MEDICAL RESEARCH INSTITUTE OF NEW ZEALAND

Research Report 2020

The MRINZ is New Zealand's leading independent medical research institute and is a charitable trust. Our medical scientists are dedicated to investigating the causes of important public health problems, to use this knowledge to improve the prevention and treatment of diseases, and to provide a base for specialist training in medical research. Our particular focus is on research which has the potential to lead to improvements in clinical management.

Chairman's Report

It is with great pleasure that I write the preface for the 2020 Annual Report of the Medical Research Institute of New Zealand. The MRINZ is New Zealand's leading independent clinical research organisation, internationally recognised for its work. Its outstanding performance is highlighted by the benchmarking of the research performance of the MRINZ using independent metrics derived from SciVal, which show the impact and quality of the research published by the MRINZ markedly outperforms that of the New Zealand universities. These findings reflect the commitment of the MRINZ to undertake quality research that challenges dogma, and has the potential to increase knowledge and change clinical practice.

The MRINZ continues to make a major international impact with its clinically-based research aimed at improving the treatment of common medical conditions. The MRINZ has research programmes in the fields of alternative and complementary medicine, asthma, cardiothoracic surgery, emerging therapeutics, intensive care, Māori and Pacific Health, medicinal cannabis, oxygen therapy, pharmacy, pleural disease, rhinothermy, stroke and rehabilitation. Major advances have been made in many of these fields in the last year with the research findings having a significant impact on medical management and public health policy.

During 2020 the MRINZ has further increased its research productivity of recent years, with one publication now every 4 days. This is an extraordinary level of output, particularly when the major impact of the COVID-19 public health measures on the clinical trials programmes is considered. This productivity reflects the depth and breadth of the innovative research programmes, the international interest in the research undertaken, and the huge commitment of all staff to complete and publish their research projects.

On behalf of the Board I thank our patient volunteers, national and international partners, and funders who have contributed to the work of the MRINZ and played a crucial role in the advances in knowledge made by our dedicated staff.

I look forward to the future with the MRINZ continuing as New Zealand's leading independent medical research institute.

David Chamberlain

BEc, FNZSA, FIAA, CMInstD

CHAIR, MRINZ TRUST BOARD

The MRINZ is the most productive independent medical research organisation in New Zealand.

Director's Report

In 2001 the Medical Research Institute of New Zealand was established as an independent medical research organisation. Since then, the MRINZ has become internationally recognised for the quality and impact of its research. The MRINZ has remained strongly committed to its mission to investigate the causes of important public health problems, using this knowledge to improve the prevention and treatment of diseases, and to provide a base for specialist training in medical research. Our particular focus is on innovative research which has the potential to lead to improvements in clinical management.

There have been many significant achievements this year. The first is the extraordinary research productivity in terms of the quality and quantity of research undertaken. In 2020 the Institute has had 96 publications, including five in the New England Journal of Medicine, six in JAMA, and two in The Lancet, the world's most prestigious general medical journals.

The second is the increasing leadership role of the MRINZ in large scale, multicentre national and international randomised controlled trials. As a result of the experience gained in these studies, the MRINZ has the unique capability to act autonomously as the trial coordinating centre in New Zealand for large-scale pivotal, clinical trials in intensive care, respiratory medicine, cardiothoracic surgery, neurology and alternative/complementary medicine. Of particular note is the MEGA-ROX study which investigates the optimal oxygen regimen in critically ill patients and is being undertaken in 40,000 patients in 14 countries worldwide, representing the largest intensive care clinical trial ever undertaken.

The third significant achievement has been the further development of close collaborative relationships with the New Zealand biotechnology sector. It has not only led to major therapeutic advances, but also economic opportunities for these New Zealand companies. Supporting the emerging New Zealand biotechnology industry represents an important ongoing priority.

The fourth significant achievement has been the restructuring of our clinical research practice and database systems to achieve internationally recognised regulatory compliance for clinical trials, an important capability for the MRINZ, and New Zealand.

In the 2020 research report we highlight these and other achievements, and acknowledge the award of the Health Research Council of New Zealand 2020 Liley Medals to Mark Holliday and Mark Weatherall.

In 2021 the MRINZ is confident it will continue to meet its goals to investigate the causes of important public health problems in New Zealand and internationally and to use this knowledge to improve the prevention and treatment of diseases.

Richard Beasley

CNZM, DSc(Otago), DM(Southampton), MBChB, FRCP(London), FRACP, FAAAAI, FFOM(Hon), FAPSR(New Zealand), FERS, FRSNZ

Key Research Outcomes

Asthma

Precision medicine & treatable traits

The MRINZ is part of an international collaborative group that has proposed a paradigm shift in the management of asthma and COPD. This 'treatable traits' approach is based on the concept that asthma and COPD represent a continuum of different diseases that share biological mechanisms and present with distinct clinical, pathophysiological, and psychosocial features that can be observed and which require individualised treatment. Having advocated for the principle of treatable trait-based management of airways disease, including in the Lancet Commission on Asthma, the focus is now on moving to research of its implementation. During 2020, the MRINZ has helped design a roadmap to implementation which lays out the research steps necessary to formalise this approach and further test its efficacy. The MRINZ has been funded by the Health Research Council of New Zealand to undertake an innovative trial to test the feasibility of treatable trait-based asthma management and this trial will be completed in early 2021 in New Zealand and Australia.

Comment: Research undertaken by this international collaborative group has the potential to lead to a paradigm shift in the assessment and management of asthma worldwide.

Treatment of mild asthma

In 2019 the MRINZ published two landmark clinical trials of a novel therapeutic approach in mild asthma, showing that a 2 in 1 combination inhaled corticosteroid (ICS)/fast-onset long-acting beta-agonist inhaler taken as required for relief of symptoms is superior to either a fast onset short-acting beta agonist (SABA) alone for relief of symptoms, or regular ICS therapy with SABA as required. The 2 in 1 inhaler budesonide/formoterol reduced the FeNO, a measure of airways inflammation, indicating that this regimen can be referred to as 'anti-inflammatory reliever (AIR) therapy'. These studies contributed to what has been described as the greatest paradigm shift in asthma management for decades, the recommendation that a 2 in 1 combination inhaler is preferred over a SABA inhaler as reliever therapy in asthma.

In 2020 a series of secondary analyses from these two landmark clinical trials has been published providing insight into the generalisability of the findings, and how 2 in 1 AIR therapy has such a major effect in reducing the risk of severe exacerbations. It was shown that AIR therapy has similar efficacy in Māori and Pacific peoples to that in New Zealand Europeans, and that there are no particular characteristics of the patient such as inflammatory biomarker profile that influences the response, indicating that the benefit is obtained across all patients with mild asthma. AIR therapy was the preferred regimen of patients with asthma who had taken this randomised treatment during the study. In another analysis of patterns of use, it was shown that the timing of ICS dose when self-titrated to beta agonist use is more important than total ICS dose in reducing severe exacerbation risk in mild asthma.

Comment: These studies have led to a paradigm shift in clinical practice in New Zealand and internationally, improving outcomes in patients with mild asthma who have a poorly recognised yet important burden of disease.

Prevention of asthma

Paediatric asthma is a major public health problem in New Zealand. Prevalence rates for childhood asthma are amongst the highest in the world. There is an urgent need for research that leads to evidence-based primary prevention strategies to reduce the prevalence of asthma. This has led to consideration of the role of novel risk factors that may increase susceptibility to the development of asthma, and may be amenable to simple public health intervention programmes. One such risk factor, for which there is substantive evidence for a potential causative role, is the frequent use of paracetamol. The first ever randomised controlled trial investigating whether paracetamol increases the risk of childhood asthma has begun, and recruitment is on track, with one half of participants having been recruited. This study, led by Professor Stuart Dalziel from the University of Auckland, in collaboration with the MRINZ, is funded by the Health Research Council of New Zealand.

Comment: This study not only has the potential to determine whether increasing use of paracetamol over recent decades has contributed to the higher asthma rates, but also could lead to intervention strategies to prevent asthma.

Alternative and Complementary Medicine

The MRINZ continues to interface with this widely accessed therapeutic sector in supporting and advising the development of clinical trial programmes for New Zealand and international pharmaceutical and nutraceutical companies. Our completion of the 950 participant study demonstrating the efficacy of kānuka honey for cold sores in the globally unique Pharmacy Research Network has paved the way for further studies, with three new trials in cold sores, eczema, and acne in 2020. Our collaboration with the NICM Health Research Institute in Sydney has led to the development of the Australian Pharmacy Research Network, with its first trans-Tasman randomised controlled trial now underway. The addition of a clinical pharmacist to the in-house MRINZ team has allowed direct support to our pharmacist investigators, providing accredited continuing professional training for each study undertaken.

Comment: This programme continues to evolve in both capacity and reputation, expanding the evidence base for complementary and over-the-counter medicines.

Cardiothoracic Surgery

Intravenous Fluid Management

Patients undergoing surgery receive a significant amount of intravenous fluid especially immediately postoperatively in the ICU. We have previously documented fluid administration practice through observational studies and demonstrated in pilot work that a strategy aimed at decreasing the amount of fluid administered is effective and may lead to better clinical outcomes.

The Fluid after Bypass Study (FAB study) is a multicentre Phase IIb study designed to determine if reducing the amount of intravenous fluid given post-operatively will reduce ventilation hours and duration of ICU length of stay. Dr Rachael Parke is Chief Investigator for the FAB study which is funded by the Heart Foundation New Zealand and the Greenlane Research and Education Fund.

Comment: The FAB study is the latest phase of a programme of research investigating the use of intravenous fluids in cardiac surgical patients. Of note, it is the first cardiac surgical study conceived and developed in New Zealand to involve all five cardiac surgical centres within the public health system. The primary manuscript arising from this study is currently under review.

Atrial fibrillation

Stroke is a major and growing public health problem worldwide. In New Zealand 24 people suffer a stroke each day and almost one third will die as a result. There are significant socioeconomic and ethnic disparities - Māori and Pasifika have double the rates of stroke for people under 65 years and functional outcomes are worse.

Atrial fibrillation (AF) is an important risk factor for ischaemic stroke, which accounts for more than 80% of all strokes. AF increases the risk of stroke five-fold and is the underlying cause for over a third of ischaemic strokes. Patients with structural heart disease have even greater risk - the combination of heart valve disease and AF results in a 17-fold increased risk of stroke and worse outcomes. New Zealand has exceptionally high rates of rheumatic fever, approximately 60% of whom will develop rheumatic heart disease requiring surgical repair or replacement of heart valves. The Left Atrial Appendage Occlusion III Study (LAAOS III) aims to assess if opportunistic removal of the left atrial appendage (LAA) in patients with AF who are having cardiac surgery will reduce the long-term risk of stroke. It is funded by the Canadian Institute for Health Research and has 120 centres worldwide including three centres from New Zealand. The study has recently completed recruitment and patient follow-up is ongoing.

Comment: Amputation of the LAA is a simple and inexpensive procedure if performed at the same time as open-heart surgery. If it is shown to be effective in reducing stroke risk then it is likely to become the standard of care in these patients.

Cryopreserved platelet

Administration of platelets is an important treatment in the management of major bleeding from any cause. Currently in New Zealand platelets have a shelf-life of only seven days as they have to be stored at room temperature. Because of this, most smaller hospitals have very limited supplies in-house and there is significant wastage of donated platelets. The New Zealand Blood Service has developed a novel method of storing platelets at -80^{0}C and a simple method of thawing and reconstitution that should enable smaller hospitals to keep a more appropriate supply on site and significantly reduce wastage.

Cardiac surgical patients are amongst the highest users of platelets and the scheduled nature of their surgery allows easier recruitment into clinical trials. We are conducting a study of the safety and efficacy of cryopreserved patients in cardiac surgical patients at the five public hospitals that perform these procedures. If we demonstrate that cryopreserved platelets are safe and effective in this patient group then they will be made available across New Zealand.

Comment: Access to platelets is significantly limited in smaller and more remote hospitals. Our Health Research Council of New Zealand-funded study (CLIP II NZ) will evaluate the safety and efficacy of cryopreserved platelets.

COVID-19

The MRINZ has been playing its part to conduct research, improve knowledge and collate evidence on COVID-19. During Alert Level 4, we surveyed New Zealand's population using social media to determine the composition of New Zealand's "bubbles". We found that bubbles mostly had one household, and a high proportion contained essential workers and/or vulnerable people. We also liaised with Regional Public Health to explore the epidemiological and clinical characteristics of COVID-19 in the Greater Wellington region. The demography of cases in Wellington reflected the imported nature of cases in the first wave, with the majority of cases being middle aged, of European descent, higher socioeconomic background and related to travel. Vulnerable communities such as the elderly, ethnic minorities and deprived households were largely spared.

Given the rising death toll of COVID-19 internationally, we analysed time-trends of mortality in 22 countries. The analysis found that the number of deaths attributed to COVID-19 is underestimated by at least one third. All-cause mortality also preceded the increase in COVID-19 mortality in most countries in which definite spikes in COVID-19 mortality occurred.

New Zealand on the other hand, had a lower burden of disease and deaths due to COVID-19 due to the stringent public health interventions. In a letter published in The Lancet, we investigated the temporal association between these public health measures and all-cause mortality. We reported that the mean weekly death rate during and post-lockdown was 11% lower than in the period 2015 to 2019.

The reduction in all-cause mortality was apparent after five weeks of lockdown, and remained below historical levels despite public health restrictions easing, during a period usually marked by an increase in mortality due to seasonal influenza and pneumonia.

To explore these observations further, we also examined the prevalence of influenza not only in New Zealand, but in the southern hemisphere, using data from the WHO and ESR. In another letter published in The Lancet, we reported that across countries in the temperate southern hemisphere, there was little influenza activity since mid-April 2020. The very low numbers of influenza cases this winter may be a welcome side-effect of the public health measures implemented to combat COVID-19.

In a third publication in The Lancet, we commented on the effective ways in which the medium of comics may engage the public in science communication about the pandemic and support mass adherence to public health measures designed to break the chain of infection.

Comment: This research programme was developed in order to tackle the lack of knowledge surrounding COVID-19. The MRINZ continues to conduct research in this field, adding to the existing literature particularly from a New Zealand perspective.

Emerging Therapeutics

Early Phase studies

The MRINZ now has an early phase clinical trials unit which undertakes 'Proof of Concept' studies of novel pharmaceutical compounds in asthma. These proof of concept studies fit between first time in human studies (Phase I studies) where safety is assessed in a small number of healthy adults and Phase II studies where both safety and efficacy is assessed in a larger number of patients with the disease of interest. These proof of concept studies usually involve administration of increasing doses of the new medication, with intensive monitoring and assessments. These are often undertaken as inpatient studies, in which patients may be admitted to a clinical trials unit for up to two weeks.

Comment: The capacity to undertake these early phase studies is based on the strong relationship the MRINZ has with our asthma volunteers, and with the Capital & Coast District Health Board Clinical Trials Unit located at Wellington Regional Hospital.

Intensive Care

Stress ulcer prophylaxis

The administration of stress ulcer prophylaxis (SUP), either with a Proton Pump Inhibitor (PPI) or a Histamine-2 Receptor Blocker (H2RB) was recommended in international guidelines and incorporated into quality-oriented checklists for care of ICU patients. Our recent data show that PPIs and H2RBs are routinely used for SUP, with the choice of medication probably not based on patient factors, but instead dependent on clinician preference or unit policy. This practice variation reflected the lack of definitive evidence comparing PPIs to H2RBs in the ICU setting. The overall influence of the opposing risks of upper GI bleeding and SUP-related infectious complications on in-hospital mortality was unknown. We led a multicentre, multinational trial comparing the safety and efficacy of PPIs vs H2RBs in almost 27,000 mechanically ventilated ICU patients. This trial was funded by the Health Research Council of New Zealand and the Intensive Care Foundation. The results, which were published in the Journal of the American Medical Association in January 2020, suggest that PPIs might increase the risk of dying in hospital compared to H2RBs. As SUP in ICU is provided to at least 2.5 million people a year, implementation of these findings is expected to save 25,000 lives per year in developed countries alone.

Comment: This international study, which included sites in New Zealand, Australia, United Kingdom, Ireland, and Canada, is to date the largest intensive care clinical trial ever published.

Timing of initiation of kidney dialysis in ICU patients with acute kidney injury

Acute kidney injury (AKI) is a common and devastating complication of critical illness. Once AKI is established, treatment is largely supportive and no intervention has been found to restore kidney function or improve overall survival. Renal replacement therapy (RRT), usually in the form of haemodialysis, is frequently needed to manage patients with severe AKI. Such patients have an in-hospital mortality that consistently exceeds 50% with delays in RRT initiation implicated as a possible contributor. The optimal timing of RRT initiation was an existing knowledge gap and a clear priority for investigation. The STARRT-AKI trial has evaluated whether earlier/pre-emptive/accelerated RRT initiation is associated with enhanced survival compared to a conservative strategy for initiation of RRT, which is driven by conventional indications and clinician judgement. This multinational trial, led in New Zealand by the MRINZ and funded by the Health Research Council of New Zealand was published in the New England Journal of Medicine in 2020. It showed that accelerated RRT initiation did not reduce mortality and was associated with an increased chance of leaving patients dialysis-dependent after six months.

Comment: The STARRT-AKI trial provides high level evidence that initiation of kidney dialysis in critically ill patients with acute kidney injury can be deferred until a clear clinical indication for dialysis is present. This approach will reduce cost and decrease the risk of patients ending up dialysis-dependent.

Duration of antibiotic therapy in ICU patients with bacteraemia

Up to 50% of antibiotic use is inappropriate, with excessive duration of treatment the greatest contributor leading to antibiotic resistance. Shorter duration antibiotic therapy (≤7 days) has been demonstrated to be as effective as longer duration in a range of infections. However, high-grade randomised trial evidence is lacking for the treatment of patients with bloodstream infection, which affects 15% of critically ill patients. The MRINZ is leading the New Zealand component of the BALANCE trial which is a large multi-centre international study to determine if critically ill patients with bloodstream infection can be effectively treated with a shorter rather than longer duration of antibiotic therapy. As well as contributing to the international effort, local recruitment will provide specific data on New Zealand patients and enhance translation of results into practice. The New Zealand contribution to the BALANCE trial is funded by the Health Research Council of New Zealand.

Comment: Antibiotic resistance is one of the major global threats to mankind, and this study will inform whether shorter antibiotic courses may be one initiative which reduces the risk of antibiotic resistance and other complications from longer courses.

Community-acquired pneumonia

Pneumonia is a common reason for admission to hospital, and the most common site of severe infection causing organ failure and need for intensive care. However, for many aspects of treatment we do not know which approaches lead to the best outcomes. In conjunction with colleagues in Australia, Europe, United Kingdom, North America and Asia we have developed a new research design which can simultaneously investigate the effect and safety of multiple different treatment options in multiple "domains" of care. The design is integrated within the usual clinical processes and patients will benefit from the knowledge that is gained as the trial proceeds. Analysis using Bayesian statistics, undertaken at regular intervals, informs the treatment allocations for new participants, and each domain continues until a clear answer is determined and the best treatment becomes usual patient care. This contrasts to the usual design where only a single hypothesis is tested, analysis does not occur until a fixed sample size is reached, and answers are often indeterminate.

In response to the COVID-19 pandemic, this study has been significantly expanded to evaluate potential treatments for this viral respiratory tract infection including corticosteroids, antivirals, immune modulation agents, antibody treatments, convalescent plasma, anticoagulation therapies, and others. This domain shows the potential for this novel trial design to respond quickly to public health crises, where there may be the lack of an evidence base for the management of newly emergent infectious diseases. The MRINZ has a senior role in the coordination and management of this trial, which is funded by the Health Research Council of New Zealand, Australia's National Health and Medical Research Council, the Canadian Institute of Health Research, and a European Union FP7 grant.

Comment: This study contributed to the evidence base that shows that steroid therapy reduces the risk of death in patients with severe COVID-19 disease, a finding which has led to this treatment becoming a standard of care within 6 months of the onset of the COVID-19 pandemic. The potential exists for this novel study design to be applied to other research questions both within and beyond intensive care medicine.

Anti-fibrinolytic treatment in severe trauma

Bleeding causes most early deaths from major trauma, and is often exacerbated by abnormalities in blood clotting. Tranexamic acid (TXA) reduces abnormal clot breakdown, and is known to reduce bleeding in other settings such as major surgery. There is some evidence from low and middle income countries that early prophylactic use of TXA improves outcomes after traumatic injury. However, as it is uncertain if the possible benefits outweigh the risks (dangerous blood clots) in advanced trauma care systems, with the availability of other rapid and effective treatments to stop bleeding and improve blood clotting, TXA is not routinely used prophylactically in New Zealand. In this study, severely injured patients at risk of abnormal blood clotting are randomly allocated to receive TXA or placebo, commenced by ambulance staff at the scene and completed in hospital, in addition to usual treatment. Patients are then assessed while in hospital and followed for six months to determine if treatment with TXA improves survival and/or reduces disability. This international trial is being led in New Zealand by the MRINZ and is funded by the Health Research Council of New Zealand, Australia's National Health and Medical Research Council, and also recently funded in Germany.

Comment: If effective without additional risk, prophylactic TXA will become standard treatment in ambulance services and Emergency Departments.

Erythropoietin in severe trauma

Severe injury activates multiple chemical pathways causing inflammation and harming vital organs, which can lead to long-term disability and death. The kidney hormone erythropoietin controls red blood cell production and is a common treatment for anaemia, and also reduces inflammation. Previous studies suggest erythropoietin may reduce death and serious disability after severe injury, without an increase in side effects.

This study will involve 2500 adults with severe injuries in New Zealand, Australia, Republic of Ireland, France and Finland who will receive either erythropoietin or a placebo injection, in addition to usual treatment. Participants will be assessed after six months to determine their survival and level of disability. The MRINZ is co-ordinating New Zealand's participation in this trial which is funded by the Health Research Council of New Zealand, Australia's National Health and Medical Research Council, and the Irish Health Research Board.

Comment: If this simple treatment can reduce death and disability after severe injury, it would have practice-changing effects worldwide.

Key Research Outcomes

Medical Cannabis

Cannabis-based medicines are a polarising field of therapeutics, with a high degree of scrutiny and disparate opinion from the public and practising clinicians. The recent evolution in legislation around cannabis, both internationally and in New Zealand, has seen a call for clinical research programmes for novel products in development. The MRINZ is a founding member of the Medicinal Cannabinoid Research Collaborative (MCRC), formed in response to the rapidly changing landscape of cannabis legislation in New Zealand, and is primarily focused on the therapeutic use of cannabis-based products. Other members of the MCRC include Caduceus Medical Development, the Institute of Environmental Science and Research, Lincoln University, Plant and Food Research, the University of Otago and Victoria University, Wellington. This collaborative group consolidates New Zealand's expertise and capability, ensuring robust clinical research of cannabis-based medicines is undertaken, with particular emphasis on molecular pharmacology, manufacturing, safety, quality control, and efficacy. We aim to set standards for the development and/or testing of pharmaceutical grade cannabis-based medicines in New Zealand and through international collaboration add to the evidence for or against the use of cannabis-based medicines in specific clinical conditions.

Under the umbrella of the MCRC we are able to conduct high quality pharmacokinetic and tolerability studies for new products, pilot studies, phase II studies and definitive phase III/IV randomised controlled trials. Through the testing of pharmaceutical grade products in defined patient populations in our multi-specialty clinician network in New Zealand, we are well positioned to integrate findings into clinical guidelines. The MRINZ is expecting to receive the first New Zealand cannabis-based medicines to commence safety and tolerability studies in 2021.

Comment: This research programme has been developed in response to the changing legislative landscape with respect to cannabis-based medicines in New Zealand. While cannabis-based medicines can now be prescribed it is important to undertake rigorous clinical trials to ensure the potential efficacy and safety is determined for different medical disorders.

Māori and Pacific Peoples' Health

The MRINZ is committed to improving Māori Health through relevant health research. In 2020 the main focus has been on workforce development and analysis of the efficacy of therapeutic interventions in Māori and Pacific participants in major randomised controlled trials.

The MRINZ has been fortunate to have the opportunity to employ Māori researchers at different levels of their medical and specialist training. Under the guidance of Dr Matire Harwood (Ngāpuhi) a team of Māori and Pacific medical research fellows has been developed, including Selwyn Te Paa (Ngāti Whātua, Ngāpuhi and Waikato-Tainui) and Johanna NeeNee (Tulaele Faleata, Lalomanu Aleipata, Salesatele Falealili of Samoa), both medical students, and Dr Jordan Te Whaiti-Smith (Ngāti Kahungunu, Ngāi Tahu, Ngāpuhi), a recent medical graduate who has a focus on health inequities in our rangatahi through his role in representing New Zealand on the Lancet Commission on Adolescent Health. Dr Alice Reid (Te Rarawa), a geriatric physician, is undertaking research on health inequities presenting through intensive care and developing a partnership with New Zealand geriatric services to better understand and promote effective strategies for frailty management.

The strong recruitment of Māori and Pacific patients in key randomised controlled trials has enabled analyses of the efficacy of novel treatment approaches specifically in these populations. In 2020 this approach has demonstrated that the novel combined 2 in 1 budesonide/formoterol inhaler taken as a reliever has similar benefit in Māori and Pacific patients to that of New Zealand Europeans in the treatment of mild asthma. In the TARGET study it was shown that in Māori a lower than recommended level of enteral feeding was just as effective and associated with fewer side effects as full calorie replacement, similar to other New Zealanders. Both these analyses showed that in both asthma and the intensive care, the recommended therapeutic approach demonstrated in the clinical trials was generalisable to all New Zealanders regardless of ethnicity.

Comment: Improving health outcomes for Māori requires a strong focus on equity and evidence-based action, and prioritising the improvement of Māori health through relevant research across the organisation.

Oxygen

Closed loop oxygen control

Oxygen is one of the most commonly administered drugs to patients who are unwell in hospital. Previous research has demonstrated that giving either too much or too little oxygen is harmful to patients and that oxygen should be adjusted to keep a patient's blood oxygen level within a "target" range. This is known colloquially as the concept of "swimming between the flags". In clinical practice this is difficult to achieve; previous studies have shown patients only spend around 60% of the time with blood oxygen levels in the target range while receiving oxygen. The MRINZ has been working with Fisher and Paykel Healthcare to investigate a novel method of oxygen delivery which involves the use of a closed-loop feedback system to automatically adjust the oxygen concentration in order to maintain blood oxygen levels within a target range. It is hypothesised that this way of adjusting oxygen will result in patients receiving the correct amount of oxygen for a greater proportion of time and thereby reducing the risk of harm from either over or under-oxygenation. A number of studies are underway investigating this novel method of oxygen delivery.

Comment: This technology is likely to improve the care of unwell patients who need oxygen in hospital and may lead to a paradigm shift in the way oxygen is delivered.

Critical illness

Oxygen is a common treatment in patients who need care in an ICU. In partnership with investigators in Australia we undertook a 1,000 participant multicentre randomised controlled trial to evaluate oxygen therapy in adults requiring life support in Intensive Care (ICU-ROX). The trial was funded by the Health Research Council of New Zealand and was published in the New England Journal of Medicine in 2020. This study suggested no overall benefit from liberal oxygen therapy and confirmed the safety of using oxygen conservatively. In patients who had suffered a cardiac arrest prior to ICU admission, conservative oxygen therapy was associated with improved patient outcomes. The ICU-ROX study laid the foundation for the Mega-ROX trial, a 40,000 participant global trial of oxygen therapy in ICU patients requiring life support, which the MRINZ is leading with funding from the Health Research Council of New Zealand and the Alpha Charitable Trust.

Comment: The Mega-ROX trial will be the largest clinical trial ever undertaken in Intensive Care, and will be the definitive study that informs clinical practice in the use of oxygen therapy in patients on life support in the ICU.

Pleural Disease

The MRINZ has had a key role in the largest randomised controlled trial of the treatment of pneumothorax (collapsed lung) ever undertaken. The study challenged the prevailing dogma that the preferred treatment is an invasive interventional approach based primarily on the insertion of a chest drain, often followed by thoracic surgery. This clinical trial was published in the New England Journal of Medicine and showed that a conservative approach, in which the patient is simply observed, with an interventional procedure only undertaken if necessary to manage a complication, is the preferred management. The rates of resolution of the pneumothorax and time to symptomatic recovery were similar for the two strategies, however the conservative approach resulted in less harm, with fewer serious side effects, fewer surgical procedures, less time in hospital, and less time off work. The study was undertaken over a five year period across 33 hospitals in Australia and New Zealand, and was funded in New Zealand by the Health Research Council of New Zealand.

Comment: The study findings should change practice in New Zealand and globally, and result in a substantive reduction in morbidity and economic cost associated with the management of pneumothorax.

Rhinothermy

The common cold is the most frequent acute respiratory illness globally with most adults experiencing between two and four colds a year. The human rhinovirus (HRV) is responsible for about two thirds of all colds and is an important cause of severe exacerbations of asthma and COPD in adults. There is no proven, effective treatment for HRV, or for the symptoms of the common cold, despite the availability of many 'over the counter' products.

HRV replication, and that of other respiratory viruses such as influenza, is inhibited in the presence of elevated temperatures within the febrile range. This has led to interest in the therapeutic intervention of rhinothermy in which heated, humidified air is delivered at high flow directly to the upper respiratory tract. The purpose of rhinothermy is to reduce viral replication and thereby reduce the severity of respiratory tract infections.

We have recently completed a large randomised clinical trial of the effects of therapeutic rhinothermy, with the delivery of humidified air, heated to 41°C for 2 hours on five consecutive days, compared with sham rhinothermy, on the severity or duration of common cold illnesses. The findings should inform not only the potential for this therapeutic approach in the treatment of the common cold, but also influenza for which there is substantive evidence of temperature sensitivity and a greater public burden of disease.

Comment: This research programme utilises novel technology developed by Fisher and Paykel Healthcare. The collaboration represents an important priority for the MRINZ as part of its commitment to support the New Zealand biotechnology industry.

Stroke

2020 was a significant year for the Stroke/Rehabilitation programme with the publication of the Heath Research Council of New Zealand-funded randomised controlled trial 'Taking Charge After Stroke – the TaCAS study'. This randomised trial showed that the goal orientated 'Take Charge session', developed in a previous clinical trial by the MRINZ, is effective for a wide range of stroke-affected individuals. This multicentre study which was based in seven district health boards in New Zealand studied 400 people discharged to community living after a stroke, showed a statistically and clinically significant effect on quality of life and independence 12 months after stroke. Rehabilitation teams around the world are starting to use Take Charge with translations of the intervention into Portuguese (for Brazil), Estonian and Russian so far. Studies using Take Charge in conditions other than stroke have been completed (COPD) and planned (mild cognitive impairment).

Comment: This study, which backs up our previously positive randomised controlled trial of the 'Take Charge session' in Māori and Pacific people with stroke (the MaPSS study) provides further evidence that this simple, cheap, safe intervention could make a significant impact on stroke outcomes in New Zealand and elsewhere. To put this in context, if two Take Charge sessions (cost $NZ 200) were provided to every person with stroke in New Zealand who was discharged to community living, around 600 more people would be independent for activities of daily living at 12 months after the stroke. We can compare this to the treatments currently provided in the early phase of acute stroke. Acute intravenous thrombolysis and mechanical thrombectomy combined, if applied at aspirational (rather than current) levels, would lead to an extra 200-250 people being independent and at considerably higher cost.

MRINZ Research Performance

In 2020, a major audit of the MRINZ's research performance was undertaken through SciVal, a research metric database that contains research metrics on over 14,000 research organisations worldwide. The SciVal database allows standardised comparisons with universities and other academic organisations, both in New Zealand and internationally. The two most commonly used output metrics to benchmark an organisation's academic impact are:

1. ***Field weighted citation impact:*** This value represents the citation level for a publication output, relative to the expected number in any given field. The values are weighted to accommodate differences in citation patterns across disciplines, allowing an adjusted comparison between organisations. A value of 1.0 means an organisation's work is being cited at the expected level, a value of 1.5 means 50% more citations than average and 0.5 means 50% less. The higher the citation index above 1.0, the higher the impact of the research.
2. ***Publications in top 10% journal percentiles by SJR:*** This represents the proportion of publications in the top cited journals. The SJR, or SCImago journal and country rank, is an independent metric that quantifies the scientific influence of journals.

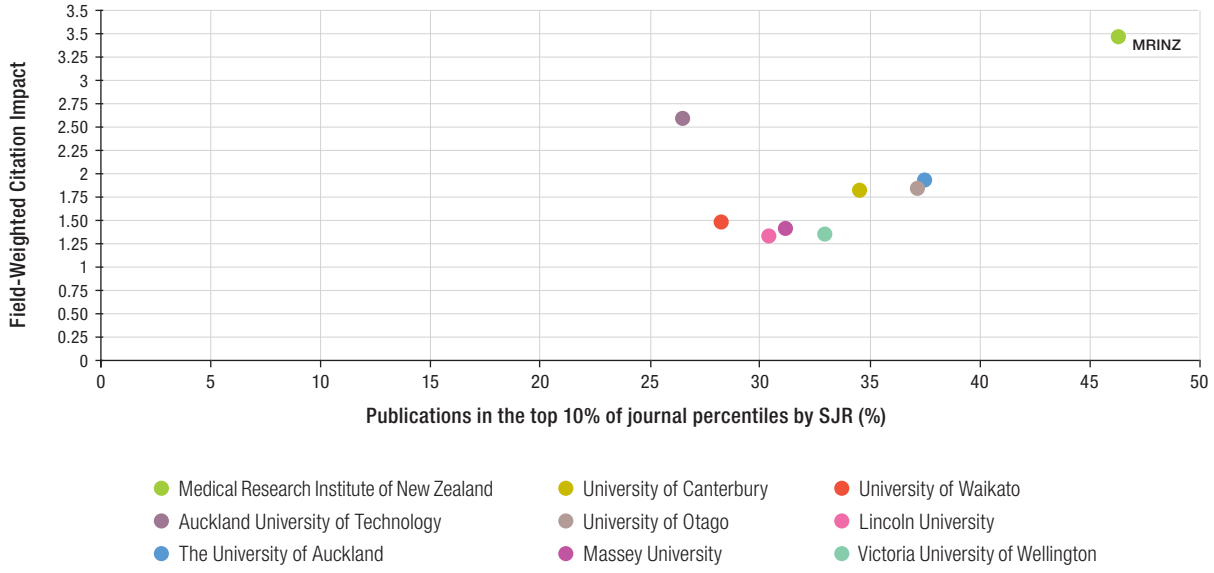
Together the above metrics can provide a standardised analysis of institutional performance relative to the rest of the world, a specific specialist field of interest or a specified group of similar organisations. The most commonly accepted data period is five years, excluding the full year immediately past to allow for complete indexing of academic output in Scopus.

MRINZ Performance 2015 to 2019

For the 2015 to 2019 period the MRINZ outperformed the New Zealand overall standard and the eight New Zealand Universities in both metrics.

Figure 1: Plot of field-weighted citation impact (y-axis) and publications in the top 10% of journal percentiles (x-axis) for the MRINZ, New Zealand overall and the New Zealand Universities.

SciVal™ database, Elsevier B.V., http://www.scival.com



The MRINZ is meeting its goal of publishing high quality research of global interest which increases knowledge and has the potential to change clinical practice.

Collaboration

The audit also assessed the capacity of the MRINZ to undertake international multi-centre randomised controlled trials. Since 2015 the MRINZ has collaborated with 432 institutions world-wide resulting in 250 publications (**Figure 2**).

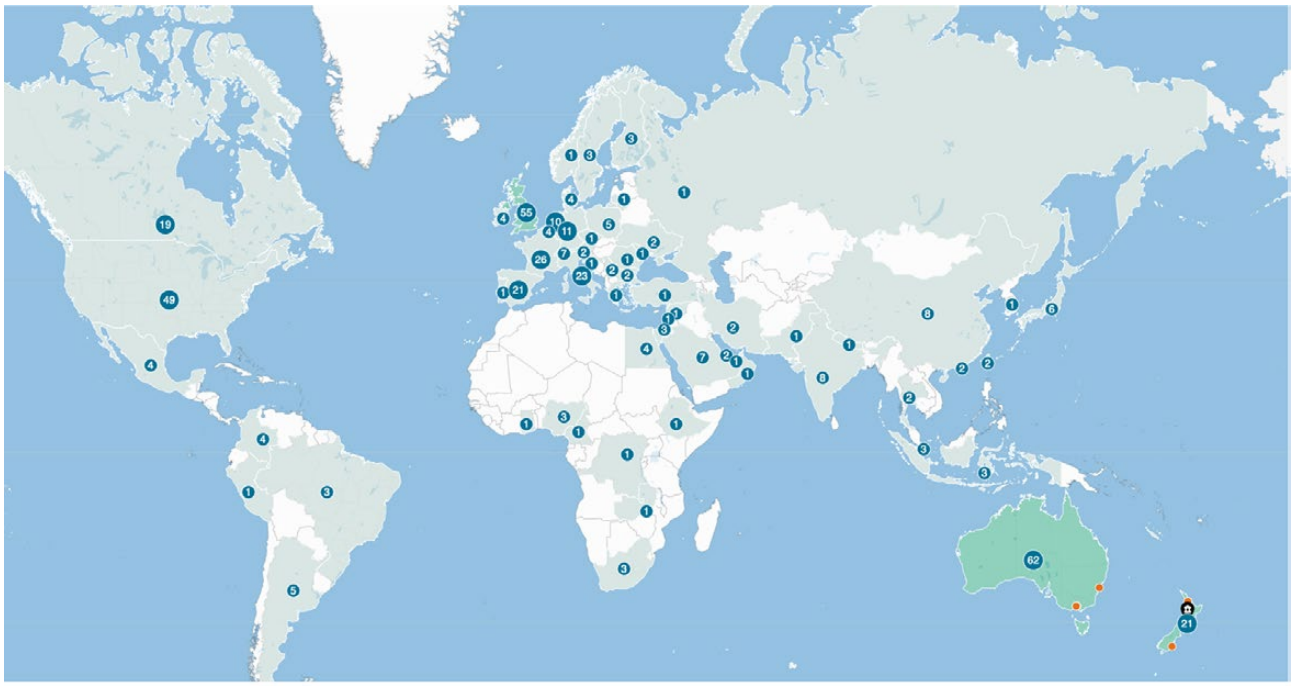
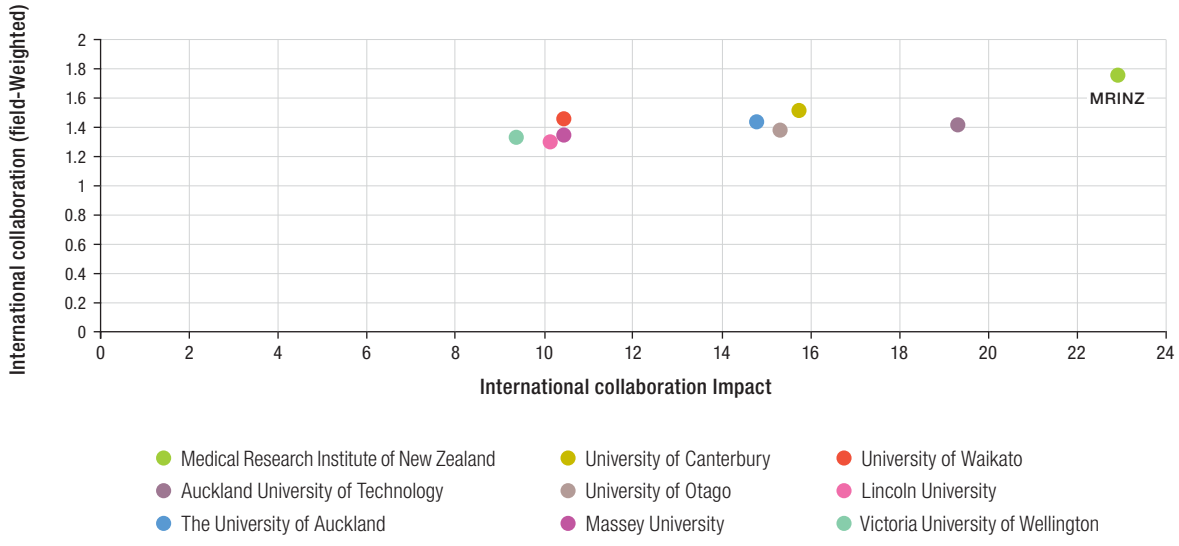


Figure 2: Institutional collaborations around the world over the period 2015 to 2020. MRINZ

The quality of publications derived from the international collaborations is shown in **Figure 3**. This demonstrates an output that is 177% the expected international collaboration worldwide for publications in the field of clinical research (*y–axis: international collaboration* [*field-weighted*]). The average number of citations for internationally collaborative MRINZ publications is 22.9 (*x-axis: international collaboration impact*).

Figure 3: Field-weighted institutional collaborations against international collaboration impact for the MRINZ versus New Zealand Universities since 2015

SciVal™ database, Elsevier B.V., http://www.scival.com



MRINZ Research Performance

Health Research Council of New Zealand Liley Medal 2020

Mark Holliday and Mark Weatherall were awarded the Liley Medal for their senior roles in the Novel START study, published in The New England Journal of Medicine in May 2019. Novel START was the first study to demonstrate that the 2 in 1 asthma inhaler budesonide-formoterol taken as needed was superior to the two recommended standard treatment approaches for mild asthma in adults. It showed that as-needed budesonide-formoterol reduced the risk of severe asthma attacks compared with regular scheduled maintenance budesonide (an inhaled corticosteroid; ICS) plus as-needed salbutamol, (a short-acting beta-agonist; SABA) and when compared with as-needed salbutamol. Importantly it was the first study to demonstrate that as-needed budesonide-formoterol reduced FeNO, a marker of airways inflammation, indicating that this regimen can be considered 'anti-inflammatory reliever therapy'.

The study has been referenced in both international (GINA) and local New Zealand asthma guidelines, as key evidence in support of their recommendations that as-needed ICS-formoterol reliever therapy is preferred to SABA reliever therapy in mild asthma, and is an alternative to maintenance ICS plus a SABA reliever. The GINA guidelines have stated that this is the most significant paradigm change in asthma management in the last 30 years.

Mark Holliday and Mark Weatherall at the Royal Society Te Apārangi Research Honours 2020 Ceremony at Government House,

The MRINZ investigates the causes and treatment of important public health problems

Collaborations

New Zealand

Auckland

Auckland City Hospital: Magdalena Butler, Yan Chen, Keri-anne Cowdrey, Stuart Dalziel, Eamonn Duffy, Karina Duffy, Eileen Gilder, Michael Gilham, Jane Hallion, Rupert Handy, Peter Jones, Davina McAllister, Colin McArthur, Rachael McConnochie, Shay McGuinness, Lynette Newby, Caroline O'Connor, Rachael Parke, Felicity Pugh, Stephen Ritchie, Sally Roberts, Samantha Ryan, Timothy Short, Catherine Simmonds, Eunicia Tan, Davina Taylor, Margaret Wilsher, Melissa Woolett

Fisher & Paykel Healthcare Ltd: Lewis Gradon, Robert Kirton, Melanie Moylan, Kevin O'Donnell, James Revie, Stanislav Tatkov, Anton Gulley, Philip Rowe, David Russell-Park

Helius Therapeutics: Paul Manning, Gavin Pook, JP Schmidt

Middlemore Hospital: Jeffrey Garrett, Dinuraj Girijadevi, Geoff Green, Alex Kazemi, Vivian Lai, Chris McKinlay, Susan Morpeth, Hamish Read, Rima Song, Eunicia Tan, Tony Williams, Conroy Wong

North Shore Hospital: Hassan Bhally, Robert Everitt, Danielle Hacking, Ywain Lawrey, Lesley Maher, Duncan Reid, Robert Russell

Optimal Clinical Trials: Barney Montgomery, Liz Smaill

Plant and Food Research: Deborah Tod

St John Ambulance: Bridget Dicker, Tony Smith, Verity Todd

University of Auckland: Innes Asher, Amy Chan, Philippa Ellwood, Matire Harwood, Peter Jones, Thomas Lumley, Richard J Milne, Ed Mitchell

Christchurch

Canterbury Health Laboratories: Meik Dilcher, Lance Jennings.

Christchurch Hospital: David Bowie, Brandon Burke, Tara Burke, David Closey, Ros Crombie, Neil Davidson, Alistair Gibson, Seton Henderson, Louise Hitchings, David Knight, Jan Mehrtens, Sarah Metcalf, Stacey Morgan, Anna Morris, Christina Quigley, Jay Ritzema-Carter, Jessica Roberts, Geoffrey Shaw, Katherine Townend, Kymbalee Van der Heyden

Princess Margaret Hospital: Carl Hanger

University of Otago, Christchurch: Lutz Beckert, Doug Sellman

Dunedin

Dunedin Hospital: Ben Brockway, Amie Eden, Dawn France, Robyn Hutchison, Pawel Twardowski, James Ussher

RMC Research: Jim Reid

University of Otago: Bob Hancox, Michelle Glass, William Leung, Trudy Sullivan

East Coast

Rua Bioscience: Manu Caddie, Damian Skinner

Hamilton

Waikato Hospital: Amelia Butler, Kelly Byrne, Cat Chang, Grant Christy, Katy Cryer, Madison Goulden, Bob Hancox, Paul Huggan, Gay Mans, Robert Martynoga, Renesh Nair, Livia Schischka, Jonathan Termaat, Kara Trask

Waikato University: Marius Rademaker

Lakeland Clinical Trials Waikato: Mike Williams

Hawke's Bay

Hawke's Bay Hospital: Matthew Bailey, Llesley Chadwick, Ross Freebairn, Dan Garner, John Gommans, Michael Park, Penelope Park

Nelson

Nelson Hospital: Alex Browne, Petra Crone, Jette Koelle, Charlotte McNab

Palmerston north

Caduceus Medical Development: Tara Creaven-Caspasso

Rotorua

Rotorua Hospital: Ulrike Buehner, Massimo Giola, Erin Williams

Lakeland Clinical Trials Rotorua: Mike Williams

Taranaki

Taranaki Base Hospital: Jonathan Albrett, Carolyn Jackson, Simon Kirkham, Cathy Vickers

Tauranga

Clinical Horizons: Andrew Corin, Colin Helm

Papamoa Pines Medical Centre: Davitt Sheahan

Tauranga Hospital: Troy Browne, Emma Downard, Jennifer Goodson, Kate Grimwade, Owen Keet, Jacqueline Shippey

Zealand Health Manufacturing: Mike Coory

Collaborations

Wellington

Asthma and Respiratory Foundation of New Zealand: Teresa Demetriou, Letitia Harding

Institute of Environmental Science and Research: Mary-Jane McCarthy, Helen Poulsen

Hutt Hospital: Carmel Chapman, Marianne Falconer, Sanjay Patel, Betty Poot, Andrew Stapleton, Justin Travers

Malaghan Institute of Medical Research: Graham Le Gros, Rob Weinkove

Ministry of Health: Nic Aaggard

P3 Research: Dean Quinn, Richard Stubbs

Regional Public Health: Tessa Luff, Annette Nesdale, Craig Thornley

Spiral: Craig Boyd, Cain Harland, Audrey Shearer, Emma Winkes, Jess Wren

University of Otago, Wellington: Michael Baker, Julian Crane, Tristram Ingham, Sharla McTavish, Giles Newton Howes, Michael Nowitz, Rob Siebers, Thorsten Stanley, Mark Weatherall

Victoria University of Wellington: Anne La Flamme, Melanie McConnell, John Miller, Katherine Nelson, Paul Teesdale-Spittle

Wellington Free Ambulance: Andrew Swain

Wellington Regional Hospital: Colin Barnes, Johnathon Barrett, Ben Barry, Tim Blackmore, Maxim Bloomfield, Richard Carroll, Andre Cromhout, Andrew Davies, Kirsha Delhaney, Bernadette de Ruyter, Marina Dzhelali, Jessica Eden Lesona, Sean Galvin, Kim Grayson, Rosemary Hall, Andrew Harrison, Harriet Judd, Grant Kiddle, Jeremy Krebs, Cassie Lawrence, Jessica Lockett, Kelly McCausland, Alexandra Millington, James Moore, Rudy Morice, Alister Neill, Mai Nguyen, Shaanti Olatunji, Kyle Perrin, Alex Psirides, Yvonne Robertson, David Robiony-Rogers, Philippa Shirtcliffe, Nicola Smith, Richard Steele, Shawn Sturland, Michael Tweed, Bob Ure, Jason Wright, Chelsea Young

Whangarei

Whangarei Hospital: Ralph Fuchs, David Hammer, Ryan Jang, Andrea Junge, Bridget Lambert, Katherine Perry

International

Nat-Intensive Care Surveillance-M.O.R.U., Asia: Abigail Beane, Rashan Haniffa, Issrah Jawad, Bharath Kumar

Australia

ANZIC-Research Centre, Melbourne, Vic: Bridget Ady, Michael Bailey, Camila Battistuzzo, Rinaldo Bellomo, Allen Cheng, Jamie Cooper, Glenn Eastwood, Tomoko Fujii, Cameron Green, Lisa Higgins, Carol Hodgson, Belinda Howe, Natalie Linke, Amanda Martin, Zoe McQuilten, Nicole Ng, Alistair Nichol, Jane Parker, Emma Ridley, Vanessa Singh, Janani Sivasuthan, Tony Trapani, Andrew Udy, Steve Webb

The George Institute for Global Health, Sydney, NSW: Frances Bass, Erika Dempsey, Simon Finfer, Martin Gallagher, David Gattas, Naomi Hammond, Dijlah Hanna, Serena Knowles, Jeffrey Lipman, Sharon Micallef, John Myburgh, Anders Perner, Dorrilyn Rajbhandari, Manoj Saxena, Ian Seppelt, Colman Taylor

Austin Hospital, Heidelberg, Vic: Rinaldo Bellomo, Glenn Eastwood, Leah Peck, Helen Young

Bendigo Hospital, Bendigo, Vic: Catherine Boschert, Jason Fletcher, Julie Smith

Cabrini Hospital, Melbourne, Vic: David Brewster, Shannon Simpson

Canberra Hospital, Canberra, ACT: Katie Jefferson, Elyse Ladbrook, Mary Nourse, Shakira Spiller, Frank van Haren

Concord Hospital, Sydney, NSW: Rosalba Cross, Helen Wong

Fiona Stanley Hospital, Perth, WA: Ed Litton, Annemarie Palermo, Susan Pellicano

Flinders Medical Centre, Adelaide, SA: Shailesh Bihari, Xia Jin, Elisha Mattheson, Tapaswi Shrestha

Footscray Hospital, Footscray, Vic: Samantha Bates, Craig French, Anna Tippett, Miriam Towns

Gold Coast University Hospital, QLD: Maimoonbe Gough, David Pearson, Mandy Tallott, Rosemary Willis

Hunter Medical Research Institute, Newcastle, NSW: Peter Gibson, Kim Jones, Vanessa McDonald

Launceston Hospital, Tas: Matthew Brain, Sarah Mineall

Liverpool Hospital, Liverpool, NSW: Lien Lombardo

Lyell McEwin Hospital, Adelaide, SA: Timothy Beckingham, Natalie Soar

Monash Medical Centre, Clayton, Vic: Dhiraj Bhatia Dwivedi, Chloe Pepin, Ben Rogers, Yahya Shehabi

Nambour General Hospital, QLD: Jane Brailsford, Anne Buckley, Loretta Forbes, Peter Garrett, John Moore, Lauren Murray

NICM Health Research Institute, Western Sydney University, NSW: Mike Armour, Alan Bensoussan

Nepean Hospital, Penrith, NSW: Rebecca Graham, Julie Lowrey, Kristy Masters, Ian Seppelt, Christina Whitehead

Queen Elizabeth Hospital, SA: Sandra Peake, Patricia Williams

Rockingham Hospital, WA: Kartik Atre, Ravi Sonawane

Royal Adelaide Hospital, Adelaide, SA: Nerissa Brown, Kathleen Glasby, Stephanie O'Connor, Benjamin Redii, Justine Rivett

Royal Hobart Hospital, Hobart, Tas: David Cooper, Rick McAllister

Royal Melbourne Hospital, Parkville, Vic: Deborah Barge, Kathleen Byrne, Adam Deane, Sarah Doherty, Christopher MacIsaac

Royal North Shore Hospital, Sydney, NSW: Frances Bass, Simon Finfer, Malcolm Fisher, Naomi Hammond, Elizabeth Yarad

Royal Perth Hospital, Perth, WA: Simon Brown, Elizabeth Jenkinson, Sharon Waterson, Steve Webb

Royal Prince Alfred Hospital, Sydney, NSW: Heidi Buhr, Jennifer Coles, David Gattas, Debra Hutch, James Wun

St George Hospital, Sydney, NSW: Deborah Inskip, Jennene Miller

St Vincent's Hospital, (Melbourne), Vic: Espedito Faraone, Jenny Holmes, John Santamaria, Roger Smith

St Vincent's Hospital (Sydney), NSW: Nerilee Baker, Hergen Buscher, Serene Leow, Priya Nair, Claire Reynolds

The Alfred Hospital, Melbourne, VIC: Jasmin Board, Emma Martin, Phoebe McCracken, David Pilcher, Andrew Udy, Shirley Vallance, Meredith Young

The Northern Hospital, Vic: Olga Burgess, Angaj Ghosh, Simone Said

The Wollongong Hospital, NSW: Wenli Geng, Samantha Jakimowicz, Martin Sterba

Thoracic Society of Australia & New Zealand: Jimmy Chien, James Douglas, Claude Farah, Greg King, Rosemary Moore, Sheree Smith, Haydn Walters

University of Newcastle: Zheng Liu, Jennifer Martin, Peter Wark

University of New South Wales: Guy Marks

University of Sydney: Sally Ioannides

University of Western Australia, Perth: Graeme Hankey, Cathy Read

Woolcock Institute of Medical Research: Helen Reddel, Juliet Foster

Canada

Alberta Health Services: Malik Agyemang, Sean Bagshaw, Jo Harris, Dawn Opgenorth, Xiaoming Wang, Dan Zuege

Grey Nuns Community Hospital, Edmonton: Dominic Carney, Krista Dewart, Larissa Fedor, Melissa Ziober

Mazankowski Alberta Heart Institute, Edmonton: David Diachinsky, Desiree Ross, Ruth Santos, Sean Van Diepen

McMaster University, Hamilton: Lisa Buckingham, Richard Whitlock

Misericordia Community Hospital, Edmonton: Erika McIntyre, Patricia O'Toole, Ella Rokosh

Mount Sinai Hospital, Toronto: Nadine Shehata

Peter Munk Cardiac Centre, University of Toronto: Aaron Conway

Ottawa Hospital Research Institute, Ottawa: Dean Fergusson

Red Deer Regional Hospital, Red Deer: Gillian Brown, Kerry Oxtoby, Carmen Petersen, Michael Russell

Royal Alexandra Hospital, Edmonton: Jon Davidow, Tove LaBlanc

St. Michael's Hospital, Toronto: Zahra Bhimani, Nikita Chavda, Alice Dang, Judith Hall, Isabelle Laksono, John Marshall, David Mazer, Marlene Santos, Jodi Shin, Rekha Thomas, Ron Wald

Sturgeon Community Hospital, Alberta: Castro Aris, Shirley Baumgartner, Glenda Corrigal, Nancy Coyne, Celine Pelletier, Oleksa Rewa, Gabriel Suen

Sunnybrook Health Sciences Centre, University of Toronto: Brian Cuthbertson, Nick Daneman, Rob Fowler, Asgar Rishu

University of Alberta Hospital, Edmonton: Sean Bagshaw, Samantha Taylor, Derek Townsend

University of Alberta Hospital (Neurosciences), Edmonton: Peter Brindley, Dyan Franco, Paul Gerun, Crystal Hancheruk, Jim Kutsohiannis, Pam Lavallee

University of British Columbia, Vancouver: Mark FitzGerald, Mohsen Sadatsafavi

Ireland

St Vincent's Hospital, Ireland: Kathy Brickell, Ciara Fahey, Leanne Hays, Nicola Hyde, Michelle Smyth

University College Dublin: Kate Ainscough, Peter Doran, Alistair Nichol

Italy

IRCCS San Raffaele Scientific Institute, Milan: Giovanni Landoni, Rosalba Lembo, Marta Mucchetti
University of Ferrara, Ferrara: Alberto Papi

Japan

The Jikei University and Jikei University Hospital, Tokyo: Tomoko Fujii

Kingdom of Saudi Arabia

King Abdullah International Medical Research Center, Riyadh: Lara Afesh, Yaseen Arabi

Collaborations

Netherlands

University Medical Center Groningen, Groningen: Marike Boezen, Djirke Postma, Maarten van den Berge

University Medical Center Utrecht, Utrecht: Marc Bonten, Lennie Derde, Sebastiaan Hullegie, Lorraine Parker, Wilma van Bentum-Puijk

Spain

University of Barcelona, Barcelona: Alvar Agusti

United Kingdom

Basingstoke and North Hampshire Hospital, Basingstoke: Clarisse Carreiras, Denise Griffin, Nicola Mechenie, McDonald Mupudzi, Richard Partridge

County Durham and Darlington NHS Foundation Trust, Spennymoor: Amanda Cowton, Chris Dawson, Louise Duncan, James Limb

Dorset County Hospital, Dorchester: Mark Pulletz, Patricia Williams

Freeman Hospital, Newcastle upon Tyne: Maite Babio-Galan, Stephen Wright

Hull and East Yorkshire Hospitals NHS Trust, Hull: Ian Smith, Neil Smith

Imperial College, London: Andrew Bush, Anthony Gordon

Intensive Care National Audit and Research Centre, London: Farah Al-Beidh, Rahi Jahan, Paul Mouncey, Kathy Rowan, Daisy Wiley

Ipswich Hospital NHS Trust, Ipswich: Stephanie Bell, Richard Howard-Griffin

James Cook University Hospital, Middlesbrough: Jeremy Henning, Keith Hugill

Medway NHS Foundation Trust, Gillingham: Claire Pegg

Mid-Essex Hospitals NHS Trust, Chelmsford: Dilshan Arawwawala

North Cumbria University Hospitals NHS Trust, Carlisle: Tim Smith, Toni Wilson

Northern Specialist Emergency Care Hospital: Bryan Yates

Nottingham University Hospitals NHS Trust, Nottingham: Tim Harrison, Amanda McNaughton, Dominick Shaw, Claudia Woodford

Peterborough and Stamford Hospitals NHS Foundation Trust, Peterborough: Coralie Carle, Andrew Cheng

Poole Hospital NHS Foundation Trust, Poole: Julie Camsooksai, Henrik Reschreiter

Queen Alexandra Hospital, Portsmouth: David Pogson, Steve Rose

Queen Elizabeth Hospital, Gateshead: Vanessa Linnett, Jenny Ritzema, Amanda Sanderson

Queen Elizabeth Hospital, Kings Lynn: Parvez Moondi, Katherine Wong

Royal Bournemouth Hospital, Bournemouth: Julius Cranshaw, Emma Willett

Royal Hampshire County Hospital, Winchester: Nicole Gregerson, Steve Wimbush

Royal Victoria Infirmary, Newcastle upon Tyne: Ian Clement, Leigh Dunn

Russells Hall Hospital, Dudley: Clare Allcock, Julian Sonsken

Salford Royal University Hospital, Salford: Ronan O'Driscoll

South Tees NHS Trust, Middlesbrough: Emanuel Cirstea, Uwe Franke

Southampton University: Stephen Holgate

St Helens and Knowlsey Teaching Hospitals NHS trust, Liverpool: Tushar Mahambrey, Amanda McCairn

University College London: Robert Horne

University Hospital of North Tees, Stockton-on-Tees: Michele Clark, Hemal Mohan

University of Oxford, Oxford: Ian Pavord

United States

Berry Consultants LLC, Austin: Lindsay Berry, Scott Berry, Michelle Detry, Roger Lewis, Elizabeth Lorenzi, Anna McGlothin, Doray Sitco

Genentech Inc, San Francisco: Ryan Ceniceros, Hubert Chen, Cecile Holweg, John Matthews, Mindy Sivasubramanian

Research in Progress

Alternative and Complementary Medicine

- Kānuka oil for the treatment of eczema and acne
- The effect of Dynamiclear on cold sores

Asthma

- The role of paracetamol in the development of asthma and allergic disorders in children
- The treatable traits approach to the management of airways disease
- The efficacy/safety profile of the ICS/LABA reliever therapy regimen in children
- The efficacy/safety profile of the AIR stepwise algorithm in adults, across the spectrum of severity
- The bronchodilator and anti-inflammatory efficacy of repeated high dose ICS/LABA in severe asthma

Cannabis-Based Medicines

- The tolerability and pharmacokinetics of pharmaceutical grade cannabis products
- The knowledge and attitudes of health professionals to the prescription of medical cannabis products

Cardiothoracic Surgery

- Left Atrial Appendage Occlusion Study
- Fluid After Bypass
- Corticosteroid Effects on inflammation, Long-term disability and Survival in patients Undergoing cardiac Surgery
- IV Iron for Treatment of Anaemia before Cardiac Surgery

COPD

- The efficacy and safety of beta-blockers in COPD patients

COVID-19

- The efficacy and safety of potential treatments in critically ill patients with COVID-19
- The long-COVID syndrome

Emerging Therapeutics

- Early phase studies of novel asthma medications

Intensive Care

- Stress ulcer prophylaxis in ICU patients
- Optimal fluid treatments in ICU
- Fever management in critically ill patients with sepsis
- Treatment strategies for life-threatening community-acquired pneumonia
- Prophylactic anti-fibrinolytic treatment with tranexamic acid in severe trauma
- Duration of antibiotic treatment for bacteraemia
- Continuous or intermittent antibiotic administration in severe infections

Oxygen Therapy

- The risks/benefits of oxygen therapy in the treatment of critically ill patients
- The physiological and clinical effects of novel oxygen therapeutic devices

Pleural Disease

- Indwelling catheter and pleurodesis vs video-assisted thoracic surgery in the treatment of malignant pleural effusion

Stroke and rehabilitation

- Self-directed community-based rehabilitation following stroke

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5. Armour M, Semprini A, Ee C, MacCullagh L, Shortt N. Efficacy of a topical herbal and mineral formulation (Dynamiclear) for the treatment of herpes simplex labialis in the community setting: study protocol for a randomised, double-blind placebo-controlled trial. BMJ Open 2020; 10: e031876.
6. Armour M, Sinclair J, Noller G, Girling J, Larcombe M, Al-Dabbas MA, Hollow E, Bush D, Johnson N. Illicit cannabis usage as a management strategy in New Zealand women with endometriosis: An online survey. J Womens Health (Larchmt) 2020; doi: 10.1089/jwh.2020.8668
7. Baggott C, Beasley R. Asthma in the anti-inflammatory reliever therapy era. Lancet Respir Med 2020; doi: 10.1016/S2213-2600(20)30465-3
8. Baggott C, Chan A, Hurford S, Fingleton J, Beasley R, Harwood M, Reddel HK, Levack WMM. Patient preferences for asthma management: a qualitative study. BMJ Open 2020; 10: e037491.
9. Baggott C, Hansen P, Hancox RJ, Hardy JK, Sparks J, Holliday M, Weatherall M, Beasley R, Reddel HK, Fingleton J. What matters most to patients when choosing treatment for mild-moderate asthma? Results from a discrete choice experiment. Thorax 2020; 75: 842-8.
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11. Baggott C, Reddel HK, Hardy J, Sparks J, Holliday M, Corin A, Montgomery B, Reid J, Sheahan D, Hancox RJ, Weatherall M, Beasley R, Fingleton J. Patient preferences for symptom-driven or regular preventer treatment in mild to moderate asthma - findings from the PRACTICAL study, a randomised clinical trial. Eur Respir J 2020; 55: 1902073.
12. Bagshaw SM, Wald R, Adhikari NKJ, Bellomo R, da Costa BR, Dreyfuss D, Du B, Gallagher MP, Gaudry S, Hoste EA, Lamontagne F, Joannidis M, Landoni G, Liu KD, McAuley DF, McGuinness SP, Neyra JA, Nichol AD, Ostermann M, Palevsky PM, Pettila V, Quenot JP, Qiu H, Rochwerg B, Schneider AG, Smith OM, Thome F, Thorpe KE, Vaara S, Weir M, Wang AY, Young P, Zarbock A. Timing of initiation of renal-replacement therapy in acute kidney injury. N Engl J Med 2020; 383: 240-51.
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Publications 2020

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MEDICAL RESEARCH INSTITUTE OF NEW ZEALAND

Investigating the causes and treatment of important public health problems

Facilities

The Institute's main offices and clinical research facility are at the Wellington Regional Hospital. There is also access to Phase II facilities including a 14 bed inpatient clinical trials unit at the Wellington Regional Hospital.

Volunteers

Database of over 15,000 adults, including around 750 patients with asthma or COPD trained in body plethysmography.

Clinical Trials Groups

The MRINZ is the New Zealand coordinating management centre for five clinical trials groups, ANZICS CTG (the Australian and New Zealand Intensive Care Society Clinical Trials Group), IOACS Net (the Improving Outcomes After Cardiothoracic Surgery Network), NZRCTG (the New Zealand Respiratory Clinical Trials Group), the NZPRN (the New Zealand Pharmacy Research Network), and the NZRRG (the New Zealand Rehabilitation Research Group).

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