchers (not listed here) across institutes and academia will be involved in the coordinated research work.

A contact list for key collaborators and leads across the different streams and infrastructure areas can be found on the WAHTN website under 'Key related documents':
https://www.wahtn.org/wa-covid-19-research-collaboration/