WAHTN
Western Australian Health Translation Network
COVID-19 RESEARCH COLLABORATION

WA COVID-19 RESEARCH COLLABORATION

Overview:

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 Department of Health; WA's five universities (UWA, Murdoch, Curtin, ECU and Notre Dame); 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 has been tasked by the WA Minister for Health, the Hon. Roger Cook MLA and the Department of Health, with coordinating a medical research state-wide response to the COVID-19 threat. The need for WA to act swiftly and decisively is great, as the global impact of COVID-19 is profound with severe implications for the health of Western Australians, the economy and public order.

Western Australia is one of the last of the advanced medical jurisdictions in the world to have sufficient time – albeit only a matter of weeks – to plan a clinical and research response. This also means WA is ideally placed to contribute to the global research response to COVID-19**.**

The WA COVID-19 Research Collaboration is a state-wide collaborative response brought together under the WAHTN. The group comprises 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 as they relate to COVID-19, the better to prepare for future pandemics.

The group have 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 collaboration is improving existing support platforms and creating new ones to support both existing clinical trials and also new and emerging proposals made possible by expected increased funding in response to the crisis.

There is still no specific treatment for COVID-19, therefore the goal of this collaboration is to rapidly provide the infrastructure and research needed to ensure all Western Australians have the opportunity to participate in world-leading research and clinical trials targeted at combating COVID-19, giving them the best chance of recovery.

It is essential at this time that we work together to find workable solutions to the COVID-19 pandemic. A coordinated research response to COVID-19 will reduce duplication and waste, and speed up the translation of research findings into improved clinical care.

Along with providing vital information and infrastructure for current treatment strategies, this work will also inform and support our approach to future pandemics. As the only body engaging with all research sectors, the WAHTN is 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.

Introduction

The Western Australian Health Translation Network (WAHTN) 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, a grouping of WAHTN and nine other similar entities facilitating coordination of research and its translation across Australia.

The global impact of COVID-19 is profound with health and possible public order 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 have 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 consequents may enable the development of effective treatments and vaccines to mitigate the current threat.

An immediate problem is that there are no specific therapeutic agents approved as effective for coronavirus infections. All the promising treatments are "off-label". Some of these treatment options include 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 include antibiotics/antiparasitics, nonspecific anti-inflammatory and immunosuppressive drugs and monoclonal antibodies. There is a need to appropriately test these and other emerging therapies. Many of these candidates are part of or being considered for trials by WAHTN researchers.

The WA COVID-19 Research Collaboration brings 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 will contribute to this endeavour.

Stream 1: The immediate core objective is 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. This collaboration will enable all researchers' access to high quality data, samples and analysis minimising duplication, reducing costs and maximising output for patient care. Clinical sample and data collection can commence within the next two weeks. Different approaches to understanding the infection that are relevant to both individual patients and the general population will be examined to triangulate treatment and outcome effects. This collaboration will be a genuinely targeted, efficient, WA-driven, response to this viral threat and be a critical part of the clinical trials conducted in WA now and into the future. This body of work is being led by South Metropolitan Health Service (SMHS), but it will be embedded across the metropolitan hospitals and have the input of all partners.

Stream 2: WAHTN has 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 COVID19 and the health implications of infection prevention control strategies. Ethics approval has been obtained and the recruitment module is being tested. CIVIC will include collection of details about lifestyle, cardiac and respiratory risk factors as well as mental health and wellbeing. These will be delivered by online systems. The plan is 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 is on existing and

imminent clinical trials, and underlying supports, it is 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.

Stream 3: Clinical Trials There is no known treatment for COVID-19, however there are several good treatment candidates that can be tested through urgent clinical trials. These trials have the potential to save lives in WA. WA scientists and clinicians are well placed to commence a number of these trials, some of which are part of a larger international collaboration. The WA COVID-19 Research Collaboration has identified several trials which have the ability to be implemented immediately, with the most chance of success here in WA, these include (but are not limited to):

- 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 preventing infections in our health care workers.
- IFN trial – determining whether inhaled interferon (IFN) administered daily to subjects tested for COVID-19 during recommended quarantine, would reduce the spread of infection around the index case and their contacts.

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 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.

Right now, WA's medical research community is working together as "Team WA". Facilitated by WAHTN, it is identifying the major research projects and programs that are the most urgent, that is those that will save lives in the next few months. Additionally, it is building capacity that will allow for new ideas to emerge and be supported quickly in this *rapidly evolving landscape*.

To this end, WAHTN has sought to develop a nimble and rigorous process for allocation of research funds that will reduce the lengthy time delays and red tape that are integral to the usual funding application process. An expert scientific panel has been assembled under the Chair of the WA Chief Scientist, Professor Peter Klinken. This panel will assist and guide the WAHTN is distributing funds quickly, where needed.

Funding agencies are being asked to be as supportive as they can of the faster and more flexible approach required to fund research in this time of rapidly spreading COVID-19.

While a collaborative approach to funding is being sought, silo funding for particular aspects of the research plan will be respected, for example, some research Foundations are only able to fund projects or infrastructure within their area health service or organisation. This can be accommodated as the collaborative plan incorporates agreed research priorities that stretch across all area health services and health research sectors in WA.

Committed Funds

The State government has committed $3M from the Department of Health. Additional funding has been pledged from a number of hospital based Foundations and a further $1M is currently being sought from Lotterywest towards this collaborative endeavour.

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 Team who reacted early and have written the protocol underpinning the pre-clinical studies.

In the immediate future, committed funds will be used primarily for:

- expanding relevant (respiratory) clinical trials;
- ensuring there is sufficient infrastructure to cope with the expansion;
- engaging people to manage the additional work; and
- establishing a centralised data and bio banking system to ensure a collaborative approach.

Of the $3M committed by the Department of Health, a proportion can be used immediately to support infrastructure (including workforce) which is needed by the broader research community before the urgency of COVID-19 cases ramps up. This includes funds to progress standardised, uniform collection and storage of samples across the metropolitan health services, and the purchase of open access biobanking software along with -80C freezers.

The remaining funds from the Department of Health plus expected additional funds from other sources will be allocated through a competitive research process that has already been released, with applications closing on 8 April 2020.

Further funding beyond that already raised and committed will be required. The estimate is currently thought to be a total of $10M over the coming 12 months. The additional funds will primarily be directed to running a number of clinical trials showing early promise, these include ASCOT, REMAP-CAP, BRACE, and IFN, amongst others. Funding will also be required for the community CIVIC study (stream 2).

Flexible Emerging Priorities Fund

Given the early stage of the pandemic, some of the most important research question may not yet be apparent. There is a need to build a flexible funding source to support innovative research in a timely manner, as novel opportunities arise.

This fund will be administered through the rigorous processes set up by the WAHTN. It will 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
- Education interruption and its consequences for children

Budget

For a full breakdown of project costs across the 3 streams of work, refer to the Indicative Budget.

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 facilities 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

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. The group meets weekly.

Advisory group:

COVID Research Response (CRR) Team:

CIVIC Study:

WA Biobank Steering Committee:

EMRIA - Emergency Medicine Research and Innovation Alliance:

Sub-groups forming around work flows.

Work flow:

The WA COVID-19 Collaboration has agreed to three primary work streams:
Stream 1 – Pre Clinical
Stream 2 - Community
Stream 3 – Clinical Trials

Detail of each stream is 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*
- TKI *IFN and BCG trials*
- EMHS *ASCOT trial*
- SJOG *REMAP-CAP trial*
- CTDMC *CIVIC trial*

WAHTN
Central Coordination

Minister for Health

Department of Health

PRE-CLINICAL
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
- IFN
- BCG
- *Emerging Trials*

Stream 1: Pre-clinical

1. CRR Project (ISARIC protocol)

Lead: Toby Richards and Merrilee Needham (SMHS)

WAHTN is ideally placed to lead an international research program to respond to COVID-19. We propose a harmonised platform of integrated research to support clinical care in WA. The COVID Research Response (CRR) team brings 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 is 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 health services, Murdoch, the Australian National Phenome Centre (ANPC), 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 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 Australian National Phenome Centre (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; ED's, critical care and now COVID19 clinics providing high-fidelity acute patient management with embedded research practices, at all tertiary hospital sites; and the Australian National Phenome Centre 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 all researchers access to high quality data, samples and analysis minimising duplication, reducing costs and maximising output for patient care.

Additional information:
Work flow charts, key personnel, sample collection protocols and procedures can be found in detail on the WAHTN website xxxxxxxxxxxxxxx

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 optimization 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.

Nowhere is the ability to deliver a rapid prognostic metric of clinical condition more important than in 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.

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.

3. Biobanking

Oversight

With Medical Research Future Funds (MRFF), WAHTN commissioned a scoping project in 2018 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.

Future plans will address feedback on the establishment of a centralised biobank in WA.
WAHTN has invested in the TKI biobank cataloguing system OpenSpecimen. Upscaling on this software 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 and maximisation of collaborations with significant cohesive data output, without waste.

Current Set up

A Biobank manager was appointed last week and 5 x -80'C freezers unpacked and switched on in Perkins South. Security has connected the freezers to BMS and we are waiting for temperatures to stabilise over weekend before arming the alarms for the freezers (Basement Perkins South).

Discussions between all parties to establish sample types and consumables required for collection sites, labelling and banking protocols. Communications with OpenSpecimen have started to set up the WA online repository with testing commencing this week.

Next Steps

- Purchasing of Freezer racks, Cryoboxes (small and large) & Cryovials.
- Consumables for central site and external sites.
- Computer requirements/availability for basement freezer area and/or office for biobank Computer system requirements to handle Open Specimen etc.
- Data extraction protocols from OpenSpecimen for samples retrieval and replacement.
- Establish collection protocols for all samples from receipt to storing at offsite locations.

- Protocols for off sites to central Perkins South Facility.
- Protocols for movement of samples between basement and ANPC.
- Determine equipment needs for each site and central depository
- Set up RPH, SCGH and FSH PathWest centres.
- Staff for sites for sample collection and organisation.
- Establish freezers & freezer service contracts

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/

5. The Clinical Data and Analytics Platform (CDAP)

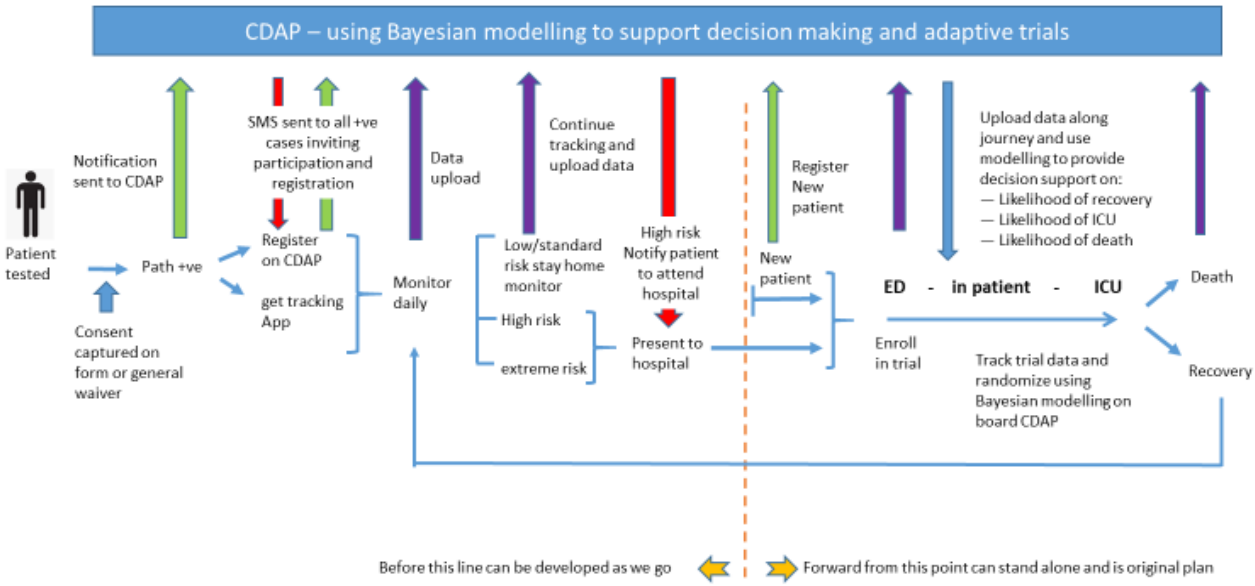
There is a critical need for health systems to be able to utilise their digitised health data for improving patient care. The Clinical Data and Analytics Platform (CDAP) will support the Australian response to the COVID-19 pandemic by creating a means to capture a broad range of clinical data and patient reported data based on the ISARIC protocol spanning the entire patient journey from diagnosis through management and into long term follow up.

Australia urgently needs a platform that:

- is a secure and nationally consistent repository of clinical, laboratory and imaging data for COVID-19 patients that is accessible by authorised users
- supports real-time analytics of the clinical data to inform best-evidence patient care;
- supports the implementation of adaptive clinical trials aimed at improving prevention, detection and treatment of COVID-19
- allows long-term (includes patient-reported) longitudinal follow up of individuals infected with COVID-19.

The Project will harness and adapt an existing suite of digital capabilities already in use within Australia. This rollout will be managed in close association with frontline clinicians who will do immediate User Acceptability Testing in real time. Moreover, the platform can accommodate existing clinical trial capabilities that are well-suited to responding to health emergencies, in particular Bayesian adaptive trials. This will permit a greater understanding of COVID-19 treatments and enable best evidence clinical decision making and patient care.

With recent changes to the Guardianship and Administration Act and appropriate governance authority the CRR will be well placed to digitalise and automate collaboration to the CDAP:


CDAP – using Bayesian modelling to support decision making and adaptive trials
Patient tested
Notification sent to CDAP
Path +ve
Consent captured on form or general waiver
SMS sent to all +ve cases inviting participation and registration
Register on CDAP
get tracking App
Monitor daily
Data upload
Continue tracking and upload data
Low/standard risk stay home monitor
High risk
extreme risk
High risk Notify patient to attend hospital
Present to hospital
Register New patient
New patient
Enroll in trial
Upload data along journey and use modelling to provide decision support on:
— Likelihood of recovery
— Likelihood of ICU
— Likelihood of death
ED - in patient - ICU
Death
Recovery
Track trial data and randomize using Bayesian modelling on board CDAP
Before this line can be developed as we go
Forward from this point can stand alone and is original plan

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.

In Wuhan, China, the case fatality rate (CFR) was elevated amongst patients with pre-existing comorbid conditions – 10.5% for CVD, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6.0% for hypertension, and 5.6% for cancer.

COVID-19 infection has 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. Thus 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 first wave of the COVID-19 pandemic caused a mental health crisis as it swept through China, and Australia should prepare to address similar problems as the number of infections increase.

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.

The coronavirus 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 mortality5-8. These otherwise modifiable CVD risk factors can be intensified by the effects of COVID-19 in isolation.

Currently, China has been implementing emergency psychological crisis interventions to reduce the negative psychosocial impact on public mental health but challenges persist.

Australia is in the cusp of COVID-19 infection explosion, thus community data on anxiety and depression must 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.

Working groups are being established in

- Mental Health – currently led by Sean Hood (UWA) and Peter McEvoy
- Sub-groups focussing on anxiety / depression / isolation
- Cardiovascular Health
- Child Health – working group currently led by Graham Hall (TKI) and others
- Workforce – led by Suzanne Robinson (Curtin) and Justin Manual (WACHS)
- Aged Care
- Respiratory – led by Fraser Brims and others
- Others to be developed, as required

CIVIC Study ethics approval has been fast-tracked and received through Curtin University Ethics Committee.

Links with established WA Cohort studies are being developed, including:

- Busselton Study – Alan James and Jennie Hui
- Raine Study – Leon Straker
- Mens Health Study – Bu Yeap
- Origins Study, TKI and others, as required

Many studies are doing their own activity so it would be good to align the work early, if possible.

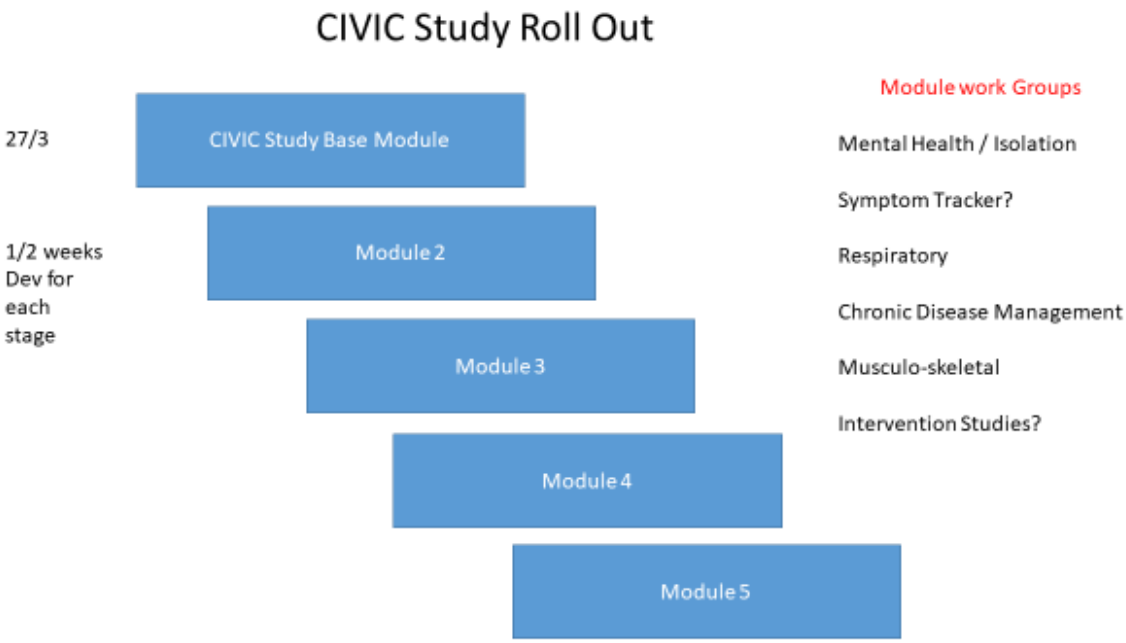
CIVIC Study data will incorporate:

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

Inter-operability

- Links with Acute Care Data system
  - Could be a look up on entry which would link symptom and history ISARIC data
  - Retain CIVIC ID number is system to link with other datasets (biobank/CDAP)

The roll-out of the base module is scheduled to commence on 6 April 2020, as per the projected timeline below.



Module Development
Modules will be developed by workgroups established from WA clinical expert groups and coordinated through the CIVIC platform.

Additional information:
Work flow charts, key personnel, sample collection protocols and procedures can be found in detail on the WAHTN website xxxxxxxxxxxxxx

Stream 3: Clinical Trials

WA's scientists and clinicians are at the leading edge of COVID-19 research. Already, many are part of international trials and collaboration that could change the course of the disease. With the relatively slower rate of infection here in WA, we have a unique opportunity to set up and participate early in a number of clinical trials that have the potential to save lives. The trials being considered under Stream 3 include the following.

1. ASCOT Trial

Treating established COVID infection to reduce deaths and improve outcomes

Overview:
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 treatments include 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 will run 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.

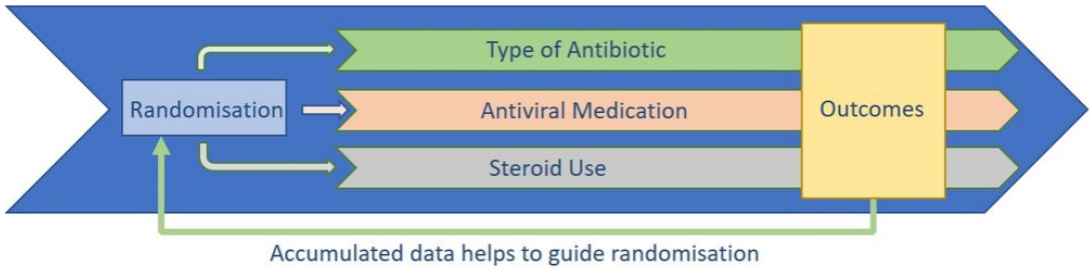
2. REMAP-CAP

A platform trial for ICU patients with COVID-19

Overview:
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)
- Immune modulation (no modulator / interferon-beta / anakinra)

Patients who are eligible for participation in REMAP-CAP will be 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

Overview:
With no vaccine and no preventative medical intervention anywhere close to providing protection for our health care workers, we need to consider alternatives. We are 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. 4000 front line health care workers in our hospitals will be invited to participate in the trial – 2000 in Perth, 2000 in Melbourne.

Timeframe:
Participant recruitment has commenced, so the need is immediate

4. THE PePCoCo Trial:

(Post-exposure-Prophylaxis Containing Coronavirus)

Stopping transmission of the virus from proven cases to their contacts

Overview:
People infected with coronavirus (SARS-CoV-2) have been known to shed virus and be contagious for up to 5 days prior to developing symptoms. This is likely to be a major driver of the rapidly expanding pandemic. This trial focusses on containing the virus by administering interferon (IFN) to positive cases and their contacts to reduce viral transmissions, particularly from those with no symptoms. We have just completed an exploratory study of interferon in Wuhan, Hubei Province, China (the original epicentre of the current pandemic). Our results indicate that IFN therapy hastened time to clearance of virus in upper airway secretions by a mean of 7 days. Since pre-symptomatic shedding of virus can start up to 5 days prior to symptom onset, our approach of a post exposure intervention to all contacts recently exposed to a case could possibly entirely interrupt the spread of the virus and with that the pandemic.

Timeframe:
Immediate, pending funding

Indicative Budget

This is indicative only while we work through what are our priorities, funding and more detailed analysis of each item.

Stream 1:

1. ADMINISTRATION SETUP

- 1 FTE Senior Trial manager coordinating oversight for WAHTN ($117k)
- 1 FTE Project Manager to coordinate funding, HR, contracts MOUs and IP ($150k)
- 1 FTE Trial Manager coordinating trial protocol harmonisation, ethics & governance ($117k)
- 1 FTE Database Manager coordinating portals & platforms ($150k)
- 1 FTE Biobank Manager ($140k)

BUDGET: $674,000

2. CLINICAL INFRASTRUCTURE AND SAMPLE COLLECTION

- 6 laboratory technicians to be placed into PathWest sites across key metropolitan sites to enable sample collection
  - 2 FTE at FSH ($240k)
  - 2 FTE at SCGH ($240k)
  - 2 FTE at RPH ($240k)
- 1 FTE Senior Database Manager to oversee large data storage, quality, validity and version control. Interface to patient data (REDCap), diagnostic pathology (PATH WEST) and BIOBANK data in a de-identified manner to all researchers ($150k)
- 1 FTE Project Manager to coordinate between the WA hospitals for data collection, also with ANPC and pan-WA researchers to facilitate research, remove duplication, promote collaboration and minimise research costs. ($130k)
- 3 FTE Trial Managers to facilitate clinical trials conducted via the research template to explore novel therapies to treat COVID-19, one for each metropolitan healthcare region
  - 1 FTE at FSH ($150k)
  - 1 FTE at SCGH ($150k)
  - 1 FTE at RPH ($150k)
- Consumables, to cover blood and urine sample collection, also PAXgene storage for genetic analysis ($1453 per 100 samples). It is envisaged that of 2.5 million people in WA, we will collect data on 100,000 patients in the next six months. This will require 1000 packs ($1.75m).
- Open label biobanking system, OpenSpecimen – including integration with REDCap system ($66,000)
- 2 x -80c freezers @ 35k each for sample storage ($70k)

BUDGET: $3,340,000

  - Personnel $1.45million
  - Biobanking (including consumables, freezers & software) $1.89million

3. RAPID ANALYTICS AND TRANSLATION

3 FTE (Laboratory technician staff and Bio-informatician) to be placed into ANPC.

They will use the deep metabolic analysis capacity of the ANPC 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.

BUDGET: $600,000

- Personnel $380,000
- Consumables and minor equipment $220,000

4. CLINICAL DATA AND ANALYTICS PLATFORM (CDAP)

The Project will harness and adapt an existing suite of digital capabilities already in use within Australia. This rollout will be managed in close association with frontline clinicians who will do immediate User Acceptability Testing in real time. Moreover, the platform can accommodate existing clinical trial capabilities that are well-suited to responding to health emergencies, in particular Bayesian adaptive trials. This will permit a greater understanding of COVID-19 treatments and enable best evidence clinical decision making and patient care.

These funds would support staff supporting the WA node of the national platform to undertake the following:

- Research Officer - Bayesian Mapping
- Community Involvement
- Project Management
- Biostatisticians (for Bayesian clinical trials)
- Community Reference Group Honorariums

BUDGET: $200,000

- circa $2M nationally
- NSW and QLD Health and Universities have already made significant commitments
- GAP for WA: $200,000

Stream 2:

5. COMMUNITY BASED RESEARCH PROGRAM SUPPORT (CIVIC Study)

- Senior Clinical Trials Project Manager ($150K)
- Software Development Team – integrated with WAHTN CTDMC – 2FTE ($240K)
- Project Coordinator ($120K)
- Administration Support ($100K)

BUDGET: $660,000

- Personnel $610,000
- Consumer fees $50,000

Stream 3:

6. Clinical Trials

BUDGET: $XX,000,000

Key Personnel

WAHTN leadership	Gary.Geelhoed@uwa.edu.au
CRR directors (Stream 1)	Toby.Richards@uwa.edu.au Merrilee.Needham@health.wa.gov.au
PathWest liaison	James.Flexman@health.wa.gov.au
Biobank	Aron.Chakera@health.wa.gov.au Michael Epis@uwa.edu.au
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Telethon Kids Institute	Jonathan.Carapetis@telthonkids.org.au
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Community Integration	Christopher.Reid@curtin.edu.au
Workforce planning and coordination	Kelly Beer@iiid.murdoch.edu.au
Post Graduates	Jay.Jay@uwa.edu.au
Medical Students	STRIVEWA@uwa.edu.au
Biobanking resources	Jennie.Hui@health.wa.gov.au

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

Appendix: Volunteer Workforce

Background
Engagement of volunteers to support COVID-19 research across sectors and institutions offers an unprecedented opportunity for WA-wide collaboration, promotion of research, and enhancing research training across the state.

Volunteers will be kept informed of progress of the programme set-up and will be called on as specific skills required, and/or contacts handed to workstream leads to coordinate their involvement as necessary.

Post-doctoral Students
Universities are currently collating details of all students undertaking research projects that are prevented by the COVID pandemic. These can be reallocated to support existing students and potentially moved to developing COVID trials (47 current ideas registered with the CRR).

Medical Students
Medical Student representatives from Curtin, UWA and UNDA will coordinate via STRIVE. The medical student population is ~1,500 across the 3 institutions. Research provides opportunities for students to meet AMA learning objectives -see below

Further Information
Discussions are currently open with SMHS to ensure appropriate access permissions and insurances for volunteers working within the project.
Discussions are currently open regarding research training resources and support for volunteers who are new to the clinical research environment.

STRIVE

The Student Research Initiative of Western Australia, STRIVE WA, is a research collaborative led by medical students from the University of Western Australia, the University of Notre Dame Fremantle and Curtin University. Their roles cover three key domains:

1. To facilitate medical student participation in audit and research.
2. To foster the growth of audit and research skills through active participation in all stages of the project cycle.
3. To advocate for student involvement in projects where there is opportunity.

In light of the COVID-19 pandemic, STRIVE WA has liaised with the state's three medical schools to oversee research-related activities in response to the outbreak. They are passionate about helping the healthcare system, devoted to playing a role in mitigating a potential health crisis and have the numbers to do so.
Their primary and secondary objectives are to:

1. Meaningfully contribute to the COVID-19 response through research-related activities
2. Enhance student learning experiences during withdrawal from clinical placements

Professor Toby Richards set up and has worked successfully with STRIVE WA in the past and is a strong advocate for student involvement in audit and research based on the platform: -
STARSurg – Student Audit and Research in Surgery

Students are able to adapt and be medically engaged from a more isolated working environment. The following graduate outcomes which apply to this initiative have been transcribed from the Australian Medical Council's 'Standards for Assessment and Accreditation of Primary Medical Programs' (see appendix for further details).