

Research

Annual Report 2021

Te Toka Tumai Auckland



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Te Whatu Ora
Health New Zealand



He kano mātauranga whakatō, he hua mātauranga puta mai.

If the seed of knowledge is planted,
the fruits of knowledge will emerge.

HIGHLIGHTS FOR 2021

▶ Targeted Interventions Improve Bronchiolitis Management in Infants.

Our own Libby Haskell (Children's Emergency Department) took the award for TOP PUBLICATION BY A DOCTORAL Student at the University of Auckland's School of Medicine 2021 Doctoral Research Showcase. Libby's paper "Effectiveness of targeted interventions on treatment of infants with bronchiolitis" is published in JAMA Paediatrics, 178 (8) pp. 797- 806.

▶ DIY artificial pancreas increases time in range vs. pump therapy in type 1 diabetes

▶ PADDI Anaesthesia trial – results are out!

▶ Our research whānau

Dr Sarah Hunter of Children's Blood and Cancer Research Unit and Dr Lynn Sadler of National Women's Health talk about research on the coalface .

▶ Vascular Interventional Research Unit scales new heights.

▶ Gene editing can work in humans, but for how long

Durability data now out on Intellia Therapeutics landmark trial of CRISPR gene editing for transthyretic amyloidosis. Nature Medicine have named this study one of 11 clinical trials that will shape medicine in 2022.

▶ Auckland Hospitals Research and Endowment Fund – grants impact report

We report on the outputs of our internal research grants programme and what an investment in research can achieve.

▶ Funding for research

Highlights of the funding successes for 2021, including Alzheimer's Foundation Fellowship for Dr Gary Cheung, Health Research Council activation grant for Dr Ali Leversha and NEWSFLASH – World first: researchers identify potential cause and treatment for obesity and insulin resistance.

▶ Publication

A total of 740 original research papers published, including 23 in the most prestigious (Top 30) health journals in the world. HOT paper on rheumatic heart disease from Starship's Dr Nigel Wilson



Targeted Interventions Improve Bronchiolitis Management in Infants

Bronchiolitis is one of the most common reasons for hospitalization among infants in developed countries. While international bronchiolitis guidelines recommend supportive care, significant variation in practice continues to exist. In this new study by Libby Haskell of the Children's Emergency Department in Starship, and her colleagues from New Zealand and Australia, the objective was to assess the effectiveness of targeted interventions compared with passive dissemination in infants with bronchiolitis.

The international, multicenter cluster randomized clinical trial (RCT), published in JAMA Pediatrics, is the first RCT to report whether targeted interventions are effective at improving bronchiolitis management. It is also one of the first to outline the effects of deimplementation of unnecessary care in acute care settings. The Australasian Bronchiolitis Guideline recommended **against** the use of common therapies and management processes that have been determined to be ineffective and potentially harmful when used in patients with bronchiolitis, including chest radiographies, albuterol, glucocorticoids, antibiotics, and epinephrine.

Medications and management processes **known to be ineffective or harmful** in infants with bronchiolitis were tossed in favour of targeted interventions in hospitals, resulting in improvements in bronchiolitis care.

The trial observed a total of 8,003 infants for the three bronchiolitis seasons before the implementation period and 3,727 infants for the implementation period. The interventions included site-based clinical leads, targeted educational delivery, stakeholder meetings, and a train-the-trainer workshop. The primary endpoint of the study was compliance with the Guideline during the first 24 hours of care.

The findings suggested that the baseline data collected before the implementation period was similar to that collected during the implementation period. Compliance with recommendations was 85.1% in the intervention hospitals compared to 73.0% in control hospitals. The analysis was by the intention to treat, and the data were collected from 26 hospitals.

The research concluded that target interventions resulted in an improvement in treatment among

infants with bronchiolitis. The findings of this study can have crucial implications for the management and intervention of the disease in infants.

“**Minimizing harm caused by unnecessary interventions in the management of infants with bronchiolitis is an important patient- and whānau-centered outcome, and it is key to health care systems delivering evidence-based, cost-effective clinical management,**” wrote the investigators.

Targeted interventions were developed based on behaviour change theories aimed at factors that influence bronchiolitis management. Examples of targeted interventions include site-based clinical leads, stakeholder meetings, training workshops, targeted educational delivery, other educational materials, and audit and feedback.

Infants from indigenous and impoverished communities are considered the most at risk for bronchiolitis, which is the leading cause of hospital admissions among infants. The increased risk stems from structural policies rooted in racism that resulted in indigenous people having a higher likelihood of residing in poverty and having less access to health care services.

DIY artificial pancreas increases time in range vs. pump therapy in type 1 diabetes

Burnside MJ, et al. 286-OR. Presented at: American Diabetes Association Scientific Sessions; June 3-7, 2022; New Orleans (hybrid meeting).

Managing type 1 diabetes can be challenging, especially in young children owing to the levels of insulin required and unpredictability around how much patients eat and exercise. Children are particularly at risk of dangerously low blood sugar levels (hypoglycaemia) and high ones (hyperglycaemia), which can damage the body and even lead to death.

In a new study carried out at Starship Child Health and other New Zealand sites, adults and children with type 1 diabetes who used an open-source automated insulin delivery system significantly increased time in target glucose range compared with baseline and with sensor-augmented pump therapy.

While open-source automated insulin delivery is not yet approved by regulatory bodies such as the FDA, people worldwide are using it to manage their diabetes. The findings have demonstrated that this is a safe and effective technology and adds to the body of evidence supporting use of open-source automated insulin delivery for improving glycemic outcomes.

Starship's Dr Craig Jefferies and his colleagues randomly assigned 48 children aged 7 to 15 years and 49 adults aged 16 to 70 years with type 1 diabetes to an automated insulin delivery system (21 children, 23 adults) or sensor-augmented insulin pump as a control group (27 children, 26 adults). Participants had type 1 diabetes for at least 1 year and were using an insulin pump and had HbA1c below 10.5% for the 6 months before the study. The automated system consisted of a Dexcom G6 continuous glucose monitor paired with a DANA-i insulin pump and the OpenAPS algorithm from a version of AndroidAPS used on a smartphone.

The study included a 4-week run-in period followed by the 24-week randomized clinical trial. The researchers assessed percent of time in target glucose range of 70 mg/dL to 180 mg/dL during the 24-week trial for the two insulin delivery groups.

The automated group, participants used automated insulin delivery 94% of the time for the study duration. Time in range increased immediately and was sustained throughout the trial for participants in the



Dr Libby Haskell

automated group. During the last 2 weeks of the trial, the automated group spent 14% more time in range than the pump group.

Study lead investigator Dr Martin De Bock presented the study at the American Diabetes Association scientific sessions in New Orleans and explained that

“For adults, particularly at night, you can see over 30% improvement in time in range on automated insulin delivery [compared with pump therapy alone], so it was very effective overnight,”

For the automated group, mean time in range was significantly greater during the final 2 weeks compared with the run-period for both adults — a 9.6% increase for final mean time in range of 74.5% — and children — a 9.9% increase for a final mean time in range of 67.5%.

Time in range did not change significantly for the pump group. International guidelines call for targeting a time in range of more than 70%. This goal was met by 60% of participants in the automated group and 15% of the pump group.

No participants experienced severe hypoglycemia or diabetic ketoacidosis during the trial. Two participants in the automated group withdrew due to hardware issues.

An interesting takeaway from the study was that people who proclaimed to be technophobic could use the open-source automated system very effectively and had no problems. Only had two people drop out despite the relatively diverse group who enrolled in the study. The authors concluded that with good support and education, automation should be offered to everyone with type 1 diabetes.

Why is time in range important? Optimal glycemic control remains challenging and elusive for many people with diabetes. The Time in Range is the

percentage of time a person with diabetes spends with their blood sugar levels in a particular target range. Increasing the time in range reduces the risk of diabetes-related complications. It's not only permanently elevated blood glucose that risks long term complications, but also fluctuating glucose levels. The more fluctuations over time the more risk towards complications such as diabetic retinopathy and diabetic kidney disease.

Continuous glucose monitoring systems determine a glucose value around the clock giving patients a consistent stream of measured values on average every five minutes. This information is vital in making those small, and sometimes constant, changes needed to live well with diabetes.



Context. Of those patients in New Zealand who are suffering from end-stage renal disease, approximately 50 per cent face their condition because of diabetes. Chronic kidney disease is a major healthcare burden on New Zealand, accounting for approximately one third of New Zealand health costs.

PADDI Anaesthesia trial – results are out!

A drug commonly used during anaesthesia before surgery at Auckland City Hospital to prevent nausea and vomiting does not increase the risk of a surgical wound infection as once feared. The results of the PADDI trial have now been published in the New England Journal of Medicine and are likely to influence anaesthetic practice around the world.

Dexamethasone is often given by anaesthetists during surgery. However, because of its effects on the immune system there has been growing concern that it may increase the risk of wound infections, particularly in vulnerable populations such as patients with diabetes. As a result, there has been a reluctance by anaesthetists to use it, even though more than half of patients are at risk of experiencing unpleasant nausea and vomiting after surgery. The same drug has recently been shown to decrease the risk of death from COVID-19 in severely ill patients.





Now, the **PADDI trial of Perioperative Administration of Dexamethasone and Infection** has found that administering a low-dose of dexamethasone during anaesthesia for surgical operations does not increase the risk of surgical wound infections. The findings showed that 8.1 per cent of patients who received dexamethasone experienced a wound infection at 30 days after surgery, compared to 9.1 per cent in the placebo group, indicating no evidence of any major differences between the groups. Dexamethasone can therefore be given safely to patients. Good management of post-operative nausea and vomiting is highly associated with patient satisfaction.

A panel of senior statisticians described the PADDI trial as having demonstrated **“exemplary statistical aspects”** from trial design and planning, through to analysis, reporting and interpretation.

PADDI is the brainchild of the Australian and New Zealand College of Anaesthetists Clinical Trial Network. One of its strengths is its large scale – 8735 patients were recruited from 55 hospitals in New Zealand, Australia, Hong Kong and South Africa. The trial recruited ## patients from Te Toka Tumai Auckland, where it was led by Associate Professor Dr Tim Short.

READ THE ARTICLE:

New England Journal of Medicine titled: Dexamethasone and surgical site infection. N Engl J Med 2021;384:1731–41. DOI: 10.1056/NEJMoa2028982

Why is this finding about post-surgical infections important? It's because these infections are common and a cause of significant mortality and morbidity. They are also incredibly expensive for the health system. The additional cost of treating a surgical site infection has been estimated as between \$40,000 and \$112,000 per patient.

In terms of value for patients, researchers from Te Toka Tumai Auckland applied this calculation in a 2018 paper published in the New Zealand Medical Journal.

“Post-surgical site infections have been estimated to cost the patient 0.5 disability-adjusted life years (DALYs). The DALY combines the likely shortening of life (years of life lost) with the loss of quality of life (years of life disabled) to measure the effect on individuals and

populations of specific illnesses and harms. The current New Zealand estimate of the Value of a Statistical Life (VoSL) is \$4 million, based on what New Zealanders state they are willing to pay in improving roads to save a life. Using methodology from the Accident Compensation Corporation to calculate the value of a year of healthy life (or avoided DALY) from this figure, each avoided DALY provides NZD\$181,000 worth of value. Hence each avoided surgical site infection provides approximately NZD\$90,000 of value for each patient.”

Source: Arthur J Morris, Sally A Roberts, Nikki Grae, Richard Hamblin, Carl Shuker, Alan F Merry (2018) The New Zealand Surgical Site Infection Improvement (SSII) Programme: a national quality improvement programme reducing orthopaedic surgical site infections. New Zealand Medical Journal, Vol 131 No 1479.





Our Research Whānau

In this issue we meet two of our best people who are bringing science to work with them everyday.

Dr Sarah Hunter is Research Manager for Starship Blood and Cancer Centre. Sarah oversees the paediatric and adolescent and young adult oncology/haematology research programme at Starship and Auckland City Hospitals. She is a board member of ANZCHOG, the Australian and New Zealand Children's Oncology Group.

I'm a nurse by background. I first worked in Auckland City Hospital when it was still the old building in the early 90s after I graduated, but then moved out to the community organisations, hospices, cancer society, where I've mainly worked with cancer and palliative care patients. I did some post graduate papers at University which then segued into a Masters degree. At the end of that I was encouraged to go on to do a PhD. My PhD question was cancer-focused. Because I had been working with the Cancer Society as a community nurse I had quite a lot to do with young people who had been diagnosed with cancer and were having their cancer therapy, and issues related to their fertility was something that came up for them. So my research was about damage to fertility and women going into early menopause because of their cancer treatment. To do that I moved around New Zealand interviewing women and talked to them about how their cancer treatments had impacted their lives, their feelings about themselves, about the future and how they saw themselves recovering from their treatments. At the end of that I'd been out of clinical nursing for quite a while and was looking to work in research. The role in Starship came up at the time. I wasn't particularly interested in it as a management position – I was just interested because it was cancer and it was research. Anyway, I was successful at getting the job.

I started on January the 7th 2011. Starship Blood and Cancer had been doing research formally for about 10 years by then, and longer in a less formal fashion. It was fairly ad hoc in the early days, but since then research has hyped up, ethical requirements have hyped up and data management has hyped up so the team gradually increased in size. **We were about 3.7 FTE in total back then, now we have 5.1. – and that's still not enough!**

“The freezing and storage of testicular tissue for that child's own use in adulthood is a process that offers the chance of fertility later in life.”

“This is very early technology around the world and while testicular tissue has now been stored for about 1000 pre-pubertal males internationally, there have been no reports of human pregnancies or babies that have resulted from the use of banked tissue.”

Dr Sarah Hunter




Starship Blood and Cancer Centre is one of only two children's cancer centres in the country. The other one is in Christchurch Hospital. Starship takes about two thirds of children and adolescents with cancer and non-malignant haematological conditions. We cover all of the North Island other than Wellington, and Christchurch covers Wellington and the rest of the South Island. Starship also houses the national bone marrow transplant unit. Although the official cut off for paediatrics is a person's fifteenth birthday and

after that they go to adult services, in practice we actually cover up until when a young person leaves school. The other reason why patients sometimes stay with our service is when they have a paediatric-style cancer and we are used to treating those cancers and giving those chemotherapy agents. Whereas if they have an adult-style cancer and they are 16 they may be better treated in adult services where those doctors have the expertise.

In paediatric oncology internationally for a service to be able to say it's giving first world-level care we need to be offering clinical trials to as many patients as we can.

The reason is that improvement in outcomes for children's cancer is largely attributable to collaborative groups getting together and doing studies from the 1970s onwards, and readily sharing the results of their research. For instance B-cell lymphoblastic leukaemia is the most common cancer diagnosis in children. A child diagnosed with B lymphoblastic leukaemia in the 60s or 70s had a 10 to 20% chance of surviving, now overall it's around 90%. An important finding over that time was that you have to keep giving intrathecal therapy after a patient goes into remission. That kind of stuff has really established the role of clinical trials in children's cancer. In New Zealand only about 150 children each year are diagnosed with cancer. That's a tiny number compared to adults diagnosed annually and for each sub-group its even tinier. So to work out the best way to treat children's cancer we need





to do international clinical trials – you can't prove anything in New Zealand on our own with our small numbers. Our participation in trials is deliberately in an international collaborative model rather than a pharmaceutical-sponsored model. We do it with multiple countries with minimal funding. We do try to have as much going on research-wise as we can. This can be therapy trials but also increasingly biology trials because children's cancers are not just adult cancers in small children; the biology is completely different. We need biology studies focused on children's cancers to work out what is happening at the cellular level, what targets do we have, what drugs do we need to be using and developing?

We are a member of the Children's Oncology Group (COG), probably the biggest children's cancer research group in the world.

COG is US government funded through the National Institutes of Health and they do pay us a small case reimbursement fee for enrolment in their studies, so essentially much of children's cancer treatment as part of research in New Zealand is funded through COG. COG trials are very well run, safety is well managed, they have very thorough data safety management. They are overseen by meticulous regulators and they will stop their studies if there is any sign of a safety signal and we feel very comfortable doing their trials. We're also involved with the Australian and New Zealand Children's Oncology Group (ANZCHOG), I've been on the board for ten years, and ANZCHOG has now formalized itself into a clinical trials group, bringing many more international collaborative group trials to Australian and NZ sites.

The clinical research associates in my team have roles that include being responsible for ethics and other approvals and maintaining those for the life of the study, all the data management and data submissions.


Half of the children on our ward at any given time might be on a trial, plus many of the children coming through our clinics. We have a way of communicating back to the clinical staff so they know whether a patient is on a trial, which trial they're on, what they need to have done today, and what is coming up, such as which scans to order, bloods etcetera. We are also responsible for reporting the work that our bone marrow transplant team does back to the international registries in the USA and Australia. This is a requirement for the international accreditation of the transplant programme, which we

get audited on, so we have to do well at it. I can say that for the last three audits we've been commended for the quality and accuracy of our data, which is really good. The other thing the team work on as part of their day to day work is the New Zealand Children's Cancer Registry, which is an opt-out registry. We're responsible for identifying all of the newly diagnosed patients, relapses and deaths. We have to make sure the families or the patients if they are old enough are informed about the registry and they have the opportunity to opt out if they don't want their data or their child's data in there. It's very very rare for anyone to want to opt out. We also do specimen management for personalized medicine, that's molecular or genetic testing, mainly overseas where there might be a particular panel that can provide the test the oncologist wants to know an answer to. For the studies we are involved in we do all of our own specimen management because we don't earn enough money to pay others, e.g. lab technicians to do it for us.

If you talk about doing research on children it can sound like you're experimenting on children and that would be terrible.

And when you talk about biology studies with children that can sound like a really bad thing because we are taking their tissue. But when you talk to families, they are often really savvy about research and will often ask for it, and mostly when its offered families will take it up, even when it's clear there's unlikely to be any benefit for their child. Some of our biology studies for instance will feed back an answer that might help a child's risk assignment or final diagnosis but often nothing is going to come back and it's just to help other children in the future. Families really get that and they will frequently say I know this won't help my child but I just want to make it better for someone else's child. So even in their moment of crisis parents are still able to look past their child to what their child's experience might do for someone else.

Early on in my tenure in this role the Ministry of Health asked the national child cancer network to look into a fertility preservation guideline, which New Zealand didn't have. When I heard about that I perked up because my PhD had been about fertility. I spoke to my boss at the time and asked him if I could go on the steering group. My boss at that time was Dr Lochie Teague and he was very good at seeing



peoples' strengths and he generously allowed me to take time to do that. I ended up taking up the Chair of the working group. We wrote the guidelines and as part of that we were very aware that for pre-pubertal children in New Zealand there was no fertility preservation option, which internationally, for girls, is ovarian tissue cryopreservation. Cancer treatment can permanently damage fertility and we wanted young New Zealanders to have the best access to fertility preservation possible. New Zealand had done a few patients privately at the patients' own expense, and it is expensive. There is a surgical procedure, tissue processing and then storage, potentially for up to 20 years or longer if you are taking tissue from a really young girl. This obviously raised questions around equity because only families that could afford the service could have it, so moving on from the guidelines we decided to write a protocol for New Zealand, which I'm principal investigator for. We went to all of the fertility providers to say "this is what we want to do, would you like to work with us?", and everyone agreed it should be Fertility Associates, a fertility provider that covers the whole country. We do the ovarian tissue collection under general anaesthetic at the same time the patient's central line is put in and it's only done for girls who have a significant risk to their fertility and a reasonable


chance of surviving their cancer treatment, because obviously it is an invasive procedure. We started this protocol at the end of 2015 and have enrolled 38 girls to date, at Starship. These girls' tissue is now all safely in storage at Fertility Associates for their own use in the future.

The latest thing we are working up at the moment is about pre-pubertal testicular tissue for boys, and boys currently have no option for this in New Zealand. The thing with this tissue is that compared with girls' ovarian tissue it's much more experimental. There have been no human babies created using cryopreserved boys' testicular tissue but the theory is that it will work and so internationally it's recommended that you do these tissue collections within an ethically approved research protocol. We've now gotten permission from the Advisory Committee for Assisted Reproductive Technologies and HDEC to work on this. What we are probably going to do is to amend the ovarian protocol to include the testicular tissue collection. We are intending to approach the Starship Foundation for funding for this, as they funded the girls' tissue. It's exciting to be doing this as at the moment those boys are missing out completely.

Because of New Zealand's national COVID response and the people who have since become household names, more of us than ever are aware of the science of epidemiology. But are epidemiologists common in our public hospitals? **Dr Lynn Sadler** explains that they are not, but ought to be, and her circuitous route to becoming a perinatal epidemiologist at Te Whatu Ora, Te Toku Tumai.

I trained as an obstetrician but changed course after 1993 when we started our family and carrying on working nights and weekends lost its appeal. Moving out of a direct patient care role was more conducive to family life and during this time I picked up some research work as well as working part time in sexual health.

Later I moved to Yale University where I undertook a Master's degree in Public Health. While on the Master's Program, an American colleague and I conceived a combined research project which was funded by the National Institute of Child Health and Human Development. The NIH funded projects in other countries when it wasn't possible to do them in America. To comply with the recommendations of the Cartwright Inquiry, National Women's Hospital, as it was called then, had developed an excellent colposcopy service database. There was already an Obstetrics database which enabled a link from the colposcopy data for the years 1988 through 1999 with births from 1989 through 2000. We wanted to find out if treatments for cervical dysplasia (a change of cells in the cervix, sometimes the precursor of cervical cancer) increase the risk of having a preterm birth. Because of



the high quality data at National Women's this was easier to research here than in the USA. We found the risk of premature rupture of membranes leading to preterm birth was strongly associated with size of cervical tissue removed from women who were treated. The work was published in the Journal of the American Medical Association and has changed clinical guidelines and practice internationally so now clinicians are much more likely to treat cervical dysplasia conservatively in women of reproductive age.

Returning to Auckland, I've been really fortunate to work for National Women's Health in an exclusively non-patient contact role as an epidemiologist for 20 years. This is a unique situation in a public hospital. During these years I have also worked for the Ministry of Health, the Health Quality and Safety Commission, and the University of Auckland. In my role as a clinical epidemiologist at the hospital, I bring my medical and obstetric training to work behind the scenes (rather than alongside patients) to improve clinical practice in a variety of ways. I spend a lot of time working with clinical data, and often am consulting with my clinical and academic colleagues. This work is important for hospitals because it means we are thinking critically about the work we do and the outcomes we achieve. The skill I bring from my epidemiology training, along with my clinical experience and training, enables an understanding of clinical data, which is especially useful given the comprehensive datasets we have available at National Women's. In addition to clinical governance, audit and quality improvement, our team in NWH produce a comprehensive annual clinical report which is used extensively by our services.

Part of my role is to help supervise other researchers in the department and I try to fit my own research around these duties. Recently I began to really think about what I'd like to achieve in research. Other colleagues had applied for Health Research Council Clinical Practitioner Research Fellowships and had been successful. To get prepared I talked to a lot of researchers I respect to get an idea of the best strategy in terms of the research I was going to pitch. The advice I received was to propose a core body of work, or direction, and add projects as they become relevant over time. The award is for five years.

My proposal has two main directions; the first is to essentially future-proof National Women's clinical databases to create a research-ready resource of maternal and neonatal data with metadata and appropriate governance.

The database will be compiled from, ultimately, three maternity datasets, neonatal data, perinatal mortality data and demographic data from the hospital clinical management system. Some of the data are not currently available for use. Other collections such as pharmacy, pathology and hospital discharge data can be added over time. I'm lucky because I have worked with these data for 20 years and so have considerable institutional knowledge. Te Toka Tumai Auckland has agreed to host the data and has commenced infrastructure development so the data are safe. It will be very satisfying to develop a data resource that will be of great value to the next generation of researchers.

Dr Lynn Sadler was awarded the New Zealand Order of Merit in 2019 for services to maternal and perinatal health



In addition to the data project, my research plan includes two observational studies and a clinical trial. All of these studies relate to birth at full dilation of the cervix. Caesarean section at full dilation is technically difficult and associated with increased risk for mother and baby, and there is also increased risk of pre-term birth in subsequent pregnancies. I'll use retrospective data initially to identify the outcomes for women and babies from this procedure, and I'll also investigate the use of a medical device to elevate the baby's head; essentially a balloon which is designed to lift the babies' head out of the pelvis during delivery. The goal of this trial is to determine if the device reduces maternal morbidity and whether it is cost effective, and to ensure that the findings of the studies are translated to practice. We'll be disseminating the results within our clinical networks and to other key stakeholders.

My HRC fellowship allows me to block off half of the week to research as it covers costs for some of my regular work to be reassigned to other staff. It has enhanced my capacity to support juniors to gain research skills and I hope to support a PhD project as part of the work program.





Vascular Interventional Research Unit scales new heights.

Over a decade ago, vascular surgical Andrew Hill and interventional radiologist Andrew Holden formed the Vascular Intervention Research Unit at Auckland City Hospital. They have now participated in well over 100 first- and early human trials with vascular and renal dialysis patients. The unit is one of the top two sites in the world as a research centre for excellence in Endoluminal Endovascular Repair.



Dr Andrew Holden

Dr Holden on the unit, the pandemic and the results of the IN.PACT AV access study.

“We are fortunate to be approached by a number of companies and investigators looking to include our unit in early human trials and postmarket registries. There are a number of important considerations: the originality of the device or procedure, whether it addresses an unmet clinical need, our ability to recruit sufficient patient numbers to the trial, and, most importantly, our capacity to manage the trial to the high level we always strive for. The “sweet spot” for our unit is an innovative and original early human device trial addressing an unmet need for a significant number of our patients. To date, we’ve been involved in a number of these trials, and the future looks promising!”

“Many of the challenges we have encountered during the pandemic by the Vascular Intervention Research Unit here at Auckland Hospital have been faced elsewhere. Initially, patients scheduled for more elective interventions were deferred, which impacted recruitment to claudication and elective aneurysm repair trials. Clinical trials involving devices for more acute indications such as critical limb ischemia and dialysis access continued, largely undisturbed. Where possible, our research coordinators worked from home, although they were obviously required in the hospital for procedures and clinic visits.

One interesting development, by necessity, has been the evolution of remote support for first- and early human trials. Prior to the pandemic, almost all support was provided in person by company and medical specialists traveling to our institution, which was a challenge given our location here in New Zealand! In association with a local audiovisual company, we have been able to provide high-quality, real-time multicamera and audio support online, such as direct transmission of imaging data without degradation. The result is an experience very similar to having the specialists in the room.”





On Paclitaxel-eluting devices.

“We had early access to this technology through our participation in research and could immediately see a paradigm shift from the frequent, severe restenosis we saw with bare nitinol stents in peripheral arteries. Following this, we participated in many early paclitaxel-coated balloon trials that directly compared patency of these devices to plain angioplasty balloons. Not only did these studies confirm paclitaxel drug coated balloons produced significantly less late lumen loss, but also, we saw this with our own eyes! Since then, we have routinely used paclitaxel-coated balloons and stents in almost all of our femoropopliteal arterial interventions, and patients have benefited from improved patency and lower reintervention rates.”

IN.PACT AV study (Medtronic Endovascular)

“Endstage renal disease (ESRD) is a form of kidney disease which occurs when both kidneys are impaired or functioning at less than 10 percent of their normal rate. The majority of patients diagnosed with ESRD require haemodialysis 2-3 times per week.

Haemodialysis access must be created through a direct connection of an artery to a vein (arteriovenous fistula or AV fistula). The formation of an AV fistula enables reliable venous access for dialysis to occur at regular intervals, and is most frequently placed in the nondominant forearm arm. However as the vein used in AV fistula formation is not intended for arterial pressures, complications can occur.

The most common complication is stenosis; either within the AV fistula or within the vein anywhere between the AV fistula and right atrium. Dialysis dysfunction due to flow limiting stenotic lesions within the AV fistula is a significant cause of morbidity and mortality amongst patients undergoing haemodialysis.


The study sets out to examine the IN.PACT AV Access Drug Coated Balloon (DCB) for safety and efficacy, when compared to the current standard of care treatment, percutaneous angioplasty. IN.PACT AV Access DCB utilises the dual action of mechanical dilation seen with PTA and also drug delivery of

Paclitaxel to the vessel wall. Paclitaxel is extensively used within the coronary & peripheral vasculature with the intent of inhibiting restenosis. Initial clinical data using the IN.PACT AV Access DCB within failing AV Fistula has shown improvements in patency and a reduction in revascularisations.

This was a prospective multicentre multinational randomised controlled trial comparing plain balloon angioplasty with IN.PACT AV access drug-coated balloon angioplasty for the treatment of haemodialysis access circuit stenosis. The trial was performed in New Zealand, the USA and Japan.

330 participants randomised 1 to 1 between the plain balloon and drug-coated balloon arms of the trial. The primary safety endpoint was freedom from serious adverse events at 30 days. The primary efficacy endpoint which was target lesion primary patency which was defined as freed from clinically driven target lesion revascularisation or access circuit thrombosis out to 6 months or 210 days. Initially patients were consented for two-year follow up but subsequently reconsented for five-year follow up.

We presented and published in the New England Journal the primary patency data which was six-month data. This was the first large, randomised trial of a drug-coated balloon in AV access to well and truly meet its primary efficacy endpoint. The primary patency of the drug-coated balloon arm was 86% which was highly significantly better than the plain balloon arm. We then saw that patency advantage sustained out to 12 months, published in the Journal of Vascular and Interventional Radiology along with an economic analysis which shows the drug-coated balloon is cost effective. Last year at the Charing Cross symposium we presented the 24-month data, again showing a significant patency advantage for the drug coated balloon over the plain balloon. It's really incredibly that we still see this patency advantage for the drug coated balloon after 36 months. The primary patency of the drug-coated balloon was 43% compared to 28.6% for the plain balloon. Just to put that primary patency data into some sort of context, we don't have many studies reporting long-term or 3-year data, but on average primary patency is normally in the order of 20-25%. So to get a primary patency of 43% was really very impressive. One of the things we've also always discussed is the number of reinterventions required to

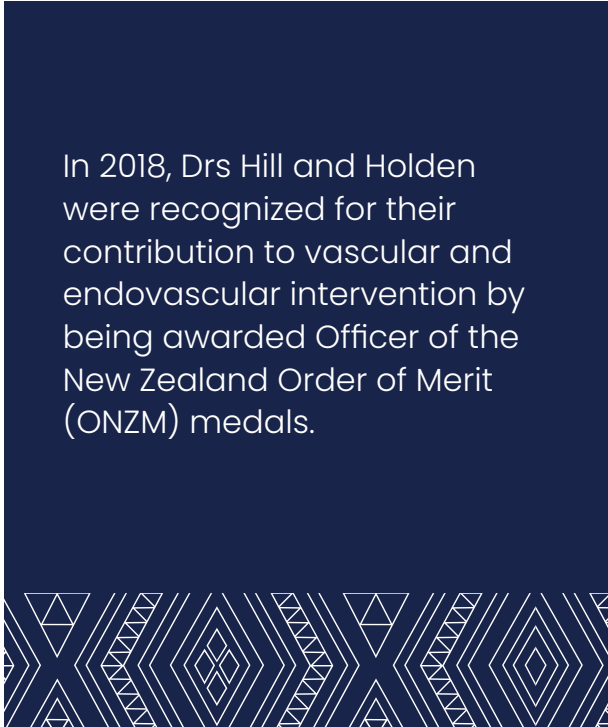


maintain target lesion patency. And what we've found is that if you look at the cohort of patients randomised to the drug-coated balloon and compare to those randomised to the plain balloon, the drug-coated balloon patients on average experienced a 21% reduction in the number or reinterventions to maintain patency. And for patients who already go through a lot in haemodialysis I think this is a very significant finding. For my patients, these durable results translate into fewer reinterventions and a better quality of life."

“But we still have some questions. For example we know 30-40% of all the fistulas that are created for dialysis failed to mature and there is some evidence to suggest that drug-coated balloon angioplasty can be very effective in actually promoting fistula maturation. That's a study we still need to have done.”

“In the past there's been some concerns about Paclitaxel and all-cause mortality. I think that's largely been resolved but I'm happy to say at three years there was absolutely no difference in all-cause mortality between the two treatment arms. So there's no safety concern with Paclitaxel. I think we now have data to say that there is a sustained patency benefit for using the IN.PACT AV drug-coated balloon and AV access intervention compared to the standard treatment of plain balloon angioplasty. And we've seen that in all locations in the AV access circuit, we've seen no safety concerns and we've now got some data saying that it's a highly cost-effective procedure. I believe we are now at the point where we really should be considering this as standard of care, really for all AC access stenosis.”

In 2018, Drs Hill and Holden were recognized for their contribution to vascular and endovascular intervention by being awarded Officer of the New Zealand Order of Merit (ONZM) medals.



Gene editing can work in humans, but for how long

Last year we reported the first clinical evidence that CRISPR gene editing inside the body can be safe and effective. Intellia Therapeutics now has the data for the No. 1 unanswered gene editing question:

Does it last?

In a landmark study published in the New England Journal of Medicine it was reported how a novel gene-editing technology (NTLA-2001) was used to treat people with ATTR amyloidosis. This is a rare and fatal disease that occurs in people born with TTR gene mutations, which cause the liver to produce abnormal, often misfolded TTR proteins.

It seems to have worked as planned. The one-time treatment appears to have turned off the TTR gene. Participants who got a low dose of NTLA-2001 saw more than a 50% decline in their blood levels of the protein. Those that received a higher dose saw 87% and higher reductions.

In a hotly anticipated readout, Intellia has now presented additional data from the phase 1 trial that recruited patients of Auckland City Hospital, one of only two recruiting sites in the world. Intellia has confirmed in interim data that the reduction in serum levels of transthyretin, or TTR, a known biomarker of disease severity, was maintained in patients after follow-up that ranged from two months to 12 months post-treatment. All this was achieved without any new concerning safety signals.

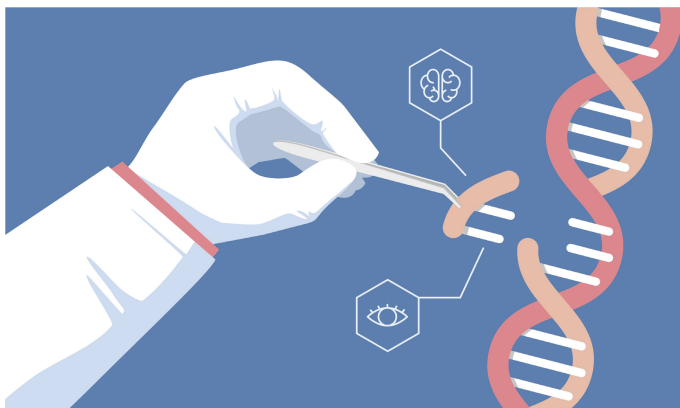
NTLA-2001 works by deploying lipid nanoparticles to the liver to drop off a two-part genome editing system. The first part is a guide RNA specific to the disease-causing gene, and the second part is a messenger RNA—the tech made famous by COVID-19 vaccines—to encode the Cas9 protein and carry out precision editing.

The latest data show that the serum reduction seen at the initial Day 28 observation was sustained through the last check-in with each of the six patients who received a dose of 1.0 mg/kg. These patients experienced reductions higher than 80% and 90%, Intellia said. The initial data release last year showed a reduction of 87%.

With some data now added to the durability question, Intellia could have itself a one-time treatment option for patients.

“In this Phase 1 study, NTLA-2001 was generally well tolerated as a single-dose treatment for ATTR amyloidosis patients with polyneuropathy, resulting in deep and durable reductions of serum TTR. These observations are consistent with animal data indicating potential life-long serum TTR suppression,” said Professor Ed Gane, Chief Hepatologist, Transplant Physician and Deputy Director of the New Zealand Liver Transplant Unit at Auckland City Hospital, and study investigator. “Importantly, these early results suggest NTLA-2001 has the potential to deliver profound benefits for patients around the world.”

Intellia plans to continue tracking the patients for the rest of their lives to record the durability data, so someday, we may have a more concrete understanding of the science behind ATTR amyloidosis.





Auckland Hospitals Research and Endowment Fund – grants impact report

Auckland Hospitals Research and Endowment Fund (AHREF, formerly A+ Trust) has invested over \$4M into investigator-led research grants since 2010 – a mix of summer studentships (value<\$6,500), small project grants (value<\$15,000) and full project grants (\$15,000 – \$50,000).

The 197 grants awarded up to 2018¹ have produced 206 high level outputs;

- ▶ **112 original research papers**
- ▶ **23 published abstracts**
- ▶ **32 conference presentations**
- ▶ **19 poster presentations**
- ▶ **8 higher degrees**
- ▶ **11 awards**
- ▶ **1 national guideline**

¹High level outputs are a lagging indicator of return on investment. The majority of our counted outputs are released between 2 and 6 years after the award of a grant. Hence this count from 2018 will have captured most but not all of the outputs likely to be generated.

Assessment of impact

A formal bibliometric analysis of our grants report is a work in progress but with the volume of publications now in the public domain alone, it is impossible to resist a somewhat crude scoresheet based on journal impact factor. Journal impact factor (JIF) is commonly used to compare the importance of journals within a field or discipline. It is a deeply imperfect measure, relying on the average number of citations for the articles a journal publishes across the subsequent few years, and is thus biased in favour of journals that publish more reviews, among other things. Nonetheless, while not a hard and fast indicator of scientific merit, JIF is a strong marker of influence on the academic community of interest. Journals with a JIF above 1.0 are considered above average, those above 10 would be top journals in the field.

	Total investment	Cost per publication	JIG average
Summer studentships	\$260,500	\$18,607	2.18
Small project grants	\$286,573	\$15,920	4.37
Full project grants	\$3,053,844	\$40,718	7.91

The first thing that needs to be pointed out about the above metrics is that cost per publication reflects only the costs to the AHREF. Many of the studies our Trust has invested in, especially the ones producing the highest value evidence (the randomised controlled trials), are very resource intensive and require funding from multiple sources. Therefore the cost per publication can best be thought of as the cost of Te Toka Tumai Auckland's participation in research of sufficient quality to produce a publication of importance. The mean JIF of 7.91 for publications from full project grants shows that since 2010 every \$40,718 invested has enabled our people to contribute to outputs well above the international average. Small project grants, for investments of only \$15,920 on average, also result in impressive publications.

One in every three summer studentships has contributed to scholarship and new knowledge with a good quality published paper.

Publications in journals are far from being the only measures of success that can be tallied up from funding research. Our investigators have communicated their findings and informed their colleagues at numerous oral and poster sessions at meetings both nationally and around the world. All of this dissemination activity advances the evidence base for clinical practice, the skills of our researchers and our reputation as a research-driven organisation.

Published articles

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Presentations

Burge, A., Nelson, M., Purdy, S., Kool, B., Leversha, A. Paed Soc NZ ASM 2019 Alison Burge¹, Moira Nelson², Suzanne Purdy², Bridget Kool³, Alison Leversha¹ ACEs and resilience in Tamaki

Cloete, E. (2016) Pulse oximetry screening at Auckland City Hospital. National Women's Annual Clinical Report Day, Auckland

Cloete, E. (2017) Can hospital-led pulse oximetry screening programmes result in equitable outcomes for newborns with critical congenital heart disease? PSNZ meeting, Wellington

Cloete, E. (2017) Improving outcomes for babies born with heart disease. Liggins Institute Public Lecture, Auckland

Cloete, E. (2017) The value of pulse oximetry screening for critical congenital heart disease. Heart Kids Conference, Auckland

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Cloete, E. (2018) Left heart obstruction: Incidence and survival. Annual Perinatal and Maternal Mortality Review Committee Meeting, Wellington

Cloete, E. (2018) Pulse oximetry screening update. National Women's Annual Clinical Report Day, Auckland

Cormack, B.E. (2014) Extremely low birthweight babies – how to get more protein in. Australasian Parenteral and Enteral Nutrition Society Annual Scientific Meeting, Auckland

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Kalluru, K., Wilsher, M.L., Milne, D.M., Ng, K.P. (2013) Prevalence of autoantibodies in idiopathic inflammatory myopathy and/or interstitial pneumonia. World Association of Sarcoidosis and Other Granulomatous Disorders, Paris.

Lee, J., Nuthall, G., Ikeyama, T. et al (2015) An International National Emergency Airway registry for Children: Comparison of tracheal Intubation Practices Across International PICU's. World Congress on Pediatric Intensive and Critical care Societies 2015

Leung, M., Poppe, T., Tottman, A., Thompson, B., Black, J., Dai, S., Harding, J., Bloomfield, F., Alsweiler, J.M. Preterm Birth and visual outcomes at 7 Years of Age. 21st Annual Meeting of the Perinatal Society of Australia and New Zealand, Canberra, 2017.

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Nelson, M., Purdy, S., Ballard, E., Burge, A., Leversha, A., 2017. Communication skills of new entrants in a sociodemographically-disadvantaged community: What implications does this have for educational pedagogy and SLT practice? Oral Presentation The New Zealand Speech-language Therapists' Association PD Symposium, Auckland

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Roberts, S., Freeman, J. (2012) Anaerobic Antimicrobial Susceptibility Test Results. Australian Society for Antimicrobials 13th Annual Scientific Meeting, Antimicrobials 2012, 23rd–25th February 2012, Brisbane, Australia.

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Tottman, A.C., Alsweiler, J.M., Woudes, T.A., Thompson, B., Gamble, G., Bloomfield, F.H., Harding, J.E. Unrecognised neurodevelopmental and health problems in school aged children born very preterm. 20th Annual Perinatal Society of Australia and New Zealand, Townsville, 2016.

Tottman, A.C., Alsweiler, J.M., Woudes, T.A., Thompson, B., Gamble, G., Bloomfield, F.H., Harding, J.E. Scarring in school-age children born very preterm. Perinatal Society of New Zealand, Dunedin, 2015.

Wijayarathne, S. (2018) Young people with type 2 diabetes and type 1 diabetes in the Auckland region: prevalence of mental health illnesses, fatty liver and macrovascular outcomes. New Zealand Society for the Study of Diabetes Annual Scientific Meeting

Williams, G., Sherring, C., Beca, J., Dalziel, S (2016) Starship paediatric early warning system: is it fit for purpose? PAEDIATRIC SOCIETY OF NEW ZEALAND 68TH ANNUAL SCIENTIFIC MEETING

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Wright, T. Infants co-admitted to Auckland's newly developed Mother-Baby Unit. Royal Australian and New Zealand College of Psychiatrists 2018 Congress, Auckland.

Posters

Amende, H., Aspden, T., Honey, M., Chan, A.H.Y., Chang, R., Ashmore-Price, H., French, A., Brackley, K. (2019) Determining patients' medicines information needs efficiently – optimising a clinical assessment tool. Auckland DHB Research Poster Week 2019 and New Zealand Hospital Pharmacists Association 2019.

Bellissima, B., Garavan, F., Tingle, M (2016) Determination of post-mortem clozapine levels in coronial autopsy cases. ASCEPT NZ 2016, Queenstown

Blincoe, A, Byrnes, C., Sinclair, J., Lim, D., Brothers, S (2015) Do Defects in the Innate Immune System Contribute to Bronchiectasis in Maori and Pacific Island Children? Auckland DHB Research Poster Week 2015 – Best Medical Poster

Campbell, D., Mrcobrada, M., Short, T.G., Devereaux, P.J. (2019) Covert stroke after non-cardiac surgery. Auckland DHB Research Poster Week 2019

Deng, C., Campbell, D., Diprose, W., Eorn, C., Robertson, N., Short, T.G., Brew, S., Caldwell, J., McGuinness, B., Barber, P.A. (2019) A pilot randomised controlled trial of the management of systolic blood pressure during endovascular thrombectomy for acute ischaemic stroke – the MASTERSTROKE pilot study. Auckland DHB Research Poster Week 2019

Depledge, J., McNair, P., Ellis, R. (2018) The Effect of Exercise and Bracing on Early Postnatal Women with Rectus Abdominis Diastasis. Auckland DHB Research Poster Week 2018

Maxwell, E., Short, T.G., Campbell, D., Weymouth, E., Sessler, D., Buggy, D. (2019) Recurrence of breast cancer after regional or general anaesthesia: a randomised controlled trial. Auckland DHB Research Poster Week 2019

Oliver, V., Cole, A., Gane. (2016) Auckland Central Liver Clinic (AACL): a pilot-project. Auckland DHB Research Poster Week 2016

Rice, K. (2017) Fontan Conversion – attempting to preserve the sinus node in anti-arrhythmia surgery. World Congress of Pediatric Cardiology and Cardiac Surgery, Barcelona, July 16–21.

Rice, K. (2017) Fontan Conversion: functional outcomes over time; a single centre experience. World Congress of Pediatric Cardiology and Cardiac Surgery, Barcelona, July 16–21.

Stanton, J., Thomas, D., Mackay, P., Jarbin, M. (2019) Self Determination Theory in the Acute Child and Adolescent Mental Health Inpatient Unit. An Exploratory Study. Auckland DHB Research Poster Week 2019

Stewart, H.A., Tottman, A.C., Alsweiler, J.M., Bloomfield, F.H., Gamble, G., Thompson, B., Woudes, T.A., Harding, J.E. Left Hand Preference and Fine Motor Outcomes in School Aged Children Born Very Preterm. 20th Annual Perinatal Society of Australia and New Zealand, Townsville, 2016.

Tilton, E., Mitchelson, B., Peat, B., Kerr, A., Jack, S., Anderson, A., Webb, R., Wilson, N. (2019) The New Zealand Rheumatic Heart Disease Registry. Auckland DHB Research Poster Week 2019

Tottman, A.C., Alsweiler, J.M., Bloomfield, F.H., Gamble, G.D., Harding J.E. Glucose variability in hyperglycaemic preterm neonates. 17th Annual Perinatal Society of Australia and New Zealand. Adelaide. 2013.

Vallely A, Hughes L, Wise M. (2016) Women's Satisfaction with a Primary Caesarean Section and Preference for Subsequent Births – An Early Postnatal Review of Attitudes. Poster presented at RANZCOG Annual Scientific Meeting, Perth.

Welch, R., Francis, A., Babbage, T., Kolbe, J., Ellyett, K (2018) Ventilatory limitation during exercise in adolescent athletes and its association with exercise induced dyspnoea. Auckland DHB Research Poster Week 2018

Wilsher, M.L., Kalluru, R., Milne, D.M., Ng, K.P. (2013) Prevalence of autoantibodies in idiopathic inflammatory myopathy and/or interstitial pneumonia. World Association of Sarcoidosis and Other Granulomatous Disorders, Paris.

Winbo, A. (2016) Pluripotential cells and LQTS: an update on research. Rhythm and Inherited Heart Diseases Symposium, September 2016, Auckland.

Winbo, A. (2016) How to strike up a conversations with a living, beating heart cell. Green Lane Scientific Sessions, October 2016, Auckland.

Degrees

Jill Depledge (Allied Health, National Women's) MHSc, AUT

Epenesa Iosua (2017) Human papillomavirus in carcinomas of the nasopharynx, oral tongue and larynx

Wikki Koopmans (LabPlus), PhD, University of Auckland, 2012. Common Variable Immunodeficiency in New Zealand: finding the molecular and cellular foundations

Moiria Nelson (2018) Language of children starting school in Tamaki: The association of linguistic diversity and social disadvantage. Master's thesis, University of Auckland

Mike Nicholls (Adult Emergency Department), Master of Health Sciences, University of Auckland, 2020. Nationwide Survey of Workplace Wellbeing in New Zealand Emergency Departments

Rachael Parke (CVICU) PhD, University of Auckland, 2014. High flow nasal oxygen therapy in patients after cardiac surgery

Jessica Parker (Community Child Health and Disability Service)

Master's, University of Auckland 2017. A Qualitative Study of Parental Help Seeking.

Jackie Robinson (Palliative Care) PhD, University of Auckland, 2017. Benefit or Burden? Exploring Experiences of the Acute Hospital as a Place of Care Amongst People with Palliative Care Needs

Awards

Alana Ainsworth – (Starship Respiratory) Best Medical Poster, Auckland District Health Board Research Poster Week 2016

Alana Ainsworth – (Starship Respiratory) American Thoracic Society 2017 Public Advisory Roundtable (PAR) Abstract Scholarship

Kim Brackley – (Pharmacy) Clinical Support Director's Choice, Auckland DHB Research Poster Week 2019.

Jill Depledge (Allied Health, National Women's) 2016 Clinical Support Directorate Award for Research, Allied Health, Scientific and Technical Awards

Frances Downen (Renal Department) Finalist – Young Investigator Award 2015

Cindy Farquhar – (National Women's Health) Health Research Council Liley Medal 2018

Groom, K., McCowan, L.M.E., Mackay, L., Lee, A., Said, J., Kane, S., Walker, S., Van Mens, T., Hannan, N., Tong, S., Chamley, L., Stone, P., McIntock, C. (2017) Editors Choice – The EPPI Trial – Enoxaparin for the prevention of preeclampsia and intrauterine growth restriction in women with a history: a randomised trial. American Journal of Obstetrics and Gynecology, 216, 296.e1-14

Anna Mulholland – (Starship Respiratory) Rising Star Award, World Bronchiectasis Conference, Milan, 2017

Anna Mulholland – (Starship Respiratory) Best Starship Poster, Auckland District Health Board Research Poster Week 2017

Script Antibiotic Treatment App (2016) Finalist – Best Awards, Digital Products. Contributors Eamon Duffy, Chang-Ho Yoon, Stephen Ritchie.

Annika Winbo (2016) Green Lane Scientific Sessions. Green Lane Trophy for best presentation



Funding for Research

In 2021 Auckland DHB researchers and their colleagues have enjoyed considerable success in obtaining funding in the millions for their research from a variety of charitable and public-good sources.

AHREF Research Grants

The hallmark of a great hospital is having a research programme of excellence. The Auckland Hospitals Research and Endowment Fund (AHREF) is a major supporter of research and the culture of research and innovation. This culture is helping reshape healthcare for our patients to ensure that they receive the best care possible. The funding has supported Auckland DHB researchers from all disciplines to undertake research across the health spectrum, from patients to population, disease to prevention, and service delivery. Here are the successful applications for 2021.

A+ Trust Project and Small Project Grants

Sharin Asadi (Starship Community) Language, movement, and impulse control in children starting school in high decile schools: Is it lower than expected, and how different is it to children starting school in low decile schools? (\$14,954)

Chen Chen (Anaesthesia) Effect of phenylephrine and norepinephrine on cerebral blood flow during general anaesthesia in adult patients having non-cardiac surgery (\$7,800)

Barbara Cormack (Paediatric Dietetics) Analysing Vitamin status and early Intravenous Nutrition in the NICU - The AVIation study (\$50,000)

Carolyn Deng (Anaesthesia) Patients' perception and understanding of postoperative neurological complications: a mixed-methods study using survey and interviews of surgical patients in New Zealand (\$49,992)

Cindy Farquhar (National Women's Health) Colorado Combined Adjuvant Therapy in in-vitro fertilisation (IVF) or frozen embryo transfer cycles for women/couples with recurrent implantation failure (RIF) (\$49,500)

Alison Leversha (Starship Community) Oral health inequity: Understanding pathways of care and opportunities for innovation (\$38,500)

Rochelle Newport (Starship Community) Hapu Māmā Oranga Niho Ki Tāmaki: Lived experience of free dental care during pregnancy (\$14,983)

Rita Sigley (Paediatric Endocrinology and Diabetes) Psychological and Diabetes self-care outcomes for Children and Adolescents attending Diabetes Camps, Auckland, New Zealand, 2023; and examination of the 'common humanity' of attending camps (\$48,658)

Michelle Wise (National Women's Health) Impact of abortion law reform on abortion services at Epsom Day Clinic (\$7,980)

A+ Trust Summer Student Grants

Amy Chan (Pharmacy) Junior doctor prescribing accuracy at Auckland District Health Board.

Amy Lovell (Nutrition and Dietetics) Understanding patient and whānau experiences of nutrition and dietetic support during childhood cancer treatment

Ryan Welch (Physiology) Steady state exercise breathing.



[NEWSFLASH] ++++++

World first: researchers identify potential cause and treatment for obesity and insulin resistance.

Researchers have shown for the first time that mesenteric (gut) lymphatic dysfunction is a potential cause of and therapeutic target for obesity and insulin resistance. The ground-breaking study, published in the prestigious journal *Nature Metabolism*, identified a profoundly damaging cycle in which a high fat diet promotes dysfunction of the mesenteric lymphatics, that in turn leads to accumulation of abdominal fat.

Notably, the study also provides evidence that intervening in this cycle by inhibiting the pathways associated with lymphatic dysfunction may be a treatment for both obesity and associated metabolic disease.

Preclinical experiments with rats carried out by researchers at Monash University and the University of South Australia were repeated in clinical samples **with funding from the AHREF (small project grant 2017)**.

Samples of small bowel and mesentery were provided by lean and obese patients undergoing surgery at the Auckland City Hospital. The samples were then processed and transported to Monash for laboratory experiments which suggest that the key observations made in the animal studies extend to humans as well.

Professor John Windsor, the study's lead investigator at Te Toka Tumai Auckland, sees this as an excellent example of transdisciplinary research that is critical for the translation of key experimental findings to the clinical setting and potential patient benefit.

Read the article: Mesenteric lymphatic dysfunction promotes insulin resistance and represents a potential treatment target in obesity. *Nature Metabolism* (2021) 3 (9) pp1175–1188.]

Alzheimer's New Zealand

Gary Cheung (Mental Health Services for Older People)
Research Fellowship (\$15,000)

[Dr Gary Cheung is a Consultant Psychogeriatrician with Mental Health Services for Older People and a Senior Lecturer in Psychiatry at the University of Auckland and conducts research in the field of old age psychiatry. He has been instrumental in introducing cognitive stimulation therapy (CST), an evidence based non-pharmacological intervention for dementia, to New Zealand.

Gary co-leads the dissemination and research of CST with Dr Kathy Peri through Alzheimers New Zealand's **Dementia Learning Centre**. He also researches how to adapt CST for Māori with Dr Makarena Dudley, who is New Zealand's leading Māori dementia researcher.

The **Alzheimers New Zealand Fellowship** will provide Gary with \$15,000 to support his research which will focus on analysing existing interRAI* clinical data to understand how the progression of cognitive impairment may be predicted.

“We brought CST to New Zealand in 2014 when the treatment was not routinely available here. Now, seven years later, a number of organisations are using it to help people living with dementia.”

“I am excited to continue my research. We have a lot of interesting data already in New Zealand through the Ministry of Health. By analysing these data we can see whether we can improve clinical practices and the quality of life for people living with dementia.”

“We will also work with colleagues in Canada on cross-country validation to see if we can use interRAI data to predict the progression of cognitive impairment over time.”

“The research environment in New Zealand is very competitive so being awarded this Fellowship is a great opportunity. I am very thankful to Alzheimers New Zealand for supporting my research.”

*interRAI assessments are comprehensive clinical assessments, which focus on a person's function. They are designed to show the assessor opportunities for improvement and any risks to the person's health, which then form the basis of a care plan.

Dr Gary Cheung

Auckland Medical Research Foundation

Clinton Lewis, Richard Doocey, Timothy Hawkins, Peter Browett, Nicole Chien (Haematology) BMI2 CAST STUDY: CYCLOPHOSPHAMIDE AFTER SIBLING-DONOR ALLOGENIC STEM-CELL TRANSPLANTATION (\$98,982)

Helen Pilmore, Michael Collins, Ian Dittmer, Germaine Wong, Paul Manley, Sally Roberts (Renal Medicine, Microbiology) COVID-19 VACCINATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE - NEW ZEALAND (C-VAK NZ study) (\$159,505)

Giuseppe Sasso, Maria-Lee Pearse (Radiation Oncology) PACE C: INTERNATIONAL RANDOMISED STUDY OF CONVENTIONALLY FRACTIONATED RADIOTHERAPY VS SBRT FOR ORGAN-CONFINED PROSTATE CANCER (\$68,320)

Anna Waylen, Tim Short, Doug Campbell, Greg O'Grady, Ben Lawrence, Sarah Nicolson (Anaesthesia, General Surgery, Medical Oncology) VAPOR-C TRIAL (\$142,668)

Australian and New Zealand College of Anaesthetists

Dr Doug Campbell, Dr Carolyn Deng, Dr Robyn Billing, Professor Tim Short, Professor Alan Barber (Anaesthesia, Neurology) Management of systolic blood pressure during thrombectomy by endovascular route for acute ischaemic stroke: the MASTERSTROKE trial (\$A69,560)

Dr Chen Chen, Dr Douglas Campbell (Anaesthesia) Effect of phenylephrine vs norepinephrine on cerebral blood flow in patients for non-cardiac surgery general anaesthesia (\$A17,255)

Cancer Research Trust

Michelle Wilson (Medical Oncology) Adjuvant tislelizumab plus chemotherapy after post-operative pelvic chemoradiation in high-risk Endometrial cancer (ADELE): a randomised phase 2 trial (\$115,051)

Cure Kids

Ben Albert (Paediatric Endocrinology and Diabetes) Ongoing follow-up for study of fish oil in pregnancy, including breastfeeding and early childhood

Health Research Council of New Zealand

Dr Emma Best (Paediatric Infectious Diseases) Understanding measles: severity and sequelae (\$1,104,966)

Dr Barbara Cormack (Paediatric Dietetics) Analysing vitamin status and early intravenous nutrition in the NICU (\$29,929)

Dr Ross Drake (Paediatric Palliative Care) RAPID paediatric palliative care and pain (\$30,000)

Dr Helen Evans (Paediatric Gastroenterology) Engagement in healthcare in young adults and adolescents after liver transplant (\$30,000)

Justin Kennedy-Good (Ara Manawa) Innovation flow in healthcare – 3D printing (\$30,000)

Dr Clare O'Donnell, Professor Robert Doughty (Paediatric and Adult Cardiology) Pilot – Developing a national Adult Congenital Heart Disease (ACHD) Registry (\$26,130)

Dr Sarah Primhak (Paediatric Infectious Diseases) Treatment of Impetigo with Antiseptics – Replacing Antibiotics (TIARA) Trial (\$160,000)

Dr Lynn Sadler (National Women's Health) Clinical Practitioner Research Fellowship (\$892,380)

Sarvnaz Taherian (Ara Manawa) Understanding the enablers of innovation in the hospital environment (\$110,000)

Dr Amelia Tekiteki, Associate Professor Helen Pilmore (Renal Medicine) Identifying the barriers to kidney transplant for Pasifika patients with ESRD (\$148,541)

Dr Alison Leversha (Starship Community) School absence and stand-down: Preventive trauma and tikanga-informed approach (\$28,410)

About this project: Education is one of the strongest predictors of good health. Tamariki who achieve at school are more likely to grow up healthy and successful.



There is a clear dose-response: the more school you attend the higher your achievement. Conversely, young people who are chronically absent, stood down or drop out of school prematurely and more likely to engage in risky behaviours and to have negative health and social outcomes.

Forty five percent of tamariki/rangatahi who die from nonmedical causes have been stood down, suspended, or disengaged from school (vs none who die from medical reasons). Māori tamariki/rangatahi are disproportionately affected: 8% of ADHB population vs 55% of those who died and stood down. The Dunedin Longitudinal study has identified poor self-regulation as the most significant risk factor for future adverse outcomes. Early childhood conduct problems are markers for future adverse outcomes. A small proportion of the population contributes to the

majority of societal costs (health, educational, justice etc). Early identification of at-risk children with early intervention and support is cost effective, will reduce health and social inequities, and enhance population wellbeing.

We will work with the Tamaki community, exploring community-driven options for prevention and intervention for truancy, absences and stand down. Combining western and indigenous knowledge we will develop a multi-level, multi-sector collaboration based on the Tamaki Makaurau Rangatahi Action Plan, the Pae Ora Māori framework and trauma-informed and tikanga-informed approaches, acknowledging neuroscience and the effect of the past: it is not what's wrong with you but what has happened to you (and your ancestors).

Neurological Foundation of New Zealand

Christina Buchanan (Neurology) PINK1 variants in early-onset Parkinson's disease in a Pan-Pacific cohort (\$83,524)

Hannah Jones (Paediatric Neurology) Investigating the role of innate immune mechanisms in autoimmune encephalitis, autoimmune movement disorders and neurodevelopment in children (\$145,748)

Hannah Jones (Paediatric Neurology) Maternal psoriasis and infant neurodevelopmental outcomes – a clinical and mechanistic study (\$229,635)

Catherine Tanumihardja (Neurosurgery) Circle of Willis neurovascular conference (\$2648)

New Zealand Society for Gastroenterology Janssen Research Fellowship

Akhilesh Swaminathan (New Zealand Liver Transplant Unit)

Starship Foundation Clinical Research Fund



Starship Child Health and the Starship Foundation share a vision to create, at Starship, an environment of world-class research, training and innovation that will better the lives of kiwi kids faster. In 2016, that vision took an important step forward with the announcement of a significant new investment in paediatric clinical research. Since then, over \$4.8M has been committed by the Starship Foundation to projects now underway. This investment enables our national children's hospital even greater ability to lead the way in evidence-based care and improved health outcomes for New Zealand's children. The Starship Foundation is proud to fund projects that save and extend lives, lift spirits, and reduce discomfort, ensure better outcome, faster recovery, and less invasive treatments, and are focused on equity and prevention to accelerate the pace of change at our national children's hospital.

Clinical research project grants awarded in 2021

John Beca (Paediatric Intensive Care Unit) Predicting long term outcomes in infants after heart surgery – a multicentre prospective trial: The NITRIC follow-up study

Cameron Grant (General Paediatrics) Prevention of wheeze-associated hospitalisations in preschoolers

Ajay Iyengar (Paediatric and Congenital Cardiac Service) The Australian and New Zealand Fontan Registry: FAN, ACE cessation & BUMP Multi-Centre Studies

Rebecca Slykerman (Paediatric Haematology-Oncology) An innovative risk calculator to predict cognitive problems in survivors of childhood cancer

Rebecca Slykerman (Paediatric Haematology-Oncology) Improving outcomes for children and adolescents living with an acquired brain injury

Elsa Taylor (Paediatric Anaesthesia) Core Outcomes in Children undergoing anaesthesia and surgery

Kate Wallace (Paediatrics and Newborn Services, Waitemata) What is the frequency and outcome of criminal investigation in children and young people seen for a medical examination for alleged sexual abuse, and what is the relationship between medical findings, charges laid and the outcome of prosecution?

John Beca's research into predicting long term outcomes in infants after heart surgery has been awarded the Athlae Lyon Research Award. This annual award was established in memory of Athlae Lyon, a founding member of the Friends of Starship, and later a long-serving member of the Starship Foundation Board of Trustees.

Publications

HOT Paper!!

Beaton A, Okello E, Rwebembera J, et al. Secondary antibiotic prophylaxis for latent rheumatic heart disease N Engl J Med. Published online November 13, 2021. doi:10.1056/NEJ-Moa2102074

A randomized, controlled trial among children and adolescents with echocardiographic evidence of latent rheumatic heart disease, the use of intramuscular penicillin G benzathine every 4 weeks for 2 years was associated with a substantial reduction in the risk of echocardiographic progression of rheumatic heart disease.

The number needed to receive prophylaxis to prevent one case of latent rheumatic heart disease progression was 13 (95% CI, 10–21).

Among those with disease progression, there was a high prevalence of moderate or severe disease at 2 years, underscoring the potential clinical impact of screening.

The study starred Starship's own **Dr Nigel Wilson**, a paediatric cardiologist and world expert on rheumatic heart disease. The study was conducted in Uganda but has enormous relevance to Aotearoa where tamariki Māori and Pacific children experience very high and unacceptable rates of this condition. Rheumatic heart disease affects more than 40.5 million people worldwide and results in 306,000 deaths annually. Echocardiographic screening can detect rheumatic heart disease at an early, latent stage. This prospective, randomized study found that antibiotic prophylaxis with

intramuscular penicillin G benzathine every 4 weeks for 2 years was associated with a substantial reduction compared to placebo in the risk of echocardiographic progression of latent rheumatic heart disease (risk difference, -7.5 percentage points; 95% CI, -10.2 to -4.7; $p < 0.001$), with the need to treat 13 children or adolescents to prevent disease progression in one. The high prevalence of moderate or severe disease at 2 years among those with progression underscores the potential clinical impact of pursuing broad efforts at screening and, if validated in additional studies, the use of secondary antibiotic prophylaxis for latent rheumatic heart disease



- Aburn GE, Hoare K, Gott M. (2021) "We are all a family" Staff Experiences of Working in Children's Blood and Cancer Centers in New Zealand—A Constructivist Grounded Theory. *J Pediatr Oncol Nurs*, 38 (5), 295–306.
- Al-Ani HH, Lu LM, Meyer JJ, Niederer RL. (2021) Cataract Surgery in Herpes Simplex Virus Ocular Disease. *J Cataract Refract Surg*, Jul 12. doi: 10.1097/jjcrs.0000000000000745.
- Al-Ani HH, Sheek L, Vincent AL. (2021) Peripheral pigmented lesions in ABCA4-associated retinopathy. *Ophthalmic Genet*, 42 (4), 383–391.
- Albert BB, Derraik JGB, Xia YY, Norris T, Zhang T, Han TL, Chang C, Rowan A, Gallier S, Souza RT, Hammond JJ, Zhou W, Zhang H, Qi HB, Baker PN. (2021) Supplementation with milk enriched with complex lipids during pregnancy: A double-blind randomized controlled trial. *PLoS One*, 16 (2), e0244916.
- Alburaiqi S, Dale RC, Crow YJ, Jones HF, Wassmer E, Melki I, Boespflug-Tanguy O, Do Cao J, Gras D, Sharpe C. (2021) Opsoclonus-myoclonus in Aicardi-Goutières syndrome. *Dev Med Child Neurol*, 63 (12), 1483–1486.
- Alexander HC, McLaughlin SJ, Thomas RH, Merry AF. (2021) Checklists for image-guided interventions: a systematic review. *British Journal of Radiology*, 94 (1121), 20200980.
- Alexander HC, Nguyen CH, Bartlett AS, Thomas RH, Merry AF. (2021) Reporting of Clinical Outcomes After Endovascular Aortic Aneurysm Repair: A Systematic Review. *Ann Vasc Surg*, 77, 306–314.
- Alexander H, Wen D, Chu M, Han C, Hadden P, Thomas R, Bartlett A. (2021) Selective internal radiation therapy for hepatic metastases of uveal melanoma: a systematic review. *Br J Radiol*, 95 (1129), 20210200.
- Alhilali M, Hearn JI, Rong J, Jain L, Bolam SM, Monk AP, Munro JT, Dalbeth N, Poulsen RC. (2021) IL-1 induces changes in expression of core circadian clock components PER2 and BMAL1 in primary human chondrocytes through the NMDA receptor/CREB and NF- κ B signalling pathways. *Cell Signal*, 87:110143. doi: 10.1016/j.cellsig.2021.110143.
- Amer MA, Herbison GP, Grainger SH, Khoo CH, Smith MD, McCall JL. (2021) A meta-epidemiological study of bias in randomized clinical trials of open and laparoscopic surgery. *Br J Surg*, 108 (5), 477–483.
- Ameratunga R, Allan C, Lehnert K, Woon ST. (2021) Perspective: Application of the American College of Medical Genetics Variant Interpretation Criteria to Common Variable Immunodeficiency Disorders. *Clin Rev Allergy Immunol*, 61 (2), 226–235.
- Ameratunga R, Jordan A, Cavadino A, Ameratunga S, Hills T, Steele R, Hurst M, McGettigan B, Chua I, Brewerton M, Kennedy N, Koopmans W, Ahn Y, Barker R, Allan C, Storey P, Slade C, Baker A, Huang L, Woon ST. (2021) Bronchiectasis is associated with delayed diagnosis and adverse outcomes in the New Zealand Common Variable Immunodeficiency Disorders cohort study. *Clin Exp Immunol*, 204 (3), 352–360.
- Ameratunga R, Longhurst H, Lehnert K, Steele R, Edwards ESJ, Woon ST. (2021) Are All Primary Immunodeficiency Disorders Inborn Errors of Immunity? *Front Immunol*, 12, 706796.
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- Ameratunga R, Woon ST, Jordan A, Longhurst H, Leung E, Steele R, Lehnert K, Snell R, Brooks AES. (2021) Perspective: diagnostic laboratories should urgently develop T cell assays for SARS-CoV-2 infection. *Expert Rev Clin Immunol*, 17 (5), 421–430.
- Ameratunga R, Woon ST, Steele R, Snell R, Medlicott N, Mears E, Leung E, Lehnert K, Jordan A, Das S, Abbott W, Longhurst H, Quiñones-Mateu ME. (2021) Perspective: the nose and the stomach play a critical role in the NZACE2-Pātari* (modified ACE2) drug treatment project of SARS-CoV-2 infection. *Expert Rev Clin Immunol*, 17 (6), 553–560.
- Anderson M, Parke R, Jull A. (2021) Effect of Cardiac Surgery on Health-Related Quality of Life in Patients Aged 75 Years or Older: A Prospective Study. *Heart, Lung and Circulation*, 30 (2), 282–287.
- Anderson N, Pio F, Jones P, Selak V, Tan E, Beck S, Hamilton S, Rogan A, Yates K, Sagarin M, McLeay A, MacLean A, Fayerberg E, Hayward L, Chiang A, Cadzow A, Cadzow N, Moran S, Nicholls M. (2021) Facilitators, barriers and opportunities in workplace wellbeing: A national survey of emergency department staff. *Int Emerg Nurs*, 57:101046.
- Anderson NE, Slark J, Gott M. (2021) Prehospital Resuscitation Decision Making: A model of ambulance personnel experiences, preparation and support. *Emerg Med Australas*, 33 (4), 697–702.
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